LAAM in the Treatment of Opiate Addiction

Treatment Improvement Protocol (TIP) Series

22

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What Is a TIP?

CSAT Treatment Improvement Protocols (TIPs) are prepared by the Quality Assurance and Evaluation Branch to facilitate the transfer of state-of-the-art protocols and guidelines for the treatment of alcohol and other drug (AOD) abuse from acknowledged clinical, research, and administrative experts to the Nation's AOD abuse treatment resources.

The dissemination of a TIP is the last step in a process that begins with the recommendation of an AOD abuse problem area for consideration by a panel of experts. These include clinicians, researchers, and program managers, as well as professionals in such related fields as social services or criminal justice.

Once a topic has been selected, CSAT creates a Federal resource panel, with members from pertinent Federal agencies and national organizations, to review the state of the art in treatment and program management in the area selected. Recommendations from this Federal panel are then communicated to the members of a second group, which consists of non-Federal experts who are intimately familiar with the topic. This group, known as a non-Federal consensus panel, meets in Washington for 5 days, makes recommendations, defines protocols, and arrives at agreement on protocols. Its members represent AOD abuse treatment programs, hospitals, community health centers, counseling programs, criminal justice and child welfare agencies, and private practitioners. A Chair (or Co-Chairs) for the panel is charged with responsibility of ensuring that the resulting protocol reflects true group consensus.

The next step is a review of the proposed guidelines and protocol by a third group whose members serve as expert field reviewers. Once their recommendations and responses have been reviewed, the Chair approves the document for publication. The result is a TIP reflecting the actual state of the art of AOD abuse treatment in public and private programs recognized for their provision of high quality and innovative treatment.

This TIP, titled *LAAM in the Treatment of Opiate Addiction*, presents current knowledge about the use of levo-alpha-acetyl-methadol (LAAM), an opioid agonist medication approved for use in 1993. LAAM suppresses opiate withdrawal symptoms for more than 72 hours, and it can be administered no more frequently than every other day. Thus, daily visits to the program clinic are not required for LAAM-maintained patients, as are visits for patients on methadone. In addition to the difference in dosing schedule, no take-home doses of LAAM are permitted under Federal regulations, and women of child-bearing potential must be tested monthly for pregnancy.

The introduction of LAAM into the current treatment system will require programs to educate staff and patients about the use of LAAM. This TIP describes the medication itself, its mode of
action, possible side effects, and interactions with other medications. A separate chapter on clinical use of LAAM presents guidelines for selecting patients who may benefit from LAAM and starting and maintaining them on the medication. A chapter on treatment planning addresses issues that may arise for counselors and patients, such as structuring free time and creating incentives for treatment progress. Issues for program managers and administrators, including staff education and costs of LAAM, are discussed in another chapter. A chapter on regulatory and ethical issues is included. As LAAM is introduced, programs will be a source of important data about its use, and the TIP presents suggestions for research in several areas.

This TIP represents another step by CSAT toward its goal of bringing national leadership to bear in the effort to improve AOD abuse treatment.

Other TIPS may be ordered by contacting the National Clearinghouse for Alcohol and Drug Information (NCADI), (800) 729-6686 or (301) 468-2600; TDD (for hearing impaired), (800) 487-4889.

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The Treatment Improvement Protocol (TIP) series fulfills CSAT’s mission to improve alcohol and other drug (AOD) abuse and dependency treatment by providing best practices guidance to clinicians, program administrators, and payers. This guidance, in the form of a protocol, results from a careful consideration of all relevant clinical and health services research findings, demonstration experience, and implementation requirements. A panel of non-Federal clinical researchers, clinicians, program administrators, and patient advocates employs a consensus process to produce the product. This panel's work is reviewed and critiqued by field reviewers as it evolves.

The talent, dedication, and hard work that TIPs panelists and reviewers bring to this highly participatory process have bridged the gap between the promise of research and the needs of practicing clinicians and administrators. We are grateful to all who have joined with us to contribute to advance our substance abuse treatment field.

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LAAM in the Treatment of Opiate Addiction

Chapter 1 - Introduction

LAAM (levo-alpha-acetyl-methadol) is a synthetic opioid agonist medication for use in the treatment of opiate addiction. It was approved by the Food and Drug Administration (FDA) in July 1993 and became commercially available in August 1993. Like methadone, LAAM creates a pharmacologic cross-tolerance to other opioids and therefore blocks the euphoric effects of those drugs while also controlling opiate craving. Methadone suppresses opiate withdrawal symptoms for 24 hours or longer, whereas LAAM achieves this effect for 48 to 72 hours or longer. Under FDA regulations, LAAM must be dispensed by approved opioid substitution therapy programs. Each program must receive approval from the single State agency (SSA) to dispense LAAM and must ensure that program staff receive training in its use.

Because of LAAM's long duration of action, after a patient's tolerance to LAAM has been established, it can be administered no more frequently than every other day. In humans, LAAM is metabolized into two active metabolites, nor-LAAM and dinor-LAAM. Both are metabolized more slowly than the parent drug. It is believed that this slow metabolism is the basis for LAAM's long duration of action. Like methadone, LAAM is similar in action to morphine. Its effects include analgesia, sedation, and respiratory depression. Tolerance to these effects develops with prolonged use, and an abstinence syndrome similar to that observed with morphine and other opiates occurs with cessation of regular use. However, with LAAM, the syndrome has a slower onset and lasts longer, with less acute symptoms (Fraser and Isbell, 1952).

Development of LAAM

LAAM is a Schedule II controlled substance and is sold under the name ORLAAM (levomethadyl acetate hydrochloride oral solution). LAAM was first developed in 1948 as an analgesic. The first study of LAAM was published a few years later by Fraser and Isbell (1952); they observed that LAAM suppressed opiate withdrawal symptoms for more than 72 hours.

LAAM creates a pharmacologic cross-tolerance to other opioids and therefore blocks the euphoric effects of those drugs while also controlling opiate craving. LAAM suppresses opiate withdrawal symptoms for 48 to 72 hours or longer.
In the late 1960s and early 1970s, as a response to widespread heroin use, interest in narcotic maintenance treatment resulted in the expansion of methadone treatment and its approval by FDA in 1972 for use in opioid substitution therapy. At the same time, clinicians began to examine its effects. Interest in LAAM during the 1970s resulted in 27 separate studies that involved a total of more than 6,000 patients. The studies varied in methodology and quality. The two major studies were conducted by the Veteran's Administration (Ling et al., 1976) and the Special Action Office on Drug Abuse Prevention (SAODAP) (Klett, 1978). Taken overall, the 27 studies established the safety and efficacy of LAAM as a maintenance medication in doses up to 100 milligrams dispensed at 48- to 72-hour intervals for extended periods (National Institute on Drug Abuse, 1993).

During the 1980s, little research was conducted or completed on LAAM, primarily because of lack of funding. However, as the human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS) epidemic began to be centered in the injecting-drug-using population, interest in expanding treatment programs for this population increased. This interest, coupled with evidence that methadone maintenance treatment provided access to this hard-to-reach population, led Federal officials to reexamine the use of LAAM. In 1990, with the establishment of the Medications Development Division at the National Institute on Drug Abuse (NIDA), Biometric Research Institute was engaged to develop a New Drug Application (NDA) for LAAM. After reviewing the submitted materials, the Drug Abuse Advisory Committee at FDA requested a study of the proposed package insert and a draft of treatment regulations for the use of LAAM in opioid substitution therapy programs.

Taken overall, 27 separate studies in the 1970s established the safety and efficacy of LAAM as a maintenance medication in doses up to 100 milligrams dispensed at 48- to 72-hour intervals for extended periods.

The final study, called the LAAM Labelling Assessment Study (LAS), was conducted in 26 methadone treatment programs throughout the United States. A total of 623 patients were recruited for the study. Seventy percent were patients transferred from methadone treatment programs; the remaining 30 percent were opiate-addicted individuals, 15 percent of whom were stabilized on methadone for less than 30 days and 15 percent of whom were not in methadone treatment. Based on results of the study and comments from treatment programs on the draft regulations, NDA 20-315 was submitted to FDA by the manufacturer in June 1993. Minor changes were made to the package insert, and FDA approved LAAM for use on August 18, 1993 (National Institute on Drug Abuse, 1993).

LAAM was approved for use in approved opioid substitution therapy programs for dosing every other day or three times per week. No take-home doses of the medication are currently allowed, but equivalent doses of methadone can be substituted to allow for travel or other emergencies. FDA regulations require that all women of childbearing potential who are taking LAAM be tested monthly for pregnancy because not enough data are available from the various preliminary studies to determine the effects of LAAM in pregnant women. The package insert recommends that women who become pregnant while receiving LAAM be transferred to methadone maintenance until they give birth, at which time they may resume taking LAAM.
Use of LAAM in Opioid Substitution Therapy Programs

During the 1980s, opiate addiction treatment programs changed dramatically. The epidemic of HIV/AIDS and the proliferation of cocaine abuse required that programs reconsider their goals and objectives. Increased availability of cocaine and crack cocaine raised concerns among some officials that take-home doses of methadone would be sold to purchase these illegal drugs. In addition, research and evaluation reports indicated that opioid substitution therapy programs were excellent sites to provide information, education, and treatment related to HIV and AIDS. Education about safer sex practices, counseling and testing, primary health care, family planning, and other relevant services can be made available in a "one stop shopping" model at a treatment center, where addicted patients can feel comfortable and safe and not experience the hostility they often encounter in mainstream health or social service settings.

As a result of these factors, public policymakers have begun to look at ways to expand substitution therapy to engage more opiate-addicted persons in treatment and service systems. Women are now entering treatment in greater numbers than ever before, and services have been initiated to meet the needs of women as well as the children who often accompany them to the treatment site.

Use of LAAM allows patients to visit the treatment site every other day or three times a week from the inception of treatment. For methadone, FDA regulations require daily visits to the clinic (at least six visits per week) during the first 3 months of treatment; after 3 months, take-home doses of methadone are appropriate for some patients. Use of LAAM can allow programs to admit more patients or focus on services other than medication dispensing.

Education about safer sex practices, counseling and testing, primary health care, family planning, and other relevant services can be made available in a "one stop shopping" model at the treatment center, where addicted patients can feel comfortable and safe and not experience the hostility they often encounter in traditional health or social service settings.

Daily clinic visits are frequently an obstacle to a patient's ongoing treatment and rehabilitation, especially if the patient is working or attending school. Because take-home doses of LAAM are not permitted, LAAM cannot be accidentally ingested by nontolerant individuals. In addition, some patients in the Labelling Assessment Study reported a preference for LAAM over methadone; they described LAAM as having a smooth action that allowed them to feel more "normal."

**Purpose of This TIP**

Medications have been used in the treatment of opiate dependence and other substance use disorders for more than three decades. While some people continue to find their use for such purposes problematic, the value of medications in alcohol and other drug (AOD) abuse treatment
has been well established over time. As this Treatment Improvement Protocol (TIP) was being prepared for publication, the Institute of Medicine published a report that further validated the concept of medication use in narcotics treatment programs (Institute of Medicine, 1995). As the use of new medications such as LAAM grows, we must continue to communicate our experiences to improve the quality of care.

Until more patients have experienced stabilization on both methadone and LAAM, comparative data will not be available to determine whether patients with certain characteristics do better on LAAM than on methadone. Previous trials of LAAM have not included sufficient numbers of new patients (i.e., those who have never been in treatment) or noncompliant patients to allow definitive statements to be made about which patients are appropriate for LAAM. As more patients receive LAAM in clinical settings and programs perform evaluation and outcomes studies, including interviews with patients to learn their preferences, these data will accumulate.

Many of the treatment professionals and administrators who reviewed the first draft of this TIP called for the document to provide very specific guidelines for deciding which patients would do better on LAAM than on methadone. Some expressed disappointment that the precise target population for LAAM was not delineated in the document. A few reviewers even asked that this TIP cite the specific percentage of opiate-addicted persons who would most benefit from LAAM treatment. Although these concerns are understandable, the response at this time is that data are not available to answer these types of questions. After more widespread experience in the use of LAAM with different groups of patients, it may be possible to select specific subgroups of those for whom LAAM would be appropriate. Some readers of the TIP will be among the clinicians, administrators, and investigators who are gaining and examining LAAM experience as it accumulates.

However, research and experience with methadone have led to some certainties about the role of maintenance medications: methadone and LAAM are useful medications, but they cannot meet all the health and social needs a patient may have. Both medications should be dispensed in a therapeutic setting and in conjunction with comprehensive health and social services that are structured to meet individual patient needs. In recent years, it has been increasingly recognized that patients who seek treatment through opioid substitution therapy programs have a wide variety of needs and a range of strengths and weaknesses that challenge the clinical skills and abilities of treatment providers. The Center for Substance Abuse Treatment (CSAT) has created this series of TIPs to document the current state of knowledge in particular areas, to provide practice guidelines, and to suggest future directions for research and investigation.

Medications have been used in the treatment of opiate dependence and other substance use disorders for more than three decades. While some people continue to find their use for such purposes problematic, the value of medications in AOD abuse treatment has been proven over time.
This TIP *LAAM in the Treatment of Opiate Addiction* is an attempt to provide single State agencies, treatment providers, clinicians, administrators, and patients with current knowledge about LAAM. Members of two panels—a Federal resource panel and a consensus panel of experts—provided input for the TIP. These two groups met in April and June, respectively, of 1994. The panels agreed that the TIP should provide guidance on current practice and objectively address issues and concerns that remain unanswered.

The Federal resource panel consisted of representatives of Federal agencies as well as other organizations (see Appendix C), concerned with the regulation and practice of substance abuse treatment and prevention. Representatives of NIDA, FDA, the Drug Enforcement Administration (DEA), CSAT, the Center for Substance Abuse Prevention (CSAP), the National Association of State Alcohol and Drug Abuse Directors (NASADAD), and others concluded that a document was needed that presented the current state of knowledge about LAAM in a balanced and objective manner.

The consensus panel of experts was nominated, selected, and convened soon after. It was composed of clinicians and researchers who were involved in both the early studies of LAAM and the more recent Labelling Assessment Study. Representatives from treatment programs and single State agencies were included, as was a medical ethicist. To ensure open and honest communication during the panel's deliberations, each participant signed a statement of confidentiality and a statement of disclosure of conflict of interest. The goal of the consensus panel was to describe the clinical, administrative, managerial, and regulatory issues raised by LAAM therapy and to achieve consensus on these issues when possible.

This TIP represents the panel's effort to assemble the current knowledge about the use of LAAM to help single State agencies and treatment providers understand this new medication. Those interested in the use of LAAM in narcotic treatment programs will find this TIP valuable, particularly front-line program staff working directly with patients and their families. Patients receiving LAAM therapy may also find the TIP helpful.

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**Concerns of the Consensus Panel**

As the consensus panel discussed and debated the clinical, pharmacological, administrative, regulatory, and practical value of LAAM as it is currently approved for use, several issues emerged. There was consensus that more experience and knowledge are needed than now exist. In addition, it is the expressed wish of the panel that NIDA, CSAT, and the other agencies concerned with the problem of substance abuse and HIV/AIDS help to address the concerns described here.
The panel recommends that training be available for all levels of staff in programs that introduce LAAM therapy. Experience in the Labelling Assessment Study indicates that patients experience improved outcomes in programs that make a concerted effort to create an informed interdisciplinary treatment staff. Counselors, nurses, physicians, and others must all support treatment decisions and work together to help patients attain treatment goals. Two resources for training and technical assistance in the use of LAAM are described in Appendix B.

It is clear that LAAM will not replace methadone in maintenance treatment. As indicated above, the details of what works, for whom, and when, are still not known. The consensus panel agreed that a thorough discussion of patient-treatment matching issues in opiate addiction treatment was needed. The panel was pleased to learn that another TIP in this series -- *Matching Treatment to Patient Needs in Opioid Substitution Therapy* -- was being developed to address these issues. The panel has no doubt that the TIP on matching will also be applicable to LAAM therapy. The TIP on matching, along with the previously published TIP *State Methadone Treatment Guidelines* and the TIP on *Assessment and Treatment of Cocaine-Abusing Methadone-Maintained Patients*, will provide valuable information for understanding the elements of comprehensive treatment and for developing individualized treatment plans. As expertise and experience in the use of LAAM grow, this body of knowledge will be periodically updated.

The two issues that most concerned the consensus panel were the use of LAAM by women of childbearing potential and the lack of take-home availability of LAAM. The panel recommends that research begin quickly to determine the safety and efficacy of LAAM during pregnancy as well as the safety and efficacy of providing take-home doses for self-administration under certain circumstances.

The two issues that most concerned the consensus panel were

- The use of LAAM by women of childbearing potential
- The lack of take-home availability of LAAM.

**The Use of LAAM by Women**

The requirement for monthly pregnancy testing caused concern and discussion among some panel members. FDA has not imposed this requirement on any other newly approved drug. No reason exists for researchers or clinicians to believe that LAAM would affect the mother or fetus any differently than other narcotic drugs taken under supervision during pregnancy, including methadone. Therefore, the panel was concerned that the required monthly pregnancy testing would be viewed with suspicion by patients and seen as an additional and perhaps unnecessary expense by program administrators.

Therefore, the panel recommends that the necessary studies in animals and humans be conducted and evaluated quickly and that the results be made widely available to patients, clinicians, and administrators. If warranted, the current requirement for monthly testing should be revised based
on these studies. In addition, family planning services should be available to all patients maintained on both LAAM and methadone, as part of a comprehensive women's health program either onsite or by referral to a cooperating facility.

The panel recommends that the necessary studies in animals and humans be conducted and evaluated quickly and that the results be made widely available to patients, clinicians, and administrators. If warranted, the current requirement for monthly pregnancy testing should be revised based on these studies.

Take-Home Doses

The absolute prohibition against take-home doses of LAAM may prevent acceptance by patients and staff. In States that prohibit or limit the use of take-home methadone, use of LAAM would provide more clinical flexibility and allow patients a degree of freedom from daily visits that they do not now enjoy. In States where narcotic treatment regulations are similar to Federal regulations, LAAM therapy would allow treatment professionals to adjust the frequency of clinic visits during the first 2 years of treatment. After 2 years, patients receiving methadone are eligible for twice-weekly visit schedules; after 3 years, schedules with once-weekly visits are possible if patients have made substantial progress in treatment. In such situations, even if patients prefer LAAM to methadone, they may want to take advantage of having fewer visit schedules and be transferred to methadone maintenance treatment.

Once patients being treated with LAAM begin to experience stability and advance in treatment, they will need take-home doses for a variety of valid personal and vocational reasons. Constant changes between LAAM and methadone could present administrative and clinical problems, including problems related to physician orders and documentation. Therefore, the consensus panel believes that the prohibition against take-home doses of LAAM should be openly discussed and considered. Studies and trials to explore the possibility of take-home doses of LAAM for appropriately screened patients should be conducted and evaluated.

It is hoped that when patients and clinicians gain experience and knowledge, LAAM therapy will provide treatment professionals and patients with another medication to add to the treatment system. After a period of clinical use, the treatment field will eventually understand where LAAM fits into the treatment system. Such knowledge will maximize the ability to match patients to appropriate treatment and assist greater numbers of persons in need of treatment.

Patient selection issues and other unanswered questions about LAAM therapy should help focus research and evaluation efforts as LAAM treatment is implemented across the country. Issues concerning pregnant women, take-home LAAM, the relationship of staff attitudes to successful treatment, use of LAAM and methadone after relapse, and the use of LAAM in difficult-to-treat or noncompliant patients and others must be examined by carefully designed studies. Focused
research efforts will help resolve some of these issues and improve treatment for all patients in opioid substitution therapy.

Overview of This TIP

The TIP is organized into six chapters. The remaining chapters are described below.

Chapter 2 Clinical Profile of LAAM reviews the pharmacology of LAAM and its actions and effects, both in the laboratory and in treatment settings. Medications that should be avoided by patients taking LAAM are discussed, as well as the side effects, indications, and contraindications of LAAM. Although this chapter may be more technical than others, the panel feels that direct treatment providers should read it carefully and understand the pharmacology of LAAM. These front-line staff are often the first to discuss such issues with patients and to respond to their concerns. Anecdotal information from the Labelling Assessment Study indicated that LAAM maintenance worked best in programs where direct treatment staff were fully trained and briefed about all aspects of LAAM therapy and had a positive attitude toward it.

Chapter 3 Clinical Application of LAAM Therapy explains the use of LAAM and describes practical concerns for clinicians in prescribing LAAM, including dosage and build-up schedules and whether to provide LAAM every other day or three times weekly. It reviews the LAS results as they pertain to different patient subgroups. Ways to approach and solve frequently occurring clinical issues concerning dosing are described.

Chapter 4 Treatment Planning reviews the first 30 days of LAAM treatment and issues and concerns that may arise. An approach to patient education that maximizes acceptance of this new maintenance therapy is described.

Chapter 5 Management and Administrative Issues provides an overview of administrative and managerial requirements for programs to become approved to use LAAM and addresses the practical application of these requirements. Issues that contribute to successful treatment programming are discussed as are issues specific to LAAM therapy, such as monthly pregnancy testing and transfer of patients from LAAM to methadone. The costs of LAAM therapy and issues involved with reimbursement, especially in managed care environments, are discussed.

Chapter 6 Regulatory and Ethical Issues provides an overview of the regulatory process for States and programs to become approved to use LAAM. The future of LAAM (and methadone) treatment regulations is discussed. NIDA's development of the Methadone Quality Assurance System, designed to assess the feasibility of a performance-based reporting and feedback system for methadone treatment programs, has led to more emphasis on treatment outcomes and quality of care than is found in traditional process reviews currently performed by FDA. In addition, the Institute of Medicine's recently published review of regulations governing methadone treatment calls for less government regulation and the adoption of practice guidelines for opioid substitution therapy (Institute of Medicine, 1995). The costs of LAAM therapy and the economic issues raised by the approval and use of LAAM are also reviewed.
Appendix A lists references cited in the TIP as well as other materials on LAAM. Training and informational materials available from the manufacturer of LAAM, as well as technical assistance available through the CSAT-implemented Opioid Addiction Treatment Improvement Project, are described in Appendix B. Appendix C is a list of individuals who participated in the Federal resource panel that helped develop this TIP. Names of those who participated in field review of an early draft of this document are listed in Appendix D.

Issues that should be the focus of future research include

• Patient selection
• Use of LAAM with pregnant women
• Take-home LAAM
• The relationship of staff attitudes to successful treatment
• Use of LAAM and methadone after relapse
• Use of LAAM in difficult-to-treat or noncompliant patients.
LAAM in the Treatment of Opiate Addiction

Chapter 2 - Clinical Profile of LAAM

LAAM (levo-alpha-acetyl-methadol) is a synthetic opioid agonist that has recently been approved by the Food and Drug Administration (FDA) for the maintenance treatment of opiate addiction (Food and Drug Administration, 1993). It is not approved for opiate detoxification treatment for either short- or long-term detoxification.

Although LAAM is similar to methadone in many ways, it has several features that make it distinct from methadone. The most significant of these features is LAAM's longer duration of action, which allows patients to visit the treatment program less frequently from treatment inception. The approval of LAAM provides a new treatment alternative in the management of opiate addiction. As such, it should be evaluated by the same standards by which other treatment options have been judged. A new medication should, for example, expand accessibility to treatment, and it should enable more effective and appropriate treatment for patients already in the treatment system. LAAM therapy offers patients such possibilities and creates opportunities for staff members to learn about and provide a new form of care.

In approving LAAM, FDA did not significantly modify the language of the regulations governing methadone treatment. The word "methadone," for example, was simply changed to "narcotic drugs" to be more inclusive. However, differences between the two agents with respect to dosing schedules, prohibition of LAAM take-home doses, and eligibility for LAAM treatment are spelled out in detail in the FDA regulations. As the States begin to approve LAAM and develop their own regulations, many may wish to follow the Federal example. Introduction of LAAM does not require States to develop extensive new regulations. (See Chapter 6 for a discussion of regulations and their development.)

This chapter describes the medication LAAM, including its metabolization, interactions with drugs of abuse and other medications, safety and side effects, and use with certain patient groups, such as women.

Any new medication should expand accessibility to treatment and enable more effective and appropriate treatment for patients already in the treatment system.
Metabolism and Mechanism of Action

The clinical utility of LAAM is based primarily on the activity of two metabolites, rather than on that of the parent drug alone. In the body, LAAM, metabolized by the liver, changes sequentially to nor-LAAM and dinor-LAAM. (Throughout this document, the term LAAM refers to the parent compound and its two active metabolites, nor-LAAM and dinor-LAAM.) Of these three compounds, nor-LAAM is the most potent. The combined duration of activity of all three of these compounds accounts for LAAM's long-acting properties. Knowledge of the basics of steady-state pharmacology is important for understanding the action of LAAM in the body. Steady-state pharmacology is described in Chapter 3 in the section "Induction Onto LAAM."

In practical terms, LAAM's longer action makes it possible for patients to visit the clinic less often than they would for daily methadone treatment. LAAM can be given either every other day or three times a week. Under current FDA regulations, LAAM cannot be given more frequently than every other day, 21 C.F.R. Part 291 Section 291.505(k)(1)(i) (1993), and no take-home doses can be given under any circumstances, 21 C.F.R. Part 291 Section 291.505 (k)(1)(iii) (1993).

Federal regulations also require clinics that use both LAAM and methadone to ensure that "dosage forms of LAAM and methadone are easily distinguished," 21 C.F.R. Part 291 Section 291.505 (1993). LAAM must be different in color and taste from methadone. Methadone is currently available in powder, tablet, and liquid forms, whereas LAAM is currently prepared only in liquid formulation for oral use. The manufacturer provides LAAM as a colorless liquid.

Clinic staff should ensure that patients who are known to abuse sedatives, tranquilizers, propoxyphene, antidepressants, benzodiazepines, or alcohol are told in very clear language of the dangers of adverse additive effects if they take these substances while maintained on LAAM.

At present, LAAM is available only from Roxane Laboratories, Inc. Methadone can be purchased from three different companies: Mallinckrodt Chemical, Inc.; Roxane Laboratories, Inc.; and UDL Laboratories, Inc. Each company markets different forms of methadone that vary in color and taste from the others.

Drug Interactions

Drugs of Abuse

LAAM's interactions with drugs of abuse have not been systematically studied in human populations, but data from the clinical studies do not suggest any unusual risk of LAAM versus other opiates in terms of drug-drug interactions with drugs of abuse. The effects of LAAM would be expected to be similar to the effects of methadone and other opioid drugs under the same
conditions. However, until conclusive data from systematic studies are available, interactions cannot be predicted with certainty.

LAAM, like methadone and other opioids, may have additive or synergistic effects when used in combination with commonly used drugs of abuse. Because of LAAM's long-acting nature, both patients and clinic staff should be aware that special caution is necessary when it is combined with drugs that depress the central nervous system, including alcohol. For this reason, clinic staff should ensure that all patients who are known to abuse sedatives, tranquilizers, propoxyphene, antidepressants, benzodiazepines, or alcohol are told in very clear language of the dangers of adverse additive effects if they take these substances while being stabilized or maintained on LAAM.

Experience during the Labelling Assessment Study (LAS) of LAAM indicated that LAAM's delayed onset of effect (from 24 to 36 hours) may lead some patients to take benzodiazepines or other drugs including opiates in an attempt to create an additive effect. Patients receiving LAAM should be counseled very specifically about its delayed onset and prolonged duration of activity, as well as the associated extra risk of effects that can induce withdrawal if patients take other drugs, even on days when they do not receive a LAAM dose. Some patients may not be candidates for LAAM if they are unable to tolerate the slow onset.

Patients receiving LAAM should also be cautioned not to use or abuse alcoholic beverages. Patients should be advised that chronic use of alcohol damages the liver and that liver dysfunction may interfere with the metabolism of LAAM. If alcohol abuse is evident, the program should ensure that the patient receives counseling and assistance in discontinuing alcohol use. If a patient abuses alcohol consistently, a switch to methadone may be warranted because daily clinic attendance will permit closer monitoring, and research has indicated that methadone may be safely prescribed for patients with severe liver damage. Although similar research on LAAM has not been completed, there is every reason to believe that use of LAAM by patients with severe liver damage is not problematic. LAAM may be used concurrently with disulfiram (Antabuse).

Medications That Can Induce Withdrawal

Mixed agonists and antagonists, such as pentazocine (Talwin), butorphanol (Stadol), nalbuphine (Nubain), and buprenorphine (Buprenex), and pure antagonists, such as naltrexone and naloxone, all may precipitate withdrawal in LAAM-maintained patients. FDA has recently approved the narcotic agonist naltrexone for use in treating alcohol craving. Clinicians must be aware and must inform patients that the use of naltrexone will precipitate withdrawal symptoms in patients maintained on LAAM or methadone. Naltrexone must not be used by patients in opioid substitution therapy.

Cross-tolerance

As a result of cross-tolerance, LAAM (like other mu agonists) reduces the effectiveness of narcotic analgesics in normal doses. Clinicians may need to adjust medications and patient pain management accordingly. As with methadone, when other narcotics, such as morphine, are used
for analgesia and anesthesia, dosages should be adjusted upward to achieve the same level of pain relief or anesthesia.

Clinicians must be aware and must inform patients that the use of naltrexone for treatment of alcohol craving will precipitate withdrawal symptoms in patients maintained on LAAM or methadone. Naltrexone must not be used by patients in opioid substitution therapy.

Interaction With Antituberculosis Drugs and Other Medications

With the rise in the prevalence of tuberculosis, many more patients are being prescribed rifampin, the bactericidal drug currently widely used to treat this disease. Rifampin has been found to reduce methadone levels in serum by up to 50 percent in patients who have been stabilized on methadone maintenance. This reduction in serum levels of methadone often results in symptoms of withdrawal. A recent study of an alternate antituberculosis medication, mycobutin (Rifabutin), showed that this medication did not alter plasma levels of methadone. Some participants had subjective complaints of discomfort, which may have resulted from suggestivity to remarks of the researchers, as noted at the consensus panel by B. Primm, M.D. Further studies of this type should be effects.

When a new medication is introduced to the market, all potential side effects must be reported. The most frequently reported side effects in the LAAM trials were insomnia, nervousness, and constipation. Other side effects observed in clinical trials are shown in Exhibit 2-1. Side effects probably caused by LAAM that occurred in less than 1 percent of patients in clinical trials include a drop in blood pressure when the patient stands (postural hypotension), muscle pain (myalgia), and tearing of the eyes.

In addition, several other reactions appeared in both controlled and uncontrolled LAAM trials. Although they were seen infrequently and their relationship to LAAM is unknown, clinic staff should be aware that these effects have been reported: hypertension, changes in cardiac activity patterns on electrocardiogram (specifically, prolongation of the QT interval and nonspecific ST-T wave changes), bradycardia, hepatitis and test indications of abnormal liver functions, absence of menstruation (amenorrhea), and the presence of pus in the urine (pyuria). Close monitoring by counselors, nurses, and medical staff in the first several months of adjustment to LAAM therapy will ensure that any side effects are addressed promptly.

Interventions

Clinicians may want to provide symptomatic treatment of side effects resulting from LAAM. Of the three most commonly reported side effects of LAAM, constipation is probably the most persistent and problematic. It also raises the potential problem of laxative dependence when patients treat themselves. Patients should be told to avoid the use of strong or harsh chemical laxatives. Stool softeners, lubricants (such as mineral oil), bulk and fiber laxatives (such as
Metamucil), and naturally occurring laxatives such as prunes may provide symptomatic relief. However, it should be noted that chronic use of mineral oil can lead to malabsorption of fat-soluble vitamins and result in a vitamin deficiency. Adequate fluid intake also is important.

The other two most frequent reactions to LAAM therapy, insomnia and nervousness, usually disappear with continued treatment. Other side effects, for example, muscle and joint pain, can be treated with nonsteroidal anti-inflammatory agents, such as ibuprofen.

Until the safety of LAAM during pregnancy is studied further, the consensus panel recommends that women of childbearing potential who enter treatment receive methadone rather than LAAM. Once treatment has progressed, the required pregnancy testing can be discussed with the patient. When informed consent is obtained and pregnancy testing is implemented, the woman can be transferred to LAAM if this is desirable.

Possible Impact of Liver Disease

Further research is needed on the impact of liver disease on patients in opioid substitution therapy programs. Although the presence of liver disease is not currently a reason to exclude a patient from treatment, the presence of severe persistent liver disease does indicate the need for caution in treatment and monitoring and may require special patient counseling. In patients with a severely impaired liver, the parent drug, LAAM, may not be as easily converted into the more active metabolite, nor-LAAM, because this process occurs in the liver. This difficulty in conversion could delay the drug's onset of effect. Such patients should be monitored closely for signs of excessive accumulation of LAAM and its metabolites.

Patients should also be monitored for signs and symptoms of dose accumulation, which include jumpiness or feeling on edge (what some patients describe as "feeling wired"), poor concentration, drowsiness, and dizziness when moving to a standing position. When patients exhibit signs of excess accumulation of LAAM, the dosage should be reduced. If significant signs of sedation are present, the clinician may omit a dose or slow the buildup.

Effects of LAAM Treatment in Specific Clinical Situations and Patient Populations

Women

Data show no differences between the sexes in response to LAAM treatment; women and men fare equally well. However, until the safety of LAAM during pregnancy is studied further, the consensus panel that developed this Treatment Improvement Protocol felt that women of childbearing potential who entered treatment should receive methadone rather than LAAM. Once treatment has progressed, the required pregnancy testing can be discussed with the patient. When informed consent is obtained and pregnancy testing is implemented, the woman can be
transferred to LAAM if this is desirable. As discussed in Chapter 1, the panel recommends that the necessary studies in animals and humans be conducted and evaluated quickly and the results made widely available to patients, clinicians, and administrators. If warranted, the current requirement for monthly testing should be revised based on these studies.

Until data are evaluated, treatment of pregnant women with LAAM is discouraged. Monthly pregnancy testing is a requirement for women of childbearing potential who receive LAAM. Women who become pregnant while on LAAM should be transferred to methadone maintenance. (More detailed information about considerations for pregnant women and nursing mothers is given in Chapter 3.)

Currently, there is no known reason to exclude patients from LAAM treatment based on HIV-positive status or AIDS.

**HIV-Infected Patients**

The effect of LAAM on the immune system is unknown, as is its interaction with zidovudine (formerly azidothymidine, or AZT) and other drugs prescribed for patients with human immunodeficiency virus (HIV) infection and acquired immunodeficiency syndrome (AIDS). Currently, there is no known reason to exclude patients from LAAM treatment based on HIV-positive status or AIDS.

**Pain Management in LAAM-Maintained Patients**

Patients receiving maintenance therapy with methadone or LAAM are often undertreated or even denied treatment for pain associated with injury, surgical procedures, or chronic conditions. It is the ethical obligation of health care providers to provide adequate pain relief for all patients. Reluctance to provide adequate treatment for pain is usually based on the belief that the maintenance dose of LAAM or methadone provides pain relief. This belief is absolutely incorrect. With long-term administration of LAAM, nearly complete tolerance develops to any analgesic effects of the medication, and the usual maintenance dose affords no pain relief.

Reluctance to provide adequate treatment for pain is usually based on the belief that the maintenance dose of LAAM or methadone provides pain relief. This belief is absolutely incorrect. With long-term administration of LAAM, nearly complete tolerance develops to any analgesic effects of the medication, and the usual maintenance dose affords no pain relief.
The inadequate treatment of pain in patients receiving maintenance therapy often leads to disruptive behavior by angry and frightened patients and discharge against medical advice, despite the obvious risks to the health of the patient (Zweben and Payte, 1990). For these reasons, program staff should work cooperatively with the patient's health care providers to assist in providing proper pain management and treatment.

**Acute Pain**

Patients on LAAM maintenance therapy for opiate addiction occasionally require treatment for pain associated with trauma or with medical, surgical, or dental procedures. Whenever possible, pain management should be discussed with care providers before surgery or dental procedures take place. Some basic principles should inform the management of acute pain in patients receiving maintenance therapy:

1. Maintenance treatment should be continued without interruption during pain management.
2. When nonnarcotic analgesia is not effective for pain management, standard opioid agonist drugs, such as codeine and morphine, are appropriate. It is important, however, for clinicians to be aware that patients will require higher doses of these drugs at more frequent intervals because of cross-tolerance to LAAM or methadone. Doses should be adjusted accordingly to achieve adequate pain relief for the patient. Doses should be administered at regular intervals rather than "as needed."
3. Agonist/antagonist drugs may precipitate severe withdrawal reactions and should not be used. These include pentazocine (Talwin), butorphanol (Stadol), nalbuphine (Nubain), buprenorphine (Buprenex), and naltrexone. More information on this subject can be found in the TIP State Methadone Treatment Guidelines.

**Chronic Pain**

Patients with chronic opioid addiction and a disorder causing chronic pain pose a clinical challenge. Those who fail to respond to more conservative management often benefit from carefully supervised adequate doses of short-acting opioid agonist drugs, provided within the context of adequate dose maintenance pharmacotherapy.

**Issues for Further Research**

The two most important areas for additional research on LAAM treatment are pregnancy (effects on the mother and the fetus, including postpartum issues such as lactation and breast-feeding) and the feasibility of take-home LAAM. Other essential research topics related to LAAM are

1. Immune response
2. Interactions with drugs of abuse, such as cocaine and alcohol (multidrug interactions)
3. Coexisting psychological problems or disorders (dual diagnoses)
4. LAAM as an analgesic for treatment of chronic pain
5. Interactions with other therapeutic drugs
6. Medically supervised withdrawal from maintenance therapy with LAAM
7. LAAM in patients with hepatic or renal disease
8. LAAM for daily use in special situations, such as in patients who metabolize the drug rapidly.

Other research areas include quality assurance studies focusing on improved treatment outcomes (for example, research on patient selection and on staff attitudes) and cost-effectiveness studies.
Chapter 3 - Clinical Application of LAAM Therapy

Both clinical and practical considerations are involved in deciding which patients are appropriate for levo-alpha-acetyl-methadol (LAAM) treatment. Patients can be inducted directly onto LAAM or can be transferred from methadone to LAAM. This chapter provides guidelines for selecting patients for LAAM treatment and stabilizing them on the medicine.

Dose scheduling is key to successfully maintaining stabilized patients on LAAM. Two factors specific to LAAM--its long-acting nature and the fact that regulations do not permit take-home doses--make dose scheduling more complicated than with methadone. Dosing can be scheduled every other day, if the clinic is open on Sunday. Three-times-weekly dosing (two 48-hour doses and a 72-hour dose) can also be used. Programs should have procedures for addressing Monday holidays and other planned and unplanned interruptions of regular LAAM dosing. For planned absences, supplemental doses of methadone may be given to patients who are allowed take-home methadone. The chapter describes approaches to addressing dosing and scheduling issues.

Selection of Patients

Research to date provides no clear-cut indicators that determine which individuals will benefit most from LAAM therapy. Until more ic effects of drugs used to supplement LAAM.

People who have been on methadone maintenance a long time but still report for medication six or seven times a week because of State or local policy on take-home methadone. These patients in particular may appreciate that fewer clinic visits are required by LAAM therapy.

Chronic relapsers, including those who have been on methadone for a long time but who remain uncommitted to the goals of treatment. Most chronically noncompliant patients do not appear to benefit from daily visits to the clinic, and many visit the clinic only because they are not allowed take-home medication. Many such patients disrupt clinic routines and, over a long period of time, have exhausted staff attempts to engage them in treatment. Members of the consensus panel felt that use of LAAM therapy with some of these patients would have the advantage of reducing disruptive clinic visits and making it easier for staff to provide care to others. Panel members understood that recommending LAAM therapy for this group was controversial; patients in this group should be carefully selected. LAAM therapy should never be used as a punishment.

Daily clinic attendance by the three groups may be reduced with LAAM therapy. Patients who have been stable on methadone maintenance for a period of years probably receive take-home
doses and would experience no reduction in visits when transferring to LAAM. However, according to Federal regulations, a patient must be in opioid substitution therapy for 2 years before he or she is eligible for enough take-home methadone to allow only two clinic visits per week. Thus, patients in the first 2 years of methadone treatment may benefit from LAAM therapy. (After 3 years of treatment, the Food and Drug Administration [FDA] regulations permit a 6-day supply of methadone for patients meeting certain conditions, thus allowing them once-a-week clinic visits. State regulations vary.)

**Practical Considerations and Clinical Factors**

In considering candidates for LAAM therapy, common sense and practical considerations should prevail. Patients with mobility problems may find LAAM treatment an attractive alternative, because fewer visits mean less frequent travel requirements. Similarly, patients in inner cities who lack transportation, those in rural areas who must drive long distances to the clinic, and those with scheduling conflicts may also find LAAM therapy a desirable alternative. Patients (such as those with dementia) for whom age or illness makes managing take-home medication difficult may also derive some benefits. Patients in States where take-home doses of methadone are not allowed or are in practice severely restricted may also benefit from the introduction of LAAM treatment. Patients in these States could have more opportunities to engage in other productive life experiences (such as employment and job training) under LAAM’s reduced dosing schedule. However, treatment choices based on these considerations alone should be avoided.

Among the appropriate target population for LAAM therapy are three main groups:

- People entering treatment, either from the street or in their first 2 years of methadone maintenance
- People who have been on methadone maintenance a long time but still report for medication six times a week because of State or local policies on take-home methadone
- Chronic relapsers, including those who have been on methadone for a long time but who remain uncommitted to the goals of treatment.

Although use of LAAM raises these and other practical issues, the decision to use LAAM should be governed by clinical factors, including the patient's desire and the belief that LAAM offers the optimal means for achieving the goals of maintenance treatment. LAAM therapy should not be selected because a clinic is trying to achieve formulas or meet quotas of LAAM patients.

The decision to use LAAM should be framed from the patient's perspective. Staff may find it useful to present the available range of opiate addiction treatment alternatives to a patient in a manner similar to that used in family planning counseling. Such conversations may extend over more than one counseling session to allow the patient to assimilate the information. (However, treatment with methadone can begin right away.) To help the patient make an informed choice,
program staff should present the advantages and disadvantages of the treatment options and give
the patient the opportunity to ask questions and to participate in the treatment selection.

Every treatment choice has particular advantages and disadvantages. For example, some patients
may need daily clinic visits as a component of their treatment program; less frequent visits may
help other patients establish a more normal routine that is not as structured around clinic visits as
is necessary when receiving methadone. For the latter group, use of LAAM offers distinct
benefits. Although use of LAAM eliminates the need for daily clinic visits, it also eliminates the
option of take-home medication. For some patients, the loss of take-home medication as an
indicator of treatment progress may present problems. For others, take-home medication may not
be achievable, and LAAM will provide an alternative method of reducing the frequency of clinic
visits.

To help the patient make an informed choice about LAAM treatment, program staff must present the
advantages and disadvantages of all treatment options and give the patient the opportunity to ask
questions and to participate in the treatment selection.

Intake and Assessment

The components of the psychosocial assessment for LAAM therapy are consistent with those for
methadone treatment. Guidelines for assessment of patients are presented in two other TIPs State
Methadone Treatment Guidelines and Matching Treatment to Patient Needs in Opioid
Substitution Therapy.

Patients who are being considered for LAAM therapy can be divided into two major groups:
those who are already in an opioid substitution therapy program and those who are not. The latter
category includes patients who are not currently dependent on opioids, for example, those
recently released from incarceration or chronic care institutions who meet FDA criteria for
admission without proof of current physical dependence, 21 C.F.R. Part 291 Section

Patients who are appropriate candidates should be offered other treatment options if they are not
able to tolerate LAAM therapy.

Criteria for Determining Eligibility: Federal Requirements

Federal eligibility requirements for methadone maintenance treatment stipulate that people with
a minimum 1-year history of opiate addiction and who have current physical dependence may
enter maintenance treatment. The minimum age requirement is 18 years; persons between 16 and
18 years of age may enter methadone treatment under certain conditions. There is no upper age
limit on entry to care. Pregnant women may be accepted for methadone treatment and, with
special medical justification, may be admitted under modified criteria. Persons with major
medical conditions are eligible for treatment, as are polydrug abusers. Details on methadone eligibility guidelines are found in the TIP State Methadone Treatment Guidelines.

Federal eligibility requirements for LAAM treatment are identical to those for methadone, with the following three major exceptions. LAAM is not approved for use by

- Pregnant women
- Nursing mothers
- Persons under the age of 18 years.

**Pregnant Women and Nursing Mothers**

LAAM is classified by FDA as a category C drug, that is, a drug for which "animal studies show adverse effects on fetus but no adequate studies in humans; benefits from drug during pregnancy may outweigh risks, OR no animal reproduction studies and no adequate human studies," 21 C.F.R. Part 291 Section 201.57(f)(6)(i)(c) (1994). Federal guidelines state that because LAAM is not approved for use during pregnancy or while nursing, "patients who are or become pregnant cannot be started or continue on LAAM, except by written order of a physician who determines this to be the best choice of therapy for the patient" (Food and Drug Administration, 1993).

Any predictions of the effects of LAAM on pregnant or nursing women and the fetus at this time are speculation. For example, because of its slower action, LAAM may produce fewer withdrawal effects on the fetus; on the other hand, LAAM metabolites might accumulate in utero. Like other mu agonist opioids, LAAM may cause respiratory depression in the fetus and other perinatal complications during delivery. It is not known whether LAAM is excreted in breast milk.

Many other drugs have been approved for use during pregnancy, even though their effects on the fetus and newborn are unknown. When there is no treatment alternative, the physician must decide whether to treat a pregnant woman. However, an adequate and proven substitute for LAAM exists - methadone. Until research has demonstrated the safety of LAAM in pregnant women and nursing mothers, it is recommended that patients who become pregnant or are nursing be transferred to methadone. Exceptions to this practice are likely to be extremely rare. The sole circumstance under which LAAM might be acceptable is when the only alternative is a return to heroin use.

Counseling concerning the potential risks of LAAM during pregnancy and nursing should be provided to both male and female patients. Women should receive written and oral information about the potential risks of taking LAAM during pregnancy, and this information should be periodically reinforced.

Regular pregnancy testing should be available in all substance abuse treatment programs; women with substance abuse problems are a high-risk population in terms of receiving poor prenatal care. Testing for sexually transmitted diseases (STDs) as well as for human immunodeficiency virus (HIV) should also be made routinely available to these patients. These tests should be offered, along with onsite access to or referral for family planning services and counseling.
Regular pregnancy testing for patients receiving LAAM may be more easily integrated into the program if it is presented as part of an overall women's health initiative.

Mandatory pregnancy testing should be presented to women as a positive treatment benefit. Testing has many benefits, provided that positive results are followed up by good prenatal care and appropriate support. Open discussion of issues related to reproductive health can strengthen the patient-staff relationship, which may in turn enhance treatment progress.

Regular pregnancy testing should be available in all substance abuse treatment programs, because women with substance abuse problems are a high-risk population in terms of receiving poor prenatal care.

**Persons Under 18 Years of Age**

Federal regulations prohibit any person under 18 years of age from entering LAAM maintenance treatment because there are no adequate studies to support its use among persons of this age. Some people question whether arbitrary limits such as these, in the absence of clinical data, are counterproductive. Studies are needed to provide a scientific basis for the exclusion of any group of patients from LAAM therapy.

**Medical and Other Considerations**

Use of LAAM has been studied in several subgroups of patients, and results are summarized below.

**Persons with comorbid medical conditions.** Persons with elevated liver enzyme levels should not automatically be ruled out as candidates for LAAM therapy. LAAM treatment is generally not recommended for persons with hepatic failure. (For further information on the effects of liver disease, see Chapter 1.)

**Persons with comorbid psychiatric conditions.** A person should not be excluded as a candidate for LAAM therapy solely on the basis of psychiatric symptoms. There is generally no reason to believe that the treatment of patients with coexisting psychiatric illness should be different with LAAM than with methadone. Psychiatric symptoms should be evaluated and treated, and decisions about maintenance therapy made in conjunction with the provision of such treatment.

Patients who do not succeed on one of the two opioid agonists available for treatment (methadone and LAAM) should be tried on the other if there are no contraindications (such as pregnancy). Anecdotal reports indicate that some patients may benefit from LAAM therapy because they experience a more level effect than with methadone; some patients receiving methadone report an "up-and-down" cycle.
 Patients with previous experience of side effects from LAAM. Persons who have experienced side effects from the drug in the past are generally inappropriate candidates for LAAM treatment.

Psychosocial considerations. Some patients have avoided opioid substitution therapy because of the stigma associated with methadone. The question of whether they are appropriate candidates for LAAM treatment cannot be answered with a simple "yes" or "no." The counselor's first task is to ensure that the patient has been given the information necessary to make an informed choice. Sensitive counseling can alleviate anxiety and facilitate rational decisionmaking.

Induction Onto LAAM

Steady-State Pharmacology

An understanding of the basics of steady-state pharmacology is essential for the safe induction of patients onto methadone or LAAM therapy. When a drug is given at regular intervals before the previous dose is eliminated from the body, there is an accumulation of the drug in the body until a steady state is reached. The term steady state refers to a condition in which the amount of a drug entering the body is equal to the amount being excreted, which allows a relatively constant serum (blood) level of the drug. For any drug, the time needed to reach steady state is a function of its elimination half-life. The half-life is the amount of time required for the body to eliminate half of a given dose of a drug.

It is important for physicians, staff, and patients to understand that the second dose is added to the portion of the previous dose that is still in the body, resulting in higher blood levels with no increase in dose. This continues until steady state is achieved.

The terms steady state and stabilization should not be confused. Steady state has been achieved when the dose of LAAM administered lasts for the intended length of time. In contrast, a patient is stable when he or she no longer exhibits drug-seeking behavior or craving. At this point, both the patient and supportive services staff can begin to focus on medical, lifestyle, and psychosocial issues, and on other treatment.

Steady state is based on multiples of the elimination half-life. Approximately four to five half-life times are needed to establish the steady state. For example, methadone has a half-life of 1 to 1.5 days (24 to 36 hours); therefore, the steady state for methadone—that is, the time at which a relatively constant dose level is present in the body—is achieved in 5 to 8 days in most patients (see Exhibit 3-1).

It takes longer to reach a steady state of LAAM in the body because the parent drug and each metabolite (nor-LAAM and dinor-LAAM) have a longer half-life than methadone. The half-life of LAAM (parent drug) is 2.6 days, that of nor-LAAM, 2 days, and that of dinor-LAAM, 4 days. Because of their different half-lives, each requires a different time to achieve steady state; the length of time is calculated by multiplying the half-life by a factor of four to five (Exhibit 3-1). Thus, although the first dose of LAAM, if it is adequate, will eliminate withdrawal symptoms,
and such symptoms should be well controlled by the second or third dose, the pharmacological steady state is not realized for 16 to 20 days.

**Method of Induction Onto LAAM Treatment**

Patients selected for LAAM therapy can be inducted onto the medication either by direct induction onto LAAM or by a standard methadone induction followed by a change to LAAM once the patient is stabilized on a methadone dose. The program's clinical staff, in consultation with the patient and family (with patient consent), can choose between these two options. With either method of induction, LAAM offers clinicians a choice in how to carry out induction—a choice that can affect outcomes. No choice should be irreversible, however, and clinicians should be open to trying another induction method if the initial decision does not appear to be effective. Although the current literature on LAAM therapy provides no clear indications to direct clinicians and practitioners in this decision, the guidelines that follow may be helpful.

**Initial Methadone Stabilization Versus Direct Induction**

Induction onto a stabilizing regimen of methadone before LAAM treatment is begun affords clinicians the ability to observe the patient on a daily basis. Such an approach can be helpful if the patient is dependent on other drugs, including alcohol. Patients who are initially inducted onto methadone may expect a more rapid onset of effect, which may be an advantage in some cases. Another potential advantage of methadone induction may be the clinician's familiarity with methadone's action and side effects.

Direct induction onto LAAM also may be preferable for certain patients because of logistical considerations. For example, patients with transportation problems or with work-related or other scheduling problems may find LAAM therapy attractive because it reduces the frequency of clinic visits.

Patients who have not had a positive experience with methadone in the past also may prefer direct induction onto LAAM. Although most methadone-maintained patients experience a very stable 24-hour dose response, some patients' response to methadone may fluctuate during a 24-hour period, perhaps because of fluctuations in blood levels of methadone caused by individual differences in metabolism. These patients may benefit from the longer action and more stable dose response to LAAM over the 48- or 72-hour period between doses.
contact, whether for medical or psychiatric reasons, as well as those who may need medication readjustment, might be cautioned against entering directly into LAAM therapy from street opiate use. These patients can be seen at the clinic on nondose days. Active alcoholics, as well as persons who abuse other sedative-hypnotics, also merit special attention.

Nonetheless, if the patient strongly desires to begin treatment with LAAM and treatment staff believe that it is in the patient's interest to do so, a treatment plan may be developed that permits this option. Arrangements could be made, for example, for daily clinic visits. The drug administration schedule need not govern the frequency of patient contact.

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**Patients Who Need Daily Contact with Staff**

If a patient needs daily contact with staff early in treatment for medical or psychiatric reasons, arrangements can be made for patients to visit the clinic daily if necessary. The drug administration schedule need not govern the frequency of patient contact.

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**Switching From Methadone to LAAM**

Once LAAM becomes available in an opioid substitution therapy program, all patients should be educated about the new medication and provided as much information as possible. Some guidelines for switching patients from methadone to LAAM are offered; however, clinical judgment should prevail in individual cases.

**Patients who are stable.** A patient who is eligible for LAAM therapy and is stable on methadone maintenance might be considered for a change to LAAM. Such individuals often do well on LAAM. Acceptance of the medication is generally greater in patients with better psychosocial functioning. Some of these patients describe a "smoother" effect with LAAM as well as a decreased narcotic effect.

**Patients who are not progressing well.** Patients who are not doing well on methadone may also be considered for LAAM therapy. This may be the case, for example, for certain patients who assimilate methadone quickly and who consequently use heroin as a supplement. Although the use of LAAM may be an appropriate option in these situations, other options, such as increasing the methadone dose, should also be considered.

**Noncompliant patients.** Some patients receive methadone maintenance for years with little progress. They do not comply with their treatment plan and chronically cause problems and disruptions in program routine. Take-home doses of methadone are not an option for these patients. A change to LAAM may be an option. It is possible that a new medication will offer therapeutic benefits to the patient and reduce disruptions in program routine caused by the daily
visits of a problematic patient. As discussed above, patients in this group who are tried on LAAM therapy should be carefully selected and monitored.

When patients are noncompliant and disruptive to clinic routines, staff should begin by counseling the patient about the effects of his or her conduct on clinic morale and operations. Efforts should be made to identify the reasons for the patient's conduct and to resolve them. Should this fail, staff may discuss treatment options, including referral to other treatment modalities in addition to LAAM.

**Initial Dose**

The process of induction onto LAAM therapy is essentially the administration of a safe initial dose, which is given to relieve the signs and symptoms of withdrawal and abstinence. Additional doses are adjusted up or down in an effort to approximate the established tolerance threshold of each patient to prevent further symptoms and to reduce or eliminate the desire or craving to continue use of illicit drugs.

During induction onto LAAM, patients may need reassurance that more time, rather than more medication, is needed if full relief is not felt within 48 hours. After all three LAAM compounds have become active and steady state has been achieved, their combined activity produces what many patients describe as feeling more "normal."

A later phase of induction involves slower, more gradual dose adjustments to establish an adequate maintenance dose that ensures the desired effects for the individual patient. The initial dose is determined by the patient's degree of tolerance.

An induction chart is provided in Exhibit 3-2. The chart is for reference only. No such chart can replace direct communication between patient and clinician. Clinicians must speak directly to a patient and to others involved in the patient's care to determine the patient's individual reactions to the medication and to adjust the dosage accordingly.

For opiate-addicted persons who are not in treatment, the initial dose of LAAM is 20 to 40 mg. Patients who are stabilized on methadone are crossed over to LAAM at a starting dose equal to 1.2 to 1.3 times their daily methadone dose, not to exceed 120 mg. Subsequent doses may be adjusted by 5 to 10 mg until the patient is stable. Doses should not exceed 140 mg. If a dose of more than 140 mg is prescribed, it must be justified in the medical record, 21 C. F.R. Part 291 Section 291.505(k)(1)(D) (1993).

Especially during induction onto LAAM, patients may need explanation and reassurance that more time, rather than more medication, is needed if full relief is not felt within 48 hours. After all three LAAM compounds have become active and steady state has been achieved, their combined activity produces what many patients describe as feeling more "normal."
Induction Schedule

In contrast to methadone, which acts quickly in the body, patients may not feel the full benefit of the initial LAAM dose for 6 to 8 hours, until the body metabolizes LAAM into nor-LAAM and dinor-LAAM. Because of this slow onset of effect, patients on LAAM may experience symptoms of withdrawal between scheduled LAAM doses during the induction phase.

Although Federal regulations prohibit LAAM from being given more frequently than every other day, methadone is an appropriate and effective supplement because of its relatively rapid onset of activity (2 to 4 hours). During the induction period, patients can be given small doses of methadone (10 to 20 mg) on days they do not receive LAAM to provide more rapid relief of any discomfort and reduce the risk that they will use illicit drugs. Persistence of withdrawal symptoms indicates that the LAAM dose is inadequate, and the induction schedule should be adjusted accordingly.

Throughout LAAM therapy, particularly during the first 2 weeks of induction, patients need a great deal of reassurance, support, and information. To a large extent, the successful implementation of treatment with LAAM depends on having well-trained staff who are available to support and educate patients. Clinical trials with LAAM showed that when program staff did not accept LAAM therapy as a potential alternative to methadone treatment or were not properly informed about counseling and casework issues, patients also tended not to accept LAAM.

Maintenance on LAAM

The goal of maintenance treatment is to develop and implement a rehabilitation program that recognizes the chronic, relapsing nature of opiate addiction and allows adequate time to ensure successful long-term remission of the addictive disorder. The treatment plan should be based on the clinical needs of the patient. Arbitrary time limits to a treatment episode are counterproductive and contrary to established principles of high-quality care. Treatment decisions should be based on ongoing dialogue between the patient, counselor, and members of the treatment team.

As is the case for methadone and other medications, the use of LAAM requires ongoing assessment and review of the treatment plan. At a minimum, FDA regulations require that treatment plans be reviewed every 90 days for the first year and every 180 days thereafter. Patient contact with treatment staff should occur as frequently as treatment plans require, and contact should be no less frequent than monthly.

Maintenance Dose Determination and Dose Adjustments

Decisions about LAAM dosages should be made on a patient-by-patient basis. Extensive research shows that inadequate dosages of methadone play a significant role in the continued abuse of illicit drugs. In clinical trials, this was also true of LAAM; therefore, each patient's LAAM dosage should be sufficient to suppress drug withdrawal symptoms, illicit drug-seeking behavior and use, and associated high-risk behavior.
Scheduling

A key issue in treatment planning is dose scheduling. LAAM doses can be given either every other day or three times a week (two 48-hour doses and a 72-hour dose). However, every-other-day LAAM dosing is an option only if the clinic is open on Sunday—that is, 7 days a week. Monday-Wednesday-Friday schedules are often convenient for clinic operation and provide the patient with a weekend with no required clinic visit. In practice, the administration schedule for LAAM may be set to fit the clinic's convenience. As far as possible, however, it should also be tailored to the individual patient's comfort, convenience, and other needs.

Clinical experience with LAAM to date indicates that patients enjoy having weekends without a trip to the clinic and that nearly all patients do extremely well on a 48-hour interval. However, the 72-hour interval, from Friday to Monday, is a problem for some patients who may experience some discomfort, usually late on Sunday, or whose anxiety about the 72-hour interval becomes a clinical issue. A primary task of the counselor is to educate and reassure the patient about LAAM's long-acting nature.

While a few patients take the same LAAM dose on Monday, Wednesday, and Friday, most will benefit from an increase in LAAM on Friday (10 to 40 percent more than the Monday and Wednesday doses) or an increase in LAAM on Friday and a small dose of methadone to be taken home and used on Sunday. For very stable and reliable patients, the best option may be a regular LAAM dose on Friday and a full methadone dose (80 percent of the LAAM dose) as a take-home dose for Sunday.

Exhibit 3-3 shows a chart used by one clinic to calculate the correct dose of LAAM and of methadone for patients on a Monday-Wednesday-Friday LAAM dosing schedule. For example, a patient on 100 mg of LAAM who is allowed take-home doses of methadone would be given a 100-mg dose of LAAM on Monday and Wednesday; on Friday the patient's LAAM dose would increase by 20 percent and he or she would take home a methadone dose of 30 mg for Sunday. As shown in the chart, for patients for whom take-home methadone is not appropriate, the approach is to increase the Friday dose of LAAM by 30 percent to cover the 72-hour period during which the patient receives neither LAAM nor methadone. (According to Federal regulations and most State regulations, all patients are eligible for one take-home dose of methadone. However, the program may decide not to allow a patient to take home any doses.)

Not enough data are available to determine whether the optimal clinical benefit of LAAM is achieved with an every-other-day or a three-times-weekly schedule. More studies are needed to
elucidate this point. For opioid substitution therapy programs, the currently approved LAAM dosing schedules raise both clinical and practical issues that should be explored.

Treatment Interruptions

Treatment programs should have plans in place to handle expected or unexpected interruptions in therapy, whether these breaks are short or long. Many circumstances, such as work-related travel, illness, funerals, planned vacations, and emergencies may arise that require patients to miss clinic visits. If it is impossible to maintain an every-other-day or three-times-weekly schedule of LAAM, methadone should be substituted to allow patients to continue treatment without interruption for absences of more than 3 days from LAAM. Because current FDA regulations do not allow take-home doses of LAAM, treatment programs should have methadone available.

Unplanned Interruptions

Disability or illness. When patients are unable to come to the clinic on their own or to be brought there with assistance because of disability or illness, authorized clinic staff can use curbside delivery and observed-dose procedures to ensure continuity of treatment. Because LAAM and methadone are tools in a comprehensive treatment program, clinics should evaluate the need for continuity of support services as well as medication in these circumstances.

Missed Doses

When doses are missed, it is critical for the clinician to evaluate the patient to determine the patient's present condition. Has the patient been using illicit drugs or taking other medications? Clear guidelines are available about the clinical management of patients who have missed scheduled LAAM doses:

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LAAM dosing options for the 72-hour (Friday to Monday) interval include one of the following:

- An increase in LAAM on Friday: 10 to 40 percent more than the Monday and Wednesday doses
- An increase in LAAM on Friday and a small dose of methadone to be taken home and used on Sunday
- A regular LAAM dose on Friday and a full methadone dose (80 percent of the LAAM dose) as a take-home dose for Sunday (only for very stable and reliable patients).

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One dose missed. For patients who miss one scheduled dose and come to the clinic the next day (that is, 3 to 4 days after the last LAAM dose), the preceding day's dose should be given and the rest of the week's schedule should be changed accordingly with a return to the regular schedule the following week. For example, for a patient on a Monday-Wednesday-Friday schedule who
misses the Monday dose and comes in on Tuesday, the schedule is changed to Tuesday-
Thursday-Saturday for that week only and returns to the regular schedule the following week.

For patients who miss a dose and come to the clinic 2 days later, when their next scheduled dose
is due (that is, 4 to 5 days after their last LAAM dose), the scheduled dose is usually well
tolerated. Some clinicians may prefer to reduce the dose slightly (for example, by 5 to 10 mg)
and return the patient to a stable dose at the next clinic visit. Good clinical judgment and
knowledge of the patient are important factors in this situation.

More than one dose missed. For patients who miss more than one dose, reinduction should
begin with an initial dose of one-half to three-quarters of the previous dose. Tolerance to LAAM
begins to drop to some extent, so that a full dose given after more than one missed dose could
result in some degree of impairment or intoxication. LAAM can then be increased by 5 to 10 mg
every scheduled day, whether the schedule of administration is every other day or three times a
week, until the patient reaches the previous maintenance dose.

More than 1 week off LAAM. For patients who miss more than a week of scheduled LAAM
doses, the induction process should be repeated.

Planned Interruptions

When take-home methadone is used as a supplement to LAAM therapy when interruptions in
treatment are anticipated, the number of doses must be calculated carefully so that it is adequate
for following the schedule. The first methadone dose should be taken 48 hours after the last
observed dose of LAAM, and the last methadone dose should be taken 24 hours before the next
scheduled dose of LAAM at the clinic.

Holidays and vacations. For patients taking LAAM every other day, the schedule can be
adjusted so that a Monday holiday falls on an "off" day. If the schedule cannot be modified,
methadone can be provided at 80 percent of the 48-hour dose, with instructions to take it 48
hours after the last LAAM dose.

For vacation and travel plans, methadone can be substituted for LAAM in the same manner as
for a Monday holiday. If 80 percent of the patient's LAAM dose is more than 100 mg of
methadone, however, clearance from the State authority and FDA may be necessary because of
To be compliant, each program must be aware of State-specific regulations in addition to Federal
regulations.

Hospitalization. Opioid substitution therapy programs are responsible for ensuring continuity of
treatment for patients who are hospitalized. Programs often find provision of this continuity to be
a problem, because some hospitals are unfamiliar with or have philosophical or ideological
objections to substitution therapy. Although methadone is available in some hospitals for
analgesia and to continue maintenance for patients, some specialty hospitals do not even stock
methadone. Hospitals initially will not carry LAAM, and methadone will have to be substituted.
They may need to consult program staff on the appropriate conversion dose of methadone to
substitute for LAAM. Programs should explore ways to educate hospitals and treating physicians in their communities about the needs of LAAM-maintained patients.

Federal regulations state that "Hospitalized patients under care for a medical or surgical condition are permitted to receive LAAM in oral form when the attending physician judges it to be advisable." In such cases, authorized clinic personnel can deliver and administer LAAM to their patients. If the attending physician does not permit the use of LAAM, the patient can be transferred to methadone, which most hospital pharmacies can provide. If doubt about the legality of providing LAAM or methadone remains after hospital staff have seen the pertinent Federal regulations, the State authority can be contacted for verification.

The best practice is for clinic staff to stay in touch with and be involved in the education of the patient's hospital clinician. For example, hospital house staff may not be aware that certain drugs, such as a mixed agonist and antagonist for pain management, should not be prescribed for patients receiving LAAM or methadone. (See Chapter 1 for more information about pain management in LAAM-maintained patients.) Communication between program and hospital staff raises confidentiality issues, and information about confidentiality should be included in treatment programs' educational presentations to the health care community. The patient's consent is necessary for this kind of program-hospital communication, but a medical emergency supersedes confidentiality regulations. If it is conducted professionally and with linkage and cooperation as goals, this kind of coordination of care can enhance the status of treatment program personnel with hospital staff.

When patients on LAAM are hospitalized, authorized clinic personnel can deliver and administer LAAM. If the attending physician does not permit the use of LAAM, the patient can be transferred to methadone, which most hospital formularies can provide.

Hospitalization, particularly of unconscious patients, raises the issue of the use of identification (ID) cards. ID cards, in turn, raise privacy issues. One large urban opioid substitution therapy program provides patients with a photographic ID card to gain admittance to the clinic. The program's experience is that some patients use their clinic card as a generic photographic ID in lieu of a driver's license; for example, they use it to cash checks, despite the fact that the card identifies them as being in treatment. "Smart cards" containing a complete medical history are already in use in the United States, Israel, and Holland and may be useful in opioid substitution therapy programs. These cards would contain electronically encoded information needed by the program to identify and monitor the patient; they would not outwardly identify the card holder as a patient.

**Overdose**

LAAM's long-acting characteristics have critical implications for the treatment of overdose or oversedation, which is more likely to occur in new patients than in dose-stable patients. Almost
all overdoses in LAAM patients involve a combination of sedative drugs. In such cases, the ABCD approach is appropriate for first aid:

- **A** - Airway: make sure it is clear.
- **B** - Breathing: ensure adequate breathing and ventilation.
- **C** - Cardiac: check cardiac status and ensure circulation.
- **D** - Drugs: Use naloxone if needed (an opioid antagonist) to counter the effects of LAAM.

In the standard treatment of overdose, naloxone may be administered. If naloxone is used, however, it is important to recognize that LAAM is long acting (effective for up to 48 hours) and naloxone is short acting (effective for .5 to 1 hour). This difference in duration of action means that the patient may respond to naloxone initially and then lapse into coma again when the effects of naloxone wear off but the effects of LAAM remain. For this reason, patients who have overdosed should be kept under observation for a minimum of 48 hours and given repeat naloxone by injection or continuous drip as needed. If a patient who has overdosed is hospitalized, house physicians may need to be educated about the different duration of activity of LAAM and naloxone. Programs should ensure that emergency services in their areas have the latest outlines for treating clients who are on LAAM for medical emergencies and who have had overdoses related to opiates, cocaine or crack, alcohol, or prescription medications.

**Withdrawal and Termination From LAAM Therapy**

Few studies have addressed the medically supervised withdrawal of LAAM patients to a drug-free state. No evidence exists, however, to suggest that withdrawal from LAAM is different from withdrawal from methadone or any other opioid. Because patient motivation is essential to success, it is very important that patients initiate the process. Any patient who asks to be withdrawn from LAAM has the right to a medically supervised withdrawal program. The decision to withdraw from LAAM treatment is a highly complex process that should take into account several factors, including level of stability, past levels of functioning without medication, and fear of detoxification (Moolchan and Hoffman, 1994).

Withdrawal and termination from LAAM therapy are highly patient-specific processes. For the LAAM-maintained patient who is psychosocially rehabilitated and wishes to achieve drug-free status, the LAAM dose can be reduced gradually at a rate determined by the patient's response. The LAAM dose levels presented in Exhibit 3-3 (earlier in this chapter) show an example of such a gradual reduction.

Clinic staff should be aware that patients often have a great fear of protracted periods of withdrawal. Because LAAM is longer acting than methadone, withdrawal is expected to have a delayed onset and protracted course, although the withdrawal may be less intense than with other opioids. Patients, however, tend to perceive a longer period as being worse, whether the actual intensity of symptoms is greater or not. Special counseling may be needed to address this aspect of withdrawal from LAAM.
For patients who wish to achieve drug-free status

- The LAAM dose can be reduced gradually at a rate determined by the patient's response.
- Patients who prefer a less protracted withdrawal phase can be converted to methadone treatment and then tapered off methadone.

As an alternative, patients who want to withdraw from LAAM treatment can be switched to methadone and then have their medication tapered. They can be transferred to methadone at 80 percent of their LAAM dose with minimal difficulty. The key issue in this decision may be the support system the patient needs; take-home methadone entails fewer clinic visits. Although patients can visit the clinic on nondose days for support services only, they are less likely to do so without the incentive of receiving a medication dose.

When involuntary withdrawal from medication is unavoidable, patients should be transferred to methadone before withdrawal is begun so that they can be observed on a daily basis and because clinical experience with methadone withdrawal is more extensive. Also, because of the shorter half-life of methadone, it may be possible to withdraw a patient more rapidly from methadone, a course which is usually desirable in involuntary situations.

When a patient knows that he or she must serve time in jail or prison, such a planned withdrawal is best. Only one jail facility in the country - Rikers Island, the central jail facility in New York City - is known to provide methadone maintenance. Most jails do not even provide methadone for detoxification. When a patient is arrested, program staff should make every effort to communicate with criminal justice authorities and to recommend that the patient be withdrawn over a period of time. Whether the patient is maintained on LAAM or methadone, some form of maintenance or detoxification is preferable to sudden withdrawal of the medication.

The decision to terminate treatment with LAAM involves the same considerations as the decision to terminate treatment with methadone. Patients should be encouraged to stay in treatment as long as necessary to allow them to make the therapeutic changes that will support a drug-free lifestyle. Patients should not be pressured to discontinue treatment to meet arbitrary deadlines. There is no evidence that any specific duration of therapy is an adequate treatment "dose." The decision to attempt to withdraw from LAAM treatment should be made jointly by the patient and the treatment team.
LAAM in the Treatment of Opiate Addiction

Treatment Improvement Protocol (TIP) Series

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Chapter 4 - Treatment Planning

In planning treatment for patients receiving levo-alpha-acetyl-methadol (LAAM) therapy, clinicians must address several unique considerations. First, the initial 30 days of treatment are of critical importance. Some patients find that adjusting to LAAM is more difficult than adjusting to methadone, because of its delayed onset of action and prolonged effect. Although persons who are being transferred from methadone to LAAM therapy generally do not have as many difficulties as those entering LAAM treatment directly, problems can occur in both groups. To support patients during this transition, treatment staff need special training in the pharmacodynamics of the drug. Flexibility and involvement of all staff members are also important. If all staff express support for the treatment regimen, patients will experience less anxiety and make better progress.

This chapter presents valuable guidelines for engaging and retaining patients in LAAM treatment. The importance of patient education is reviewed, and suggestions for issues to address in education sessions are provided. A discussion is included of typical issues that may arise in counseling sessions, such as adapting to dosing schedules and structuring increased time away from the clinic. Reinforcing treatment progress may be a challenge for counselors who are used to working with patients maintained on methadone; with methadone, patients often receive take-home medications in recognition of their progress in treatment. However, no take-home LAAM is permitted. This chapter presents some suggestions for reinforcing treatment progress. Other clinical issues, such as relapse, urinalysis, and discharge planning are also briefly addressed.

For more detailed discussions of clinical issues related to treatment planning, the reader is referred to two other Treatment Improvement Protocols (TIPs) in this series, State Methadone Treatment Guidelines and Matching Treatment to Patient Needs in Opioid Substitution Therapy. The Center for Substance Abuse Treatment (CSAT) has also prepared a valuable handbook Treatment of Opiate Addiction With Methadone: A Counselor Manual, which is part of its Technical Assistance Publication (TAP) series. The manual includes patient questionnaires that help focus counselor-patient discussions of important treatment issues, such as recognizing stress, staying busy, developing healthy eating and exercise habits, and preventing relapse. These questionnaires can be used with both methadone- and LAAM-maintained patients.
**Patient Education**

Patient education is essential to successful outcomes for patients in LAAM therapy. A comprehensive education plan that takes into account the patient's educational background, ethnicity, and culture is an integral part of the treatment plan. Patient education should be initiated early in the treatment process and should be ongoing. Information should be presented, clarified, and reinforced at every opportunity.

Patient education is essential to a successful outcome for patients in LAAM therapy. A comprehensive education plan that takes into account the patient's educational background, ethnicity, and culture is an integral part of the treatment plan.

Although certain principles of patient education apply to all persons being treated for a chronic disease, individuals undergoing treatment for opiate addiction have additional requirements. Patients may be divided into two categories:

- Those who are new to the opiate addiction treatment system
- Individuals who have a treatment history but who are new to LAAM therapy.

While all patients need basic information about opioid substitution therapy, the focus of education differs for each group.

It should be noted here that clinical trials with LAAM have clearly shown that when program staff do not accept LAAM therapy as a potential alternative to methadone treatment or are not properly informed about counseling and casework issues, patients also tend not to accept LAAM treatment. Therefore, even the best efforts to educate patients can be undermined by staff with negative attitudes about LAAM. As discussed in Chapter 5, every effort should be made to provide staff members with appropriate training about LAAM therapy and to ensure that their questions or fears about its use are addressed.

Although this chapter focuses primarily on patient education about LAAM therapy, the need for patient education in numerous areas, such as human immunodeficiency virus (HIV) risk reduction, alcohol and other drug (AOD) abuse, nutrition, health care, parenting, and so forth should not be overlooked. The TIP *Matching Treatment to Patient Needs in Opioid Substitution Therapy* provides several recommendations for patient education. In addition, patients' families and significant others also benefit greatly from education about LAAM therapy.

**Patients Newly Admitted to Opioid Substitution Therapy**

Patients who have not previously participated in an opioid substitution therapy program need to understand the treatment options that are available and how they differ from one another. Staff should describe treatment alternatives and explain the differences between LAAM and
methadone. The nature and goals of opioid substitution therapy should be presented. An effort should also be made to allay patients' concerns about the social stigma associated with this type of therapy. Staff should also be prepared to counter the prevailing idea that the sole objective of treatment is to become drug free, an idea which tends to alienate those who need and want continuous maintenance treatment. Patients should be helped to view LAAM as medicine and not as a drug.

Issues specific to the individual program, especially those relating to clinic management, services, hours of operation, and administrative matters, should be thoroughly discussed. Policies governing involuntary withdrawal from treatment should also be explained. The program's policies should be posted in public areas throughout the facility. All information should be continually reinforced in individual sessions with the patient. New patients should be given a copy of the program's policies and rules. Ample opportunity should be allowed for patients' questions. When available, programs should provide patients with a patient handbook that includes all relevant program-specific information necessary for patient compliance. The handbook should be written so that all patients can understand the expectations and the rules. The handbook should be available in the patient's first language, where applicable.

**Patients Newly Admitted to LAAM Therapy**

Patients who have received or are currently receiving treatment for opiate addiction and who are being inducted onto LAAM therapy also need to be educated about the unique aspects of LAAM and how it differs from methadone. For these patients, the first issue to be addressed is the action of LAAM, particularly with regard to its delayed onset and duration of effect. It is of utmost importance to warn patients about the dangers of using other drugs while waiting for the onset of action of LAAM.

The change from daily dosing to every-other-day or Monday-Wednesday-Friday dosing has broad implications for patients. Many patients may be initially unaware of how the schedule change will affect them. Counselors should help patients explore in detail the lifestyle changes that will accompany the LAAM dosing schedule. Patients will have more unstructured time and less clinic contact; they may need support in finding ways to deal with this new situation. The involvement of the patient's family and significant others, although not essential, should be encouraged, if appropriate. In addition, the issue of LAAM dosing during vacations, emergencies, and other unanticipated interruptions in treatment should also be explored. (See Chapter 3 for approaches to handling planned and unplanned interruptions in treatment.)

It is of utmost importance to warn patients about the dangers of using other drugs while waiting for the onset of action of LAAM.

Because of the reduced dosing frequency of LAAM, many patients may view this therapy as a kind of quick-and-easy solution. Staff should emphasize that LAAM, like methadone, is a
maintenance medication, and that success in treatment requires that the patient make significant changes, often over an extended period of time.

As described in Chapter 3, the rationale for not using LAAM for women who are pregnant or nursing and the need for monthly pregnancy tests for women of childbearing potential should be explained to both male and female patients. These issues should be explored in detail with female patients.

Patients should be reassured about the efficacy of LAAM. Although newly approved, LAAM is not a new drug and is no longer experimental. Staff should explain that LAAM has been successfully used with nearly 6,000 persons enrolled in programs across the country over the last several decades and that, when used as approved, it is safe and effective.

Patients being treated for opiate addiction may not remember information presented during the early stages of treatment, before their condition has stabilized. Constant and consistent reinforcement by all members of the staff is critical, and opportunities should be sought to review treatment goals and other issues that affect a patient's progress. For example, when female patients of childbearing potential elect to try LAAM therapy, the monthly pregnancy test provides an opportunity not only to assess a woman's progress in treatment but also to explore issues related to sexuality, family planning, and reproductive health.

Patient education can be delivered in an individual meeting or a group session. Programs may find it helpful to schedule group orientation and education sessions, as well as discussion groups, for patients who are beginning LAAM therapy; the groups will help them establish appropriate expectations and allow patients to share experiences and problem-solving strategies.

Written materials can reinforce and supplement oral messages. All clinics should provide simple, patient-appropriate educational materials. They may develop their own materials or use those developed by others. All materials should be reviewed for appropriateness for the specific population being served. Non-English versions should be available if appropriate for the clinic population.

**Counseling and Case Management**

The emotional and psychological needs of patients during the initial phases of treatment for opiate addiction are often considerable and intense. Treatment programs that offer medications such as LAAM should be focused on the patient, with a positive, trusting, hopeful philosophy. Counselors should not be policing or punishing, but rather motivating in their approach. Most patients experience marked differences in their physical and emotional feelings while on LAAM therapy. There may be a danger that patients will begin to feel "too well too fast." Education is important for both staff and patients, and its goals should include fostering an understanding of the chronicity of the disease of addiction. Feelings of physical well-being, although desirable, do not always equate with cure.
There may be a danger that patients may begin to feel "too well too fast." One goal of education is to foster an understanding that physical feelings of well-being, although desirable, do not always equate with cure.

**Duration and Frequency of Counseling Sessions**

During the first few weeks of treatment, efforts to relieve the patient's anxiety concerning the effects of LAAM and to reassure the patient about the efficacy of treatment are of paramount importance. Group counseling can play an important role in this area. Individual counseling sessions during this period may have to be longer or more frequent than those that follow. The frequency and duration of visits, both during the first weeks of care and throughout the treatment course, should be dictated by patients' individual needs. Because use of LAAM eliminates the need for discussing arrangements for take-home doses, this time may be used to address other substantive concerns of the patient.

Patients who have recently entered LAAM treatment often have questions about dosages and dosing intervals. When a patient maintains that his or her dosage is inadequate, the reason may not be purely medical. All staff members should be aware of the many factors that can cause a patient to feel that his or her dosage is inadequate. The patient's dosage should be reevaluated, and the treatment team should discuss the issue. However, Federal regulations stipulate that only a physician may prescribe or adjust a patient's dosage. Each team member should be aware of his or her specific role in medication ordering, administration, and monitoring. Regardless of occasional differences of opinion over what is best for a patient, the team should speak to the patient in a consistent voice that mirrors the program philosophy and mission statement.

**Issues in Counseling Patients Receiving LAAM Therapy**

Staff who counsel patients maintained on LAAM should be prepared to deal with some issues that differ from those faced by methadone counselors. A few of the most prominent issues are discussed here.

**Dosage Level**

Dosing issues are more complex with patients receiving LAAM than with those receiving methadone. As described in Chapter 3, the physician often must order two doses, a Monday-Wednesday dose and a Friday dose. Dosage determinations should be based on an assessment of medical need. Arbitrary guidelines such as "lower is better" are inadvisable. The patient's psychological concerns are valid considerations in dosage determination, particularly if dosing is done on Monday, Wednesday, and Friday, rather than every other day.

Some treatment programs are slow to accede to a patient's request for a higher dose. Reliable information about LAAM levels in the patient's blood is of significant benefit to clinicians who are concerned about increasing a patient's dosage.
Dose Scheduling

The 72-hour interval between Friday and Monday is a common source of anxiety and discomfort. For some patients, oral reassurance will help ease the psychological distress. Many patients will need an increased dose of LAAM on Friday. If the patient continues to experience discomfort during the 72-hour interval, methadone can be introduced for the interval.

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Patient preference for scheduling is not predictable. Some prefer an every-other-day schedule if the program is open 7 days a week. Many patients who are relatively stable prefer the three-times-weekly schedule, which eliminates weekend visits. Variations such as these underscore the need to respect patient preferences whenever incentives that are consistent with their style and the characteristics of their patients.

Compliance with LAAM treatment counts toward methadone take-home privileges. For some patients, this privilege will be an incentive for them to comply with LAAM treatment. Staff should be sure that patients have this information. A patient who has been maintained on LAAM for 2 years may be eligible for five take-home doses of methadone a week (that is, a twice-weekly visit schedule); upon completing 3 years, a weekly methadone visit schedule may be possible.

Incentives may be financial. Some programs, for example, reduce patient fees by a set amount for every educational session attended; others offer vouchers or food coupons (Silverman et al., 1993). Another incentive, albeit one that should be used with great discretion, may be increased program privileges, such as being excused from attending a group session. If a patient is employed, for example, an appropriate incentive might be to excuse him or her from participating in a vocational counseling group. If a patient has family problems, however, he or she should not be excused from family counseling, no matter how remarkable his or her progress in other areas of rehabilitation. The counselor should never overlook the obvious fact that a patient may be doing well only because of faithful attendance at counseling sessions and that removing that opportunity may be counterproductive.

Increased vacation time may also be used as an incentive. There are two ways to provide medication for vacation. The patient can be transferred to methadone temporarily, and take-home doses can be provided or a courtesy visit can be arranged to a clinic in the area that the patient will be visiting. The LAAM can be dispensed by a clinic there.
Empowerment

Involving patients in decisionmaking and giving them opportunities to make choices are empowerment techniques that will enable them to feel confident to take charge of other aspects of their lives. The beneficial effects of empowerment techniques may be particularly noticeable for LAAM-maintained women when counseling on pregnancy and related issues is provided. Empowerment may also strengthen the patient's ability to develop vocational goals or to take action to improve dysfunctional family relationships.

Family Issues

Patients' families and significant others should be educated about the same issues for LAAM as for methadone. For patients switching from methadone to LAAM, the change in dosing schedule may allow patients to spend more time with family and friends.

Relapse

Because addiction is a chronic, relapsing condition, many LAAM patients will relapse to heroin use (or the use of other drugs, including alcohol). When relapse occurs, staff members' first concern should be to determine what triggered the relapse. The first question that should be asked is whether the patient's LAAM dosage is adequately blocking the effects of heroin. Relapse to heroin use does not necessarily signify the need for a change to methadone. Patience, understanding of the patient's needs, and a thorough reexamination of the patient's clinical status and treatment plan are necessary before any change is made.

Treatment Incentives for Use With LAAM-Maintained Patients

- Providing positive feedback on patient progress ("You're doing a great job!")
- Ensuring that patients recognize the improvements in their physical and mental health
- Ensuring that patients know that compliance with LAAM treatment counts toward methadone take-home privileges
- Reducing patient fees by a set amount for every therapeutic session attended
- Providing vouchers or food coupons
- Increasing program privileges, such as reducing required contacts with staff
- Arranging vacation time.

Discharge Planning

The process of tapering the LAAM dosage to achieve drug-free status is not substantially different from the process used for methadone. As with methadone, patients who express the
desire to discontinue LAAM therapy should be fully evaluated for their social environment, clinical status, and personal reasons for wanting to discontinue maintenance treatment.

Withdrawal from LAAM is not the termination of treatment but the beginning of a new phase of treatment. Some patients may benefit from naltrexone after discontinuation of medication. Naltrexone can be used to prevent relapse in some patients. However, clinicians must be aware of lingering abstinence symptoms and be sure that the patient is free of all opioid substances.

Like medication, psychosocial support should be tapered rather than suddenly withdrawn. These two components of therapy may not always work in tandem. Some patients may need psychosocial support long after opioid substitution has been discontinued. Issues such as treatment phasing and ensuring that patients receive appropriate levels of psychosocial support and services during all phases of treatment are addressed in more detail in another TIP in this series, Matching Treatment to Patient Needs in Opioid Substitution Therapy.

As with methadone, patients who express the desire to discontinue LAAM therapy should be fully evaluated for their social environment, clinical status, and personal reasons for wanting to discontinue maintenance treatment.

Patient Monitoring: Routine Testing

Urinalysis

No reagent is commercially available for screening urine for the presence of LAAM. (LAAM can be detected in urine using thin-layer chromatography and gas chromatography/mass spectrometry). Therefore, patients should be observed taking their medication and should speak to the dispensing nurse after swallowing. Anecdotal evidence exists for possible cross-reactivity of LAAM with methadone reagents in one enzyme immunoassay, the Abbott ADX, which could lead to misinterpretation of results.

Some States may not approve LAAM until there is a screen for it. The pharmacokinetic profile of LAAM makes "double dipping"—receiving treatment from two programs—a potential danger, but the use of registries, sufficient informed consent, and adequate patient tracking should prevent this problem. If regulations eventually permit take-home doses of LAAM, urine tests will become important to ensure that patients are taking LAAM properly.

Urine screening of LAAM patients for drugs of abuse is recommended. A positive screen can prompt a discussion with the patient that may lead to an adjustment in the treatment plan or resolution of another issue that is jeopardizing compliance. (See State methadone guidelines for a thorough discussion of urinalysis.)
Pregnancy Testing

The required monthly pregnancy tests for women of childbearing potential present an additional issue in treatment planning for female patients receiving LAAM. As discussed in Chapter 3, such testing can add a positive dimension to treatment if it is offered within the context of concern for the woman's overall health and, should she desire pregnancy, for that of her fetus.

Review of the Treatment Plan

Treatment plans should be individualized to meet patient needs and rate of recovery. Patients should be familiar with the components of their treatment plan and agree to work toward the stated goals and objectives. Federal regulations require that treatment plans be reviewed every 90 days for the first year and every 180 days thereafter. These are regulatory minimums and may not reflect individual patient needs. Regular reviews and revisions should be made to ensure that all services are being provided, progress is evident, and needs are met.
LAAM in the Treatment of Opiate Addiction

Treatment Improvement Protocol (TIP) Series

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Chapter 5 - Management and Administrative Issues

Levo-alpha-acetyl-methadol (LAAM) is currently the only approved alternative to methadone for opioid agonist maintenance treatment of opiate addiction. The integration of LAAM therapy into the existing treatment system poses new challenges. Several issues will arise not only for care providers within a clinical context, but also for administrative and management staff. Use of LAAM affects the management and operation of treatment facilities. Its impact on the facility's functioning, staffing and administrative needs, costs, and quality monitoring are discussed in this chapter.

Every opioid substitution therapy program is part of a community, and program administrators and staff must make efforts to maintain good community relations. Readers are referred to another Treatment Improvement Protocol (TIP) in this series, State Methadone Treatment Guidelines, which has a separate chapter on developing a multifaceted, proactive plan to establish and maintain ongoing relationships with community leaders and systems.

Setting

Single State agencies should advise and regularly update eligible providers on the current State regulations pertaining to the use of LAAM. As more States approve LAAM, and as treatment providers use LAAM more widely, it will initially be administered within a "closed system," that is, by clinics currently approved and licensed to dispense methadone. As experience with LAAM grows, however, it may gain a broader role within the treatment system. Future settings for the delivery of LAAM treatment may include outpatient psychiatric clinics, primary care clinics, managed care providers, and mobile vans.

Whether or not additional providers seek to make LAAM therapy available in other settings, it must be clearly understood that these providers must also have methadone medication available for the many times that LAAM cannot be provided, such as for take-home doses for travel, the 3-day interval, and emergency situations when the patient cannot visit the clinic. Thus, while a program may specialize in LAAM, it would not be feasible for it to operate without dispensing methadone as an adjunct medication. Currently, Federal regulations require that programs dispensing LAAM also be approved for dispensing methadone.

Future settings for the delivery of LAAM treatment may include outpatient psychiatric clinics, primary care clinics, managed care providers, and mobile vans.
To the degree that expansion of the treatment settings in which LAAM is provided broadens accessibility to treatment, it should be encouraged. At the same time, it is essential that decisionmakers and staff be aware of considerations that attend the nature of the medication itself and of opiate addiction treatment in general. Expansion of program sites is of no value in itself. Poor physical plants that are not equipped or staffed properly may have a negative impact on patient outcome. Each program should offer as broad a range of services as possible; only in this way will staff be able to match patients and services effectively.

Because the dosing schedule for LAAM is different from that of methadone, programs may want to keep the two pharmacotherapies somewhat separate. Establishing "LAAM-only" clinics has been suggested. In settings where cost control is a priority, there may also be a move to separate the dispensing of medication from the provision of support services. As explained above, the establishment of LAAM-only clinics would be of dubious utility because Federal regulations do not permit take-home doses of LAAM. In addition, new patients may require ns, like other issues attending the introduction of LAAM therapy into treatment programs, must be made by program directors and staff according to the goals and priorities of the program and the needs of the surrounding community.

In deciding how and to whom to administer LAAM treatment, program staff should look for options and points of negotiation. For example, a program may decide to determine whether any patients currently receiving methadone desire to switch to LAAM. Some individuals might welcome such a change. The reduced demand on the clinic resulting from fewer visits by LAAM patients might allow for an overall expansion in treatment slots.

Programs should be creative in finding ways to improve the delivery of treatment services. The use of LAAM with different patient groups must be further researched. The use of LAAM with iatrogenically addicted patients (patients dependent on opiates as a result of medical treatment), the use of LAAM with dually diagnosed patients, and the use of residential facilities for patients maintained on LAAM remain unresolved issues. This type of treatment would require an agreement that ensures that the methadone clinic continues to dispense the medications. It is possible to provide "courtesy dosing" of LAAM by using mobile facilities to provide treatment in homeless shelters or criminal justice facilities.

**Hours of Operation**

Flexibility is essential in setting hours of operation of clinics dispensing LAAM. Hours of operation must accommodate patient needs. Programs that are open 6 days a week may wish to consider adopting a 7-day-per-week schedule when they add LAAM therapy to the treatment regimen. If this schedule is impossible, they might consider scheduling the 72-hour break in the patient's dosing schedule in the middle of the week, rather than over the weekend. In this way, the program would be open for phone calls or visits by LAAM patients who need extra support. However, as discussed in previous chapters, once patients are stabilized on LAAM, most prefer not having to visit the clinic on weekends.
Extending hours of daily operation, perhaps by putting staff on flex-time schedules, merits consideration, since it would allow employed patients or those with personal responsibilities to visit the clinic before or after work.

**Staffing Considerations**

Other new medications are being developed for the treatment of opiate addiction and may be approved in the coming years. The introduction of LAAM treatment marks an evolutionary step within opioid substitution therapy, which to date has relied on only one agonist medication. As the spectrum of opioid pharmacotherapies broadens, staff must become better able to assess patients and to determine which agent is most appropriate at a given point in the patient's course of treatment. Fulfilling these responsibilities will require preservice and inservice staff training. LAAM, like any other medication used in chemical dependency treatment, is more effective for most people if offered in conjunction with comprehensive supportive services, counseling, and case management services by well-trained staff.

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LAAM, like any other medication used in chemical dependency treatment, is more effective for most people if offered in conjunction with a variety of comprehensive supportive services, counseling, and case management services by well-trained staff.

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**Staff Attitudes and Training**

Health professionals from many disciplines will be involved in the safe and effective use of LAAM. Training programs are needed for physician assistants and nurse practitioners, who often have key roles in opioid substitution therapy programs. Staff attitudes and knowledge have a direct effect on the acceptance of LAAM treatment by patients. The decision to introduce LAAM treatment should not be made without proper staff education and training. Program managers or other decisionmakers should think through the implications of the decision to offer LAAM treatment to their patients, and staff members should be involved in this process whenever possible. Because LAAM has unique pharmacologic properties, clinics must develop new procedures and protocols before offering the medication to patients.

Anecdotal evidence from the National Institute on Drug Abuse (NIDA) and Food and Drug Administration (FDA) Labelling Assessment Study (LAS), described in Chapter 2, indicates that staff attitudes toward LAAM therapy may be the single most important factor in positive treatment outcomes *(Payte, 1992)*. Staff attitudes provide the context within which LAAM treatment is delivered. A positive context can mean the difference between treatment success and failure. Although the counselor may have the most contact with patients, every member of the staff must demonstrate support for patients receiving LAAM. Programs should also monitor whether the use of LAAM affects staff attitudes toward methadone patients who do not switch to LAAM.
Before they can effectively care for and counsel patients and families, staff must be thoroughly versed in the advantages and disadvantages of LAAM treatment. This process entails the exploration of a broad range of historical, attitudinal, and economic factors that surround the use of LAAM. Some staff may be resistant to change—even positive change. One challenge to program managers may be to overcome resistance to change. Frequent opportunities for staff discussion of the planned change should be provided. Given the absence of evidence that LAAM treatment produces universally better patient outcomes, some staff may question the need for offering it as a therapeutic option.

LAAM is an anomaly: it is a "new" drug that underwent initial testing two decades ago. Because of this history, LAAM is surrounded by misperceptions, some of which present obstacles to its acceptance as a treatment option. Staff of new programs receiving licensing for the first time should have a minimum number of required training hours in the pharmacology of LAAM. Staff of ongoing programs should be able to show that they have had a sufficient number of hours of training in the use of LAAM and provide evidence of their knowledge and understanding of its treatment potential.

Staff must be attuned to Federal regulations that differ from those for methadone. Monthly pregnancy tests are required for women of childbearing potential. The regulatory definition of this term has not been spelled out. For example, some clinics may interpret this term to include women who have undergone tubal ligation or who receive contraceptive implants or injections, since none of these methods is 100 percent effective. Staff may need special training to counsel patients on reproductive issues.

Other factors relate to the changing climate of health care and economics. LAAM therapy may be more expensive than methadone treatment, which is related to the cost of required monthly pregnancy testing and the cost of the medication itself. Because the dosing schedule reduces by half the number of weekly visits, many staff are concerned that managed care providers will enact policies that require them to transfer as many patients as possible to LAAM and then to greatly expand staff caseloads. These concerns, although real, are in many cases unfounded. Education of staff, reinforced by regular interdisciplinary staff meetings, can allay misperceptions and make staff more comfortable in recommending and using LAAM, as well as improve patient-treatment matching.

As LAAM therapy is used in additional treatment settings and as existing programs adopt new protocols to accommodate its pharmacology and the needs of patients receiving it, staff roles
may change. Counselors will learn to function in an expanded treatment environment. Some may wish to specialize; for example, programs may have counselors who deal only with patients receiving LAAM. However, to optimize staff flexibility, programs should consider assigning mixed caseloads (that is, both methadone and LAAM patients) to staff during the LAAM introduction period. Programs should consider current methadone caseloads, staff skills, and resources when assigning initial LAAM cases. Another way to integrate LAAM cases might initially be to choose the most skilled and effective counselors for LAAM cases. It should be kept in mind that therapy with LAAM does not necessarily mean a reduced number of patient visits, especially in the early weeks of treatment. Patients may receive medication 3 days a week, but their treatment plans might require them to come to the clinic daily to be monitored and to receive other services.

Training must prepare staff to use imagination in their vision of future settings for the delivery of LAAM therapy. The approval of LAAM may help managed care providers to make available opioid substitution therapy services. This trend may benefit patients, provided that attention is paid to quality assurance measures. For example, inclusion of substitution therapy in managed care settings might lead to a better geographic distribution of clinics; such services would no longer be centered in the inner city. Smaller clinics, run by groups of physicians, could treat small groups of patients.

A more equitable geographic distribution of treatment settings might provide treatment access to larger numbers of patients. It might make treatment more attractive to persons in rural areas as well as to an emerging cohort of heroin users, many of whom are middle-class persons living in the suburbs. As new treatment settings are considered, the single greatest risk may be the tendency to separate administration of LAAM from the health and psychosocial services needed to ensure its effective use. Staff must be prepared to ensure that access to health and human services is a part of any narcotic treatment program.

It should be kept in mind that therapy with LAAM does not necessarily mean a reduced number of patient visits, especially in the early weeks of treatment. Patients may receive medication 3 days a week, but their treatment plans might require them to come to the clinic daily to be monitored and to receive other services.

FDA approval of a program's request for a license to dispense LAAM is contingent on all clinic staff's receiving training during the first 2 years after the program's approval. The manufacturer of LAAM, Roxane Laboratories, Inc., can arrange such training for substance abuse counselors and other health professionals. These training resources are described in more detail in Appendix B.

Programs also may wish to adapt existing training documents, such as the Counselor's Manual for Methadone Treatment, published by the Center for Substance Abuse Treatment as part of its
Technical Assistance Publication (TAP) series. Some of this information may need to be tailored for use with LAAM patients.

As the use of LAAM grows, hospital staff and medical students will need information on LAAM. Such information is especially important for emergency room staff, who must be forewarned about the pharmacokinetic profile of LAAM and the possibility of overdose (see Chapter 2). Clinics that dispense LAAM should make sure that local hospitals know of their presence in the community.

Patient-to-Counselor Ratio

Minimum counselor staffing ratios governing methadone treatment programs are defined by the States and vary widely. In several States, maximum patient-to-counselor ratios of 50:1 are set by regulation. Introduction of LAAM treatment into some programs may simply change the dosing frequency of medication, rather than the structure or goals of the overall treatment program. In such cases, the patient-counselor ratio may not change. If, however, the use of LAAM changes the overall treatment program, the ratio may change.

As new treatment settings for providing LAAM are considered, the single greatest risk may be the tendency to separate the drug from the health and psychosocial services needed to ensure its effective use.

Programs should attempt to exceed the minimum requirements. Another TIP in this series, *Matching Treatment to Patient Needs in Opioid Substitution Therapy*, recommends a maximum counselor caseload of 35 patients. When counselors' caseloads are smaller and staff are better supervised, patients' progress in treatment generally improves.

The degree of patient need should be a factor in determining counselor-to-patient ratios; for example, a counselor providing care for a large number of patients in the early weeks of LAAM treatment should have a smaller caseload. When a substantial number of counseling services are provided offsite, programs should build this factor into the staffing formula. Needs-based ratios permit staff to spend more time with patients who need and want counseling, which helps make staff more productive.

Recordkeeping and Storage of LAAM

Patient records must clearly indicate which medication the patient is receiving. Product storage recommendations are set forth in the manufacturer's insert that accompanies the medication. No additional precautions are needed.
Medication Dispensing

To safeguard against errors in dosing, a program should develop protocols for dispensing. The solutions used to mix methadone and LAAM must be of different colors. Larger clinics may consider establishing separate dispensing windows for the two medications.

Attention must be given to appropriate dispensing procedures for liquid medications. Programs that have little or no experience in this area must develop careful systems for documenting and reconciling the amount of liquid in the bottle with the doses removed so that Drug Enforcement Administration (DEA) and State standards are met. Regulations set forth by State boards of pharmacy must be observed. Under no circumstances should LAAM be rebottled. Proper procedures must be followed for disposal of empty containers. Staff must take precautions to ensure that the patient swallows the medication at the time it is dispensed. The simplest way to do this is to have the patient speak to the dispensing nurse after swallowing the medication.

Costs

A recent cost-benefit study in California found that the average cost per year to treat a person in continuing outpatient methadone treatment was about $2,400, or about $50 per week (California Department of Alcohol and Drug Programs, 1994). New York State has established a range of reimbursement rates for methadone patients, ranging from $60 per week for some for-profit programs to $100 for not-for-profit programs (annual range, $3,120 to $5,200). Costs of around $3,500 have been widely cited as average for continuing methadone maintenance.

Costs of providing LAAM treatment will vary among States and will depend on the client mix, the range of services offered, payer issues, and a host of other factors. Cost comparisons between methadone and LAAM treatment must be made with care. Data from evaluation and cost studies of LAAM must be gathered from numerous sources and analyzed before the relative costs of these treatments can be understood. The difference in costs between methadone and LAAM can be offset by many variables.

The cost of LAAM will depend on specific program issues such as whether program capacity will increase, staff productivity will be aided, or community perceptions will improve. The financial impact of LAAM on the chemical dependency treatment system is unclear at this time.
the higher cost of the medication itself and the cost of pregnancy testing. A discussion of cost considerations from the perspective of health care reform is also included.

Cost of LAAM per Dose

The cost of a daily 65-mg dose of methadone ranges from 34 cents to 51 cents. Thus, the weekly cost for methadone medication ranges from $2.40 to $3.56. The cost of a week's supply of LAAM (three 78-mg doses) ranges from $7.92 per week ($2.64 per dose) to $9.89 ($3.30 per dose). These are costs only for the actual medication, which represent a small percentage of total program costs. Programs must take into account a host of other cost elements, such as cost for salaries, facilities, and support services.

Unit of Pricing

Some programs calculate costs based on a flat or aggregate rate, while others disaggregate costs for different types of services. Setting flat rates—that is, agreeing to provide services based on an average rate of cost per patient per week—sometimes poses undue burdens on programs that offer a wide range of services. Pricing by unit of service rendered may be more equitable.

Attempts to compare costs of LAAM and methadone treatment and estimate cost differences are under way. However, such studies must be carried out with care so that results are not misleading. In many cases, cost differences are ultimately a matter of tradeoffs. For example, decreased time in preparing take-home doses may free staff to complete additional paperwork during working hours. Because LAAM patients receive fewer doses of medication per week, less nursing or pharmacist time is needed for medication preparation. This reduction may make it possible to assign these employees to other important duties. Additionally, patient visits may decrease if LAAM is widely used, but clinics using LAAM may attract new clients who have had difficulty with methadone. Until further data are available, the net effect of LAAM treatment on program operating costs cannot be sufficiently addressed.

Pregnancy Testing

Pregnancy testing is a predictable cost associated with the use of LAAM in female patients of childbearing potential. The cost of pregnancy testing is estimated at $10 per month. Between one fourth and one third of all patients in opiate addiction treatment are women of childbearing potential.

In many cases, cost differences between LAAM and methadone are ultimately a matter of tradeoffs. For example, decreased time in preparing take-home doses may free staff to complete additional paperwork during working hours.
Health Care Funding Reform and Cost Considerations

Although cost is a key factor in patient-care decisions in all health care delivery systems, cost should not be the single driving factor. The principles of managed care, which is the model for many funding reform efforts, are in many ways the antithesis of those of narcotic dependency treatment. Managed care functions as a gatekeeper; for persons in opiate dependency treatment, treatment success depends on continuous services, including medication and case management.

In setting costs, programs should focus on patients' needs for services, not on the specific medication selected. Programs will have to be able to explain to reimbursers that a reduction in the number of visits for medication may not reduce overall costs. If a program has analyzed its costs, it can present the data necessary to make an effective case to reimbursers.

Programs will have to examine LAAM costs in the continuum, making sure they are delivering the most cost-effective treatment possible. Making treatment "cost-effective" does not necessarily mean increasing the number of patients per week, but rather allocating as efficiently as possible administrative costs related to delivery of services, such as administrative activities, salary, equipment, and medication.

With reform, several different reimbursement strategies will come into play. A common strategy is capitation, which provides a set fee for each patient, including patients who "do well" and those who are "chronic relapers," and which is based on the assumption that not every enrollee uses a high level of services. The ability to control costs and to correctly predict the program's patient mix will make capitation easier and will enable programs to compete in a managed care environment. Programs must find ways to determine their costs and their patient mix. Programs have many types of costs to consider, including salaries, facility and utility costs, supplies and equipment, insurance, laboratory services, and administrative costs (utilization review, standing committees such as pharmacy boards, etc.). Conducting such complex cost analyses may not be realistic for smaller programs. The implementation of managed care may spur smaller programs to merge with other programs in order to survive.

In fact, the most important result of health care reform for treatment programs may be the integration of different treatment modalities. Programs may form associations to standardize procedures and costs. Different treatment modalities may form alliances to offer a full range of care. Despite the fears, mistrust, and resentment that may accompany such change, the benefits of association will become readily apparent with the first successful bid for a contract from an integrated program.

Perspectives on cost change with the players and their concerns. The consumer, or patient, is concerned with coverage or cash outlay and whether the same services can be had for less elsewhere. The provider is concerned with the source of funding and how funds are distributed. Society is concerned with the consumption of huge amounts of public dollars, although the cost of treatment for substance abuse is minimal in comparison with the costs incurred by untreated patients in the criminal justice system, in HIV treatment, and in medical care and other health systems. In this regard, it is important to bear in mind that the costs of treatment should be compared with the costs of not having a service available.
LAAM Cost Offsets

Programs that are providing information to policymakers and funders should be especially aware of the cost offsets that result from alcohol and other drug (AOD) abuse treatment. Such cost offsets have been strongly documented by recently published results of the long-term study of AOD treatment in California, which found that for every dollar spent on substance abuse treatment, more than $7 in future costs were saved (California Department of Alcohol and Drug Programs, 1994). These savings were largely in relation to reductions in criminal activity and in the number of hospitalizations for health problems.

The study examined the costs to society (net productivity loss) and to the taxpayer (theft, expenditures for welfare and disability, and so forth). Specifically for ongoing methadone maintenance treatment, the study found that an untreated opiate-addicted person cost society $92 per day in the year before treatment and $62 per day during treatment. Respective taxpayer costs were $53 and $23. The daily cost of treating an individual in a methadone maintenance program in California at the time of the study was $6.37. Thus, from the view of society and the taxpaying citizen, treatment paid for itself on the day it was delivered.

In addition, a nationwide survey on the effectiveness of treatment conducted by the National Association of State Alcohol and Drug Abuse Directors (NASADAD) also clearly documented significant cost offsets related to decreases in hospitalization and crime and an increase in employment (Young, 1994).

In addition to these types of cost offsets, initial investments in incorporating LAAM into treatment programs will be paid off if the new medication prompts an educational process that helps upgrade and diversify staff capabilities or gives rise to different approaches to outcomes evaluations and funding mechanisms. Incorporating LAAM therapy as a treatment alternative can stimulate the pace of the process of quality improvement. The availability of LAAM treatment may expand the number or type of patients who will enter treatment.

It is not appropriate to set caps on reimbursement for opioid substitution therapy or any kind of chemical dependency treatment, any more than it is appropriate to cap reimbursement for treatment of other chronic diseases.

Reimbursement

Reimbursement issues may arise in systems that integrate methadone and LAAM treatment into a service delivery system so that the same provider delivers both drug-free treatment and opioid substitution therapy. Drug-free modalities tend to be reimbursed on a fee-for-service basis, whereas substitution therapy programs usually receive a comprehensive fee. Both kinds of reimbursement (fee-for-service and comprehensive fee) will be needed. Programs may need to establish a minimum number of clinic visits patients will need to qualify for comprehensive fee
reimbursement. In fact, a definition of what constitutes a "patient visit" may need to be developed.

There is a trend in some States toward disaggregating methadone treatment rates, so that there are separate rates for dispensing visits, urine test visits, and counseling visits, as opposed to a single comprehensive daily or weekly rate. In response, funding sources might disaggregate reimbursements, which might lower reimbursements. Different types of reimbursement mechanisms should be used. It is not appropriate, however, to set caps on reimbursement for opioid substitution therapy or any kind of chemical dependency treatment, any more than it is appropriate to cap reimbursement for treatment of other chronic diseases.

It is possible that a managed care organization might view LAAM treatment as more cost effective than methadone treatment, specifically when reimbursement is based on the number of visits to the clinic, and the organization might therefore decide to reimburse only for LAAM treatment. Although this is a possible scenario, it is more likely that programs may seek to dispense only LAAM, which is not a viable treatment approach.

As LAAM therapy is incorporated into an increasing number of treatment programs, funding for its use will become a major issue, as will accountability and accessibility. The availability of Federal block grant money could be affected by requirements to introduce LAAM therapy into State treatment systems. Many publicly funded programs receive funding from several sources rather than a single source. Programs have been forced to seek other sources because funding, especially at the State level, has significantly decreased in recent years and patients' needs, particularly their medical needs, have increased. Some scenarios of future funding predict a decrease in block grant funds, with those dollars going to pay for substance abuse benefits under a national health care reform program.

Regardless of specific reforms in health care funding that will be made in various States, programs must become increasingly creative in providing comprehensive services and developing mechanisms for reimbursement. Private, for-profit programs will not be able to rely solely on cash payment for comprehensive services, and all programs will have to be keenly aware of what the various components of treatment actually cost.

More data and further research are needed on the actual long-term costs of treatment for the chronically relapsing population. Patients in narcotic treatment programs tend to use care frequently and intensively, particularly in the first few years, because they have neglected their health and welfare.

**Quality of Care**

The standards of care governing the administration of LAAM are the same as those that apply to all programs providing treatment services for chemical dependency. State standards, although they may be helpful, are not of consistent quality. National standards, as published in the TIP *State Methadone Treatment Guidelines*, are recommended.
Regardless of specific reforms in health care funding that will be made in various States, all programs will have to be keenly aware of what the various components of treatment actually cost.

The choice between methadone and LAAM treatment should be driven by patient need rather than program benefit. When a program has alternative treatments to choose from, it should be better able to focus on patient needs when developing treatment plans. When treatment is patient driven, the quality of care is improved.

**Monitoring Program Quality**

Managed care has directed new attention to the importance of quality assurance and outcomes monitoring. All chemical dependency programs, regardless of size, should develop and use written quality assurance protocols.

NIDA has published a technology transfer package to help program administrators and staff who have no previous experience or formal training in evaluation. The package will help them to plan and conduct evaluations of their programs. The package is titled, *How Good Is Your Drug Abuse Treatment Program?*, and it includes an overview and case study manual, an evaluation guide, a resource manual, and looseleaf worksheets and agendas. It is available free of charge from the National Clearinghouse for Alcohol and Drug Information.

**Quality Assurance**

LAAM treatment offers an opportunity for program staff to review and reevaluate current quality assurance procedures and develop new systems to ensure the appropriate administration of medications and provision of other services. Factors that such systems should monitor include the number of dosage changes, the number of adverse reactions, and the number of pregnancy and tuberculin skin tests performed. Compliance with recordkeeping requirements should also be monitored.

Some programs ensure quality by hiring an internal auditor who performs the same functions as inspectors from FDA, the State, or the Joint Commission on Accreditation of Health care Organizations (JCAHO). Internal auditors generally review program information monthly. Other programs form internal quality assurance teams that assume responsibility for developing monitoring instruments, ensuring that these instruments are properly used, and reporting to the administration concerning problems identified and actions taken. Staff turnover and patient retention are important indicators that should be evaluated by an internal quality assurance team. When a subcontractor performs a service, the program should be certain that the subcontractor maintains adequate quality assurance procedures.

In some settings, quality assurance is integrated into an institutional total quality management (TQM) system. Under the TQM approach, interdisciplinary teams discuss a particular issue, identify problems, and make recommendations concerning their resolution. A program considering the introduction of LAAM might wish to form a team specifically for the purpose of
developing appropriate quality assurance systems to govern the administration of this new medication. The team might investigate such matters as provision of informed consent, pregnancy testing, urinalysis, and response to counseling.

A program considering the introduction of LAAM might wish to form a team specifically for the purpose of developing appropriate quality assurance systems to govern the administration of this new medication.

States have the opportunity to exercise leadership in the development of quality assurance measures. Program administrators and staff should be prepared to offer guidance to States wishing to develop such measures.

**Staff Quality Assurance Measures**

The quality of care provided by a treatment program depends to a great extent on the quality of counseling services provided by its staff. For veteran counselors, LAAM treatment offers new incentives and challenges. In opioid substitution therapy, counseling can have a major impact on patient retention and, ultimately, on treatment outcomes (Ball and Ross, 1991). For these reasons, it is important for programs to support their counseling teams and to evaluate the performance of individual counselors.

Counseling approaches vary broadly, both among programs and among counselors at a single program. More uniformity in counseling approaches is needed. Programs should consider developing counseling protocols and minimum requirements for counselors. Staff should be trained to implement counseling protocols.

The effectiveness of counseling may be increased by greater attention to counselor-patient matching. Frequent reinforcement and feedback are beneficial, as are ongoing training and opportunities to participate in case conferences and to offer input into management decisions. Programs should develop ways of evaluating counselor effectiveness.

**Outcomes Monitoring**

The introduction of LAAM treatment provides an opportunity to develop and refine procedures needed to measure patient outcomes. Careful studies can greatly increase support for opioid substitution therapy. Outcomes monitoring is a relatively new area for the field of chemical dependency treatment. Another TIP in this series, *Developing State Outcomes Monitoring Systems for Alcohol and Other Drug Abuse Treatment*, addresses the importance of monitoring treatment outcomes in the current health care environment and offers useful guidelines for evaluating treatment outcomes. Chapter 5 of the TIP *Matching Treatment to Patient Needs in Opioid Substitution Therapy* is a step-by-step guide to designing and conducting program-level monitoring of patient outcomes.
Patient outcomes may be monitored in a variety of ways:

- A standard assessment instrument can be used at periodic intervals to monitor progress in treatment. One example is the Addiction Severity Index (ASI) (McLellan et al., 1980), which measures patients' progress in seven diagnostic domains (drug abuse, alcohol abuse, medical needs, psychiatric needs, family and social support systems, legal needs, and vocational needs). A variety of other instruments are described in the NIDA publication Diagnostic Source Book on Drug Abuse Research and Treatment (Rounsaville et al., 1993). The effective use of any assessment instrument requires staff training, the cost of which is offset in the long run by improvements in the delivery of services and thus a stronger competitive presence in a managed care environment.
- Results of urine testing for drugs of abuse are useful measures of treatment progress.
- A program's rate of treatment retention is an important measure. Both staff and those who pay for treatment are aware that retention in treatment is a positive indicator. It is a clear sign of patient satisfaction. Retaining a patient in treatment increases the chance of a successful outcome.
- The number of patients leaving against medical advice should be monitored, since their leaving may indicate problems in the operation of the program.

Outcomes measures of LAAM treatment must be carefully defined and must be based on an acknowledgment that drug abuse is a chronic, relapsing disease. Some outcomes measures that may have initial appeal are not, in fact, valid indicators of progress or lack of progress in treatment. A transfer from LAAM to methadone, for example, is no more a negative outcome than is a transfer to an alternative antibiotic agent for a patient with a refractory infection. In each case, the change simply indicates the need to explore other options. Likewise, the number of patients who complete medically supervised withdrawal from LAAM or methadone is not an outcome measure in the same sense as a negative urine test for illicit drugs. The significance of completed detoxification depends on its importance in a given patient's overall treatment plan.

**Consideration of Public Policy Issues**

The focus of opioid substitution therapy programs should be the use of substitution medication in concert with other necessary program services to help patients reach treatment goals. Treatment must be delivered in the context of a complete service delivery system. Treatment programs should carefully assess patients to ensure that they can avoid relapse and have the opportunity to lead happy and productive lives. Programs should provide services onsite or by referral and provide case management to ensure that patients use health and human service resources in the community.

Medication has been used to treat opiate dependence, cocaine addiction, alcoholism, and other substance use disorders for some time. What makes the use of specific medications more palatable than others for some people is not always clear. However, the viability of using medications for substance use disorders is clear.

As a society we have not committed the resources to provide comprehensive substance abuse treatment for all who need it. Over the last 30 years, we have steadily reduced what we are willing to spend to treat opiate addiction. Epidemics of HIV, tuberculosis (TB), sexually
transmitted diseases (STDs), and other infectious diseases require that we halt behaviors that fuel those epidemics and stabilize patients who are in crisis. Medication-managed treatments are important means to this end. The leading edge of advances in drug "technology" has been in the streets (for example, more potent heroin), and medications are needed to counter the consequences of chronic use of these potent substances.

The introduction of LAAM treatment brings the opportunity to further promote the modality of opioid substitution therapy. Use of LAAM increases program options in terms of treating narcotic addiction and may help modify the stigma that is associated with maintenance treatment. LAAM treatment allows for reduced clinic attendance and so may broaden the population that can be given medication by extending treatment to those who need a treatment plan that includes fewer individual medication visits. Use of LAAM decreases demands on staff in a predictable fashion and may enable programs to move closer to providing treatment "on demand" (that is, no waiting lists). By reducing the use of intravenous drugs, it reduces the risk of exposure to HIV. Introduction of LAAM therapy may change attitudes toward methadone and broaden the number of third-party payers who are willing to reimburse for services delivered

Outcomes measures of LAAM treatment must be carefully defined. Some outcomes measures that may have initial appeal are not, in fact, valid indicators either of progress or lack of progress in treatment. A transfer from LAAM to methadone, for example, is no more a negative outcome than a transfer to an alternative antibiotic agent for a patient with a refractory infection. In each case, the change simply indicates the need to explore other options.

**Concerns Regarding Use of LAAM**

The consensus panel raised several concerns about the introduction of LAAM treatment:

- A dangerous risk exists that introduction of LAAM will reinforce a focus on medication, rather than on comprehensive treatment. LAAM therapy may incorrectly be seen as a treatment modality in and of itself, resulting in 3-day-per-week dispensing programs without adjunctive counseling and other usual services.
- Insurance companies might ultimately choose to reimburse only LAAM maintenance treatment. Appropriate education of third-party payers is essential.
- The use of LAAM might revive public unease about the concept of opioid substitution therapy.
- The use of LAAM might act as a catalyst for providers to use the "interim methadone maintenance regulations" when doing so may not be appropriate. The "interim" concept was developed because of the shortage of treatment slots and the widespread existence of waiting lists. Interim treatment focuses on the use of medication with provision of minimal services.
- Because of the dosing schedule for LAAM, some patients may binge on the days on which they do not need to visit the program. Appropriate assessment will identify such patients, and treatment plans can be adjusted accordingly.
• If a program cannot get funding for monthly pregnancy tests, it may choose not to offer LAAM therapy or not offer it to the program's female population, eliminating an option for women that may be available for men.
• For-profit programs may increase the number of patients, without providing additional staff, simply to increase profits.

The number of treatment slots funded by Federal block grants has effectively decreased in the last 6 years. LAAM therapy could be perceived as a "quick solution" for this problem. LAAM treatment should not be used as a rationale for not increasing treatment slots in response to realistic per capita treatment needs. Neither should it be used to maintain an absolute number of slots or to decrease the number of slots relative to the population in need.
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**Chapter 6 - Regulatory and Ethical Issues**

This chapter provides an overview of the Federal regulations governing the use of levo-alpha-acetyl-methadol (LAAM), which are a subset of the regulations for all opioid substitution therapy programs (see Exhibit 6-1). The chapter also presents suggestions for States that desire to develop their own LAAM regulations. How the use of LAAM might affect other systems, such as the public health system, is described. Ethical issues involved in introducing LAAM treatment are discussed.

The Center for Substance Abuse Treatment (CSAT) has developed two publications that provide information about the regulation of opioid substitution therapy. The first, *State Methadone Treatment Guidelines*, is another Treatment Improvement Protocol (TIP) in this series that provides guidelines for States and programs to provide high-quality care in compliance with the regulations. The second publication *Approval and Monitoring of Narcotic Treatment Programs: A Guide on the Roles of Federal and State Agencies* is part of CSAT's Technical Assistance Publications (TAP) series. To those seeking to establish an opioid substitution therapy program, the latter offers a step-by-step overview of what to expect from Federal and State agencies during the program approval and monitoring process. Sample application forms are provided. Both publications are available free of charge from the National Clearinghouse for Alcohol and Drug Information.

**Approval of Treatment Programs to Dispense LAAM**

**Approval Process**

Opioid substitution therapy programs seeking to become approved to administer LAAM must apply to the Food and Drug Administration (FDA) and to the State in which they intend to operate. Federal programs, such as those operated by the Department of Veterans Affairs, may use LAAM treatment even if the State in which they are located has not yet approved LAAM for use by treatment programs.
Opioid substitution therapy programs seeking to become approved to administer LAAM must apply to the Food and Drug Administration and to the State in which they intend to operate.

Typically, an application must also be made to the Drug Enforcement Administration (DEA) and notice given to the single State agencies (SSAs). At present, only programs that are approved to use methadone are eligible for approval to administer LAAM.

Some States require programs to obtain approval, some certification, and some licensure. Some States are still in the process of obtaining the necessary approvals or amending regulations to permit use of LAAM. (All States have their own controlled substances laws and must reschedule LAAM from a Schedule I to a Schedule II drug in order to allow clinics access to it [see below].) The SSAs can advise treatment providers about whether LAAM is currently available in their States and about the steps to follow to add LAAM therapy to their treatment regimens. Providers should contact their State methadone authority. It and the SSA are the best sources of information regarding local licensing and regulatory requirements. The SSA is responsible for ensuring that use of LAAM is approved, that all licensing and approval requirements are met, and that programs are in compliance with the laws of the State.

The addition of LAAM therapy to a clinic's treatment options will necessitate an expansion of the program's philosophy and mission statement. As a result, program manuals, consent forms, and treatment approaches may need revision. Forms related to release of information may also need revision. In addition, programs may need to rewrite protocols for the dispensing and storage of drugs to meet DEA requirements. Many of these revisions can simply follow the method used by the Federal Government in revising the Federal Narcotic Treatment Regulations. The word "methadone" was struck out wherever it occurred and the term "narcotic drugs," a more inclusive term for the class of medications that includes methadone and LAAM, was substituted. This method of revision obviates the need to revise the basic regulations each time a new medication is introduced; language pertinent to the new medication may simply be added (see Exhibit 6-1).

All opioid substitution therapy programs are subject to a thorough inspection process related to the safety and security of inventory and storage control for medications. Some States also require an onsite review focusing on program protocols, qualifications of clinical staff, and patient records.

Regulatory monitoring, whether by the State or another oversight body, focuses on patient outcomes as well as compliance with recordkeeping procedures. Members of inspection teams may wish to conduct interviews with patients and staff to better evaluate patient outcomes. Individuals with backgrounds in treatment should have a role in the design and implementation of regulatory monitoring procedures. All regulatory monitoring should be followed by technical assistance in areas of identified need. Punitive approaches are counterproductive and may contribute to poor patient retention in programs.

During the Labelling Assessment Study of LAAM, the DEA insisted that programs keep methadone and LAAM medications separate; that is, each medication should have a distinct
dispensing vehicle and be stored separately (although not necessarily in separate safes). Patient records should be coded so that records for patients receiving LAAM can be easily identified. Programs must establish methods of distinguishing clearly between methadone and LAAM patient records or files, particularly in dispensing and inventory procedures. This requirement should be continued in the interest of patient safety and adequate accountability of medications, especially in States where local regulations do not differentiate between LAAM and methadone.

The inspecting agency (that is, DEA or the local drug control agency) should clarify its requirements related to the separation of methadone and LAAM in terms of inventory control, storage, dispensing, and administration to ensure safety, efficacy, and ease of operation.

Patient records should be coded so that records for patients receiving LAAM can be easily identified. Programs must establish methods of distinguishing clearly between methadone and LAAM patient records or files, particularly in the dispensing and inventory procedures.

The Future of LAAM Regulation

FDA is moving into an era of opioid substitution therapy as a general, expanded concept of therapy, as opposed to a more narrow modality named after a specific medication--methadone. The introduction of LAAM therapy for narcotic addiction treatment is likely to pave the way for the introduction of other medications that are opioid substitutes and for adjunct treatment medications.

States that prefer to write their own regulations for LAAM, as well as those that have regulations related to methadone and wish to add LAAM to them, should be encouraged to do so in such a way that the regulations need not be rewritten each time a new opioid addiction medication using Schedule I or II compounds is introduced. This process can be accomplished by using generic terms such as opioid substitution therapy, narcotic addiction treatment (the Federal term), narcotic treatment services, or narcotic addiction therapies, rather than LAAM therapy. This language will facilitate future revision of the regulations.

States should consider an expedited regulatory mechanism for scheduling new medications, thereby encouraging treatment programs to utilize the latest developments in pharmacological therapy, as long as the technology and indications are not radically different (such as an antagonist medication rather than an agonist medication). States may want to consider how regulations must vary if a new medication were classified as a Schedule VI drug rather than a Schedule II drug, allowing greater flexibility and use by physicians in office practice.

All States have their own controlled substances laws and must reschedule LAAM from a Schedule I to a Schedule II drug in order to allow clinics access to it. The mechanism for rescheduling varies by State. States may want to explore the use of an automatic scheduling process that would mirror (or replicate) Federal scheduling of new medications for use in treatment. The alternative can be a long process requiring the approval of several State agencies
before rescheduling takes place. (As of this writing, LAAM has still not been rescheduled in some States.) Such processes create barriers to programs that want to offer the latest advances in pharmacological therapy.

States are strongly encouraged to write regulations to incorporate "sunsetting"--that is, a mechanism requiring that regulations be reviewed and updated within a specified period of time (for example, 3 years, as in Texas). This review would allow the regulations to reflect advances in the field (new medications and new treatment modalities) in a timely manner.

States are strongly encouraged to write regulations to incorporate "sunsetting"--that is, a mechanism requiring that regulations be reviewed and updated within a specified period of time (for example, every 3 years).

Regulations should emphasize that medications and services must be delivered together, in a complementary fashion, for any treatment medication. Programs using LAAM therapy must have the capability to administer methadone as needed in order to adequately address patients' needs, ensure their safety, and resolve problems of individual patients. Considerations must include necessary patient travel, vacations, program holidays, disasters, inclement weather, and other logistical issues. Serious consideration should be given to modifying the regulations to allow take-home doses of LAAM in cases in which there is a clinical need. (See Chapter 3 for suggested ways of handling interruptions in treatment.)

Training requirements should be included in State regulations, which should specify a minimum amount of staff training required per year in order to be licensed to operate. Minimum annual training should include some basic coverage of pharmacology. For example, 24 hours of annual training might include 3 hours of psychopharmacology and an additional 12 hours related to opiate addiction treatment. Because data about LAAM therapy is still accumulating, training should be constantly upgraded.

Role of the States

Any State agencies that regulate dispensing and pharmacy would normally be involved in the program approval process. States that regulate dosage and other clinical matters should ensure that their regulations are consistent with the new clinical guidelines for methadone maintenance; they should not use the same criteria for LAAM as for methadone. Regulations should avoid drug-specific requirements (such as specifying dose levels) and should be based on treatment efficacy rather than solely on community, philosophical, or ideological concerns.

Role of Treatment Programs

States that develop a certification or licensure process and regulations should involve providers (and consumers) within the State in the development of certification protocols and new
regulations. When appropriate, States should contact programs in other States that have had experience with LAAM (through clinical trials) and their SSAs, as well as the National Institute on Drug Abuse (NIDA) and the Center for Substance Abuse Treatment, when developing or revising regulations.

Treatment programs should serve as the primary sources of data on therapeutic protocols, advances, and the need for regulations. Programs should be proactive and work cooperatively with States by investing the time and energy in the regulatory process to develop useful and practical regulations and encourage regulatory changes. With the current restrictions on LAAM, such as lack of take-home doses and restrictions on use in pregnant women, it is not possible to use the new medication to its greatest potential for patients' needs. Clinical personnel should be proactive in focusing on optimal patient needs and working toward regulations that will better meet those needs.

**Treatment Standards**

SSAs should evaluate opioid substitution therapy programs that incorporate LAAM treatment by using a combination of outcomes variables and process variables. Outcomes evaluations in alcohol and other drug (AOD) abuse treatment programs have thus far focused on discharged patients, an approach that is highly inadequate for measuring the success of maintenance therapies. It is hoped that the introduction of LAAM therapy will move the evaluation process toward an effective and clinically relevant one in which outcomes variables are based on patient achievements (and quality-of-life improvements as a result of the treatment process), not on the numbers of patients "successfully" discharged (McLellan and Durell, submitted for publication).

The expansion of narcotic addiction treatment to include LAAM therapy puts programs in a position to improve outcomes evaluation. Outcomes variables should be defined in a way that measures progress rather than failure. A program should evaluate treatment outcomes with an instrument that is predictable, reliable, valid, and targeted to the goals of the program--and communicate the results of that process to the State, in order to add to the information base from which regulatory change derives. (See Chapter 5 for a discussion of outcomes measures.)

**Integration of AOD Treatment With Other Health Care Services**

Patients who need opioid substitution therapy should be assessed by a clinician who is familiar with the treatment alternatives but who does not have a stake in which modality is chosen. Thus, some form of centralized intake may be required. Such a system must use a standardized assessment procedure for patients, who may have a variety of problems. The availability of treatment slots must be known. Assessment staff must understand the types of treatment offered and the populations served, as well as the characteristics of both patients and programs that will facilitate optimal matching of patients to appropriate treatment modalities. States that have target cities programs should be further along in the development of centralized intake and standardized assessment systems.
Treatment programs serve as the primary sources of data on therapeutic protocols, advances, and the need for regulations. Clinical personnel should be proactive in working toward regulations that will better meet patient needs.

States should ensure that several systems and agencies work together to integrate services. These include the substance abuse treatment, mental health, public health, criminal justice, and primary medical care delivery systems. This approach will assist programs in the transition to managed care. Thus, it behooves States and programs to integrate the services of all systems. If they do not, they run the risk of being subject to the decisions of an outside agent that may not integrate services in a quality-focused manner.

**Use of LAAM: Effects on Other Systems**

The introduction of LAAM treatment has implications for other areas of the substance abuse treatment system, not just opiate addiction treatment programs. The introduction of LAAM treatment will have effects on other systems and organizations, as discussed below.

**Public Health Services**

It has been suggested that, like methadone maintenance, LAAM could stretch the public health treatment dollar by reducing the spread of sexually transmitted diseases and human immunodeficiency virus (HIV) (through needle sharing) and integrating public health and substance abuse treatments. The anticipated reduction in waiting lists due to the introduction of LAAM treatment may also eventually result in decreases in HIV and acquired immunodeficiency syndrome (AIDS) and the associated risk and incidence of tuberculosis. Success with either methadone or LAAM maintenance results in a stabilized patient in treatment, and continuing treatment has been shown to reduce high-risk behavior, improve overall health, and reduce health care costs related to other medical complications. These are important public health concerns.

HIV imposes huge costs in health and human terms. Mainstream medicine--including managed care companies, health maintenance organizations, and other health care providers--may be willing to accept LAAM because it is new and may be implemented in a more innovative way than the current methadone maintenance treatment programs. It is also being introduced at a time when harm reduction is an important public health consideration.

**Criminal Justice System**

Regulatory restrictions and the past hostility of prison administrators to opioid substitution therapy make it unlikely that many prisons will provide this treatment, but prisons that have licenses to dispense methadone should expand their capabilities to include LAAM treatment. In fact, LAAM should be easier for prison health authorities to provide because of the reduced dosing schedule.
Until LAAM is widely used, prison staff may not know how to handle patients receiving LAAM. Criminal justice system staff (including judges) should receive the same type of education that is provided to health care providers to familiarize them with the pharmacology and use of LAAM.

States should write regulations that encourage methadone or LAAM maintenance of patients whose expected period of incarceration is short (less than 3 months).

Social Service Organizations

Fewer clinic visits will give LAAM-maintained patients a more flexible schedule, allowing them to better avail themselves of the services of social service organizations. Such organizations include agencies that provide legal, vocational, educational, and family social services, such as job training programs.

Insurance, Reimbursement, and Funding Organizations

Insurers frequently set caps on the number of visits to treatment programs of any kind. They often do not distinguish ongoing maintenance treatment as a separate modality that requires frequent visits. Treatment programs and others in the substance abuse treatment system should work to ensure that funding agencies, payers, and insurance companies receive education about the cost-effectiveness of opioid substitution therapy, including LAAM treatment. This will help insurers understand that it is not appropriate to arbitrarily cap the number of visits.

Medical costs associated with untreated opiate addiction can be high. Patients who enter opioid substitution therapy usually suffer from years of neglected health and welfare. Thus, in the first year of treatment, costs may be greater than in later years. However, once the patient enters treatment, the program can provide some assurance that the patient will receive appropriate and cost-effective services. In particular, programs can help patients access primary care rather than hospital and emergency room care, access which will reduce costs. Because the use of LAAM offsets other medical costs, insurers should cover LAAM therapy and be willing to reimburse costs of required pregnancy tests. Insurers should view health problems in substance-abusing patients in the same way as those in other populations.

Ethical Issues in the Administration of LAAM

The decision to medicate with LAAM or methadone should be made with a focus on the patient rather than on financial considerations or programmatic convenience. Programs with a patient
mix that includes both publicly funded and private-pay patients should ensure that the source of reimbursement does not dictate the medication or other treatment services delivered. Programs must evaluate their treatment decisions in light of good ethical practice and not succumb to the temptation to overload their program staff with more patients than can be treated in a comprehensive, patient-focused manner.

Informed Consent and Confidentiality

Informed consent is an ongoing process of interaction between staff and patients about treatment decisions. Its goal is to lead to informed choice. Patients must understand the nature and purpose of the treatment; its potential risks, side effects, and benefits; any interactions with other drugs or treatments; and alternative therapies.

Programs are encouraged to develop an educational process that includes the following elements, documented in the patient record with a signature:

1. Patient hears the information (adequate disclosure).
2. Patient understands the information (assessment that disclosure was comprehended).
3. Staff assesses patient voluntariness (voluntariness is absent when a patient makes a choice solely out of desperation or other emotional reactions) and reasons for making the choice (capacity for decisionmaking). Program staff are then obligated to make the best choice based on this assessment.

The confidentiality issues attending the administration of LAAM are identical to those surrounding all other forms of AOD abuse treatment. Several TIPs in this series have separate chapters that present detailed guidelines for providing substance abuse treatment in compliance with the Federal confidentiality regulations. For example, the reader is referred to Chapter 5 of the TIP Simple Screening Instruments for Outreach for Alcohol and Other Drug Abuse and Infectious Diseases. Issues addressed include the proper use of consent forms and communicating with other agencies. CSAT has also prepared a separate document Confidentiality of Patient Records for Alcohol and Other Drug Treatment, as part of its Technical Assistance Publication (TAP) series. The TAP contains sample patient consent forms and other forms for programs to use in releasing information to other agencies.

Noncompliance and Termination

In the process of providing patient education and obtaining informed consent, women should be told specifically that if they become pregnant while receiving LAAM, the physician will switch them to methadone. Staff should ensure that a patient understands this information. After the pregnancy, patients may be transferred back to LAAM.

Providing information about the consequences of noncompliance should be part of the informed consent process. The criteria for noncompliance should be clear to patients and should not differ for LAAM and methadone patients. Programs should avoid terminating patients from treatment for continued substance abuse problems. Rather, programs should seek improved or alternative
treatment plans or methods that may better meet patients' needs.

Treatment is not punishment, and patients should not be changed involuntarily from one medication to another nor should the treatment be changed in any way that they might perceive as a punishment. Clinic staff should ensure that a patient understands the reason for any medication change.

**Advertising**

It has been reported that some programs have engaged in unethical advertising practices. For example, some programs have told patients that they would receive extra take-home medication if they brought a new patient into treatment. Some programs have advertised that they give higher doses and more take-home doses than "competing" programs in the area.

Advertising by opioid substitution therapy programs should be approached with great care and sensitivity--especially advertising in print or electronic media. A program may seek to "market" its services in places where referrals are likely to be found, such as emergency rooms, detoxification centers, police stations and other criminal justice agencies, and health and human service agencies. Churches and other groups that help community members in distress can also be approached. In certain geographic regions, it may be valuable to recommend that clinics form associations for self-regulation of issues such as advertising.

**Quality of Care**

Some patients are not ready to engage fully in treatment. The question of whether it is appropriate to use LAAM while delivering minimal clinical services until the patient engages in treatment should be examined carefully. "Minimal" services usually involve an initial assessment of severity of substance abuse, which allows clinicians to determine the level of care a patient will receive when he or she enters treatment. In some situations, case management is provided for patients whose conditions require immediate and ongoing attention. In addition, some further contact is necessary for urinalyses to ensure that the patient is not using other substances. This level of services may be appropriate for patients who are unable to engage in treatment for psychosocial or medical reasons. Minimum treatment should include TB testing and HIV prevention education, which is required under Federal block grant regulations.
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Roxane Laboratories, Inc., manufacturer of LAAM, provides onsite training to clinics that have received Food and Drug Administration (FDA) approval to administer LAAM. Training can be tailored to address the needs of physicians, nurses, counselors, or administrators. Depending on the needs of the clinic, training may be conducted in a couple of hours or a full day. A number of informational brochures, as well as a videotape, are available for physicians, counselors, and patients. There is no charge for the training. More information can be received by writing to Roxane Laboratories, Inc., P.O. Box 16532, Columbus, Ohio 43216, or by calling (614) 276-4000.

Single State Agencies and the Opioid Addiction Treatment Improvement Project

CSAT implemented the Opioid Addiction Treatment Improvement Project (OATIP) as a nationwide initiative to enhance the quality and scope of drug treatment for opioid-dependent populations in order to improve treatment effectiveness. The primary purpose of technical assistance to single State agencies is to improve clinical services management, quality assurance activities, evaluation, and compliance with State and Federal regulatory requirements. The services include national technical assistance (onsite and offsite); workshops with State AOD directors, opioid addiction treatment providers, and other key agents in related areas; and information dissemination on opioid treatment.
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LAAM in the Treatment of Opiate Addiction
*Treatment Improvement Protocol (TIP) Series 22*

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LAAM in the Treatment of Opiate Addiction
*Treatment Improvement Protocol (TIP) Series 22*

[Exhibits]

**Exhibit 2.1 Possible Side Effects of LAAM**

<table>
<thead>
<tr>
<th>Whole body</th>
<th>Respiratory</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weakness, loss of energy (asthenia)¹</td>
<td>Cough²</td>
</tr>
<tr>
<td>Back pain², chills²</td>
<td>Rhinitis²</td>
</tr>
<tr>
<td>Fluid accumulation (edema)²</td>
<td>Yawning²</td>
</tr>
<tr>
<td>Hot flashes (males 2:1)²</td>
<td></td>
</tr>
<tr>
<td>Flu syndrome and malaise (11 percent)</td>
<td>Cardiac</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Hypertension³</td>
</tr>
<tr>
<td><strong>Gastrointestinal</strong></td>
<td>Electrocardiogram (EKG) changes¹</td>
</tr>
<tr>
<td>Abdominal pain¹</td>
<td>Postural hypotension</td>
</tr>
<tr>
<td>Constipation¹</td>
<td>Slowed heart rate (bradycardia)</td>
</tr>
<tr>
<td>Diarrhea²</td>
<td></td>
</tr>
<tr>
<td>Dry mouth²</td>
<td>Hepatic</td>
</tr>
<tr>
<td>Nausea and vomiting²</td>
<td>Hepatitis³</td>
</tr>
<tr>
<td></td>
<td>Abnormal liver function tests³</td>
</tr>
<tr>
<td><strong>Musculoskeletal</strong></td>
<td></td>
</tr>
<tr>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Joint pain (arthralgia)&lt;sup&gt;1&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Muscle pain (myalgia)</td>
<td>Skin and Appendages</td>
</tr>
<tr>
<td></td>
<td>Rash&lt;sup&gt;2&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>Sweating&lt;sup&gt;1&lt;/sup&gt;</td>
</tr>
<tr>
<td><strong>Nervous System</strong></td>
<td></td>
</tr>
<tr>
<td>Abnormal dreams&lt;sup&gt;2&lt;/sup&gt;</td>
<td>Special Senses</td>
</tr>
<tr>
<td>Anxiety&lt;sup&gt;2&lt;/sup&gt;</td>
<td>Blurred vision&lt;sup&gt;2&lt;/sup&gt;</td>
</tr>
<tr>
<td>Decreased sex drive&lt;sup&gt;2&lt;/sup&gt;</td>
<td>Tearing</td>
</tr>
<tr>
<td>Depression&lt;sup&gt;2&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Euphoria&lt;sup&gt;2&lt;/sup&gt;</td>
<td>Urogenital</td>
</tr>
<tr>
<td>Headache&lt;sup&gt;2&lt;/sup&gt;</td>
<td>Difficult ejaculation&lt;sup&gt;1&lt;/sup&gt;</td>
</tr>
<tr>
<td>Decreased sensitivity to stimulation (hypesthesia)&lt;sup&gt;2&lt;/sup&gt;</td>
<td>Impotence&lt;sup&gt;1&lt;/sup&gt;</td>
</tr>
<tr>
<td>Insomnia (9.1 percent)</td>
<td>Absence of menstrual periods (amenorrhea)&lt;sup&gt;3&lt;/sup&gt;</td>
</tr>
<tr>
<td>Nervousness&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Pus in the urine (pyuria)&lt;sup&gt;3&lt;/sup&gt;</td>
</tr>
<tr>
<td>Sleepiness, unnatural drowsiness (somnolence)&lt;sup&gt;2&lt;/sup&gt;</td>
<td></td>
</tr>
</tbody>
</table>

<sup>1</sup> Side effects occurred in more than 3 to 9 percent of patients and were probably related to LAAM.

<sup>2</sup> Side effects occurred in 1 to 3 percent of patients and were probably related to LAAM.

<sup>3</sup> Side effects occurred with "low frequency in controlled and uncontrolled studies. They are not known to be causally related to the administration of the drug."

Side effects with no superscript occurred in less than 1 percent, unless otherwise indicated.

Adapted from ORLAAM: Levo-alpha-acetyl-methadol for the Management of Opiate Dependence: Information for Physicians. No date.
### Exhibit 3.1 Half-life and Steady-State Times of Methadone and LAAM

<table>
<thead>
<tr>
<th>Medication</th>
<th>Half-life</th>
<th>Time to Steady State</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methadone</td>
<td>1 to 1.5 days</td>
<td>5 to 7.5 days</td>
</tr>
<tr>
<td>LAAM</td>
<td>2.6 days</td>
<td>10.4 to 13 days</td>
</tr>
<tr>
<td>Nor-LAAM</td>
<td>2.0 days</td>
<td>8 to 10 days</td>
</tr>
<tr>
<td>Dinor-LAAM</td>
<td>4.0 days</td>
<td>16 to 20 days</td>
</tr>
</tbody>
</table>

### Exhibit 3.2 Phases of LAAM Dosing

<table>
<thead>
<tr>
<th>Phase</th>
<th>Purpose</th>
<th>Range in Milligrams</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial dose</td>
<td>Relieve abstinence symptoms</td>
<td>20-40 mg</td>
</tr>
<tr>
<td>Early induction</td>
<td>Reach tolerance threshold</td>
<td>Plus or minus 5-10 mg q dose</td>
</tr>
<tr>
<td>Late induction</td>
<td>Establish adequate dose (desired effects)</td>
<td>Plus or minus 5-10 mg q 5-10 days</td>
</tr>
<tr>
<td>Maintenance</td>
<td>Maintain desired effects (steady-state occupation of opiate receptors)</td>
<td>Usually 60-60-60 to 140-140-140 mg or 130-130-180 mg. May be greater than 140 or less than 60 mg</td>
</tr>
</tbody>
</table>

### Exhibit 3.3 Sample Monday-Wednesday-Friday Dose Scheduling Chart

<table>
<thead>
<tr>
<th>Sample Monday-Wednesday-Friday Dose Scheduling Chart for Patients on LAAM Who Are and Are Not Allowed Take-Home Methadone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients Allowed Take-Home Methadone</td>
</tr>
<tr>
<td>Mon.</td>
</tr>
<tr>
<td>-------</td>
</tr>
<tr>
<td>140</td>
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<tr>
<td>135</td>
</tr>
<tr>
<td>130</td>
</tr>
<tr>
<td>125</td>
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<tr>
<td>120</td>
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<td>8</td>
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<td>6</td>
</tr>
<tr>
<td>4</td>
</tr>
<tr>
<td>2</td>
</tr>
<tr>
<td>0</td>
</tr>
</tbody>
</table>

* Friday (72-hour) dose = 20 percent increase over Monday and Wednesday (48-hour) doses

** Methadone dose = 30 percent of Monday and Wednesday (48-hour) doses

*** Friday (72-hour) dose (with no methadone) = 30 percent increase over Monday and Wednesday (48-hour) doses

**Exhibit 6.1 Federal Narcotic Treatment Regulations**

| Federal Narcotic Treatment Regulations: Language Specifically Relating to Use of LAAM |
(d)(1)(iii)(B)(6)

Patients who are or become pregnant should not be started or continued on LAAM, except by the written orders of a physician who determines this to be the best choice of therapy for that patient. Clinics providing treatment with LAAM must advise all patients of childbearing potential of the risks of LAAM and make a medical evaluation available to all patients who become pregnant while taking the drug. An initial pregnancy test shall be performed for each prospective female patient of childbearing potential before admission to LAAM comprehensive maintenance treatment and monthly pregnancy tests performed thereafter on such female patients in LAAM comprehensive maintenance treatment. Analysis of such tests shall be performed in a laboratory approved under the Clinical Laboratory Improvement Amendments of 1988 or in a laboratory certified by a State or private accrediting body approved by the Health Care Financing Administration.

(d)(1)(iv)(B)

A person under 18 years of age shall not be admitted to LAAM maintenance treatment.

(k)(1) LAAM

(i) Dosage and responsibility for administration. After a patient's tolerance to LAAM is established, LAAM shall be administered no more frequently than every other day. Dosage of LAAM shall be individualized at doses, frequencies, and under conditions of usage described in approved labeling and as follows:

(A) New patients. The persons responsible for the program shall ensure that the initial dose of LAAM to a patient whose tolerance for the drug is unknown does not exceed 40 milligrams.

(B) Stabilized methadone maintenance patient. The persons responsible for the program shall ensure that the initial dose of LAAM for a previously stabilized methadone maintenance patient is less than or equal to 1.3 times the patient's daily methadone dose, not to exceed 120 milligrams.

(C) A licensed physician shall assume responsibility for the amount of the narcotic drug administered or dispensed and shall record, date, and sign or countersign in each patient's record each change in dosage schedule.

(D) The administering licensed physician shall ensure that a single dose of LAAM greater than 140 milligrams is justified in the patient's record.
(ii) *Dosage form.* LAAM may be administered in oral form when used in a maintenance treatment program. Hospitalized patients under care for a medical or surgical condition are permitted to receive LAAM in oral form when the attending physician judges it advisable. Although syrup concentrate or other formulations may be distributed to the program, all oral medication is required to be administered in a liquid formulation. Clinics that administer both LAAM and methadone shall take appropriate measures, including contrasting color and taste, to ensure that dosage forms of LAAM and methadone are easily distinguished.

(iii) *Take-home medication.* Take-home doses of LAAM are not permitted. A patient who is eligible for one or more take-home doses of methadone under paragraph (d)(6) of this section and who is unable to conform to the applicable mandatory LAAM dosing schedule because of exceptional circumstances such as illness, personal or family crises, travel, or other hardship, or official State holidays, may be temporarily transferred to methadone. Take-home doses of methadone for a patient eligible for a planned temporary discontinuation of treatment with LAAM shall be individualized at doses, frequencies, and under conditions of usage described in the approved labeling and the applicable provisions for take-home methadone medication under paragraph (d)(6) of this section. The maximum number of take-home doses of methadone shall be determined in accordance with the provisions of 21 C.F.R. Part 291 Section 291.505(d)(6)(v) and (d)(6)(vi) (1993).