

KAP Keys Based on TIP 43

Medication-Assisted Treatment
for Opioid Addiction in Opioid
Treatment Programs

Knowledge Application Program

KAP Keys

For Clinicians

Based on TIP 43

*Medication-Assisted
Treatment for Opioid*

*Addiction in
Opioid
Treatment
Programs*



U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Substance Abuse and Mental Health Services Administration
Center for Substance Abuse Treatment
www.samhsa.gov

KAP Keys Based on TIP 43 Medication-Assisted Treatment for Opioid Addiction in Opioid Treatment Programs

Introduction

KAP Keys were developed to accompany the Treatment Improvement Protocol (TIP) Series published by the Center for Substance Abuse Treatment (CSAT), Substance Abuse and Mental Health Services Administration (SAMHSA). These KAP Keys are based entirely on TIP 43 and are designed to meet the needs of the busy clinician for concise, easily accessed “how to” information.

For more information on the topics in these KAP Keys, readers are referred to TIP 43.

Other Treatment Improvement Protocols (TIPs) that are relevant to these KAP Keys:

TIP 37: *Substance Abuse Treatment for Persons With HIV/AIDS (2000)* **BKD359**

TIP 40: *Clinical Guidelines for the Use of Buprenorphine in the Treatment of Opioid Addiction (2004)* **BKD500**

TIP 42: *Substance Abuse Treatment for Persons With Co-Occurring Disorders (2005)* **BKD515**

Information Obtained About and Provided to Patients During Screening and Admission 1

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Essential Information Obtained About Patients

- Risk of suicide and other emergencies
- Age (patients younger than 18 must meet Federal and State eligibility requirements for admission to an opioid treatment program [OTP])
- Method and level of opioid use and pattern of daily preoccupation with opioids
- Other substances of abuse (e.g., alcohol, nicotine, illicit drugs) and prescription and over-the-counter medicines used
- Treatment history, preferably from previous providers (requires patient's informed written consent)
- Recovery environment (i.e., do living environment, social network, co-residents, and housing status support or jeopardize treatment and recovery?)
- Other recovery resources (e.g., family, friends, significant others, neighbors, co-workers, insurance status, employment, education, spirituality)
- Other compulsive behaviors (e.g., gambling, sexual disorders)
- Patient motivation and reasons for seeking treatment

Essential Information Provided to Patients

- Orientation to medication-assisted treatment (MAT): treatment methods, optional programs, treatment requirements, roles and responsibilities of all those involved
- Handbook (in patient's first language): information needed to comply with treatment requirements
- OTP information requirements and methods: written consent to treatment, program recordkeeping and confidentiality, patient rights, grievance procedures, discharge policies
- Facility safety instructions and rules
- Information on family planning, gynecological health, menopause, pregnancy testing (for women)

See TIP 43, pages 43–53.

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Medication-Assisted Treatment for Opioid Addiction
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- Physical examination
- Laboratory tests (possibly including TB, hepatitis, HIV, sexually transmitted disease tests plus initial drug test and 8 random drug tests per year)
- Determination of opioid addiction and treatment history, extent of other substance use and treatment, medical history

Induction Assessment

- At least daily checks for signs of overmedication (intoxication or sedation) or undermedication (withdrawal symptoms) during initial dosing
- Assurance that patients are not using benzodiazepines or alcohol during induction
- Observed dosing to ensure medication ingestion
- Dosage adjustments until steady state is reached

Comprehensive Assessment

- Determination of patient motivation
- Continuing assessments of substance use
- Cultural background assessment
- Assessment of psychosocial factors (e.g., mental health, sociodemographic status, family and social network, spiritual support, physical or sexual abuse history, housing, legal status, employment and military status, sexual orientation, insurance and financial status, recreational activities)

See TIP 43, pages 49–60.

Pharmacotherapeutic Medications for Opioid Addiction Treatment

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	Methadone	LAAM	Buprenorphine	Buprenorphine/ Naloxone	Naltrexone
Available Formulations	Oral solution, liquid concentrate, tablet/diskette, and powder	Oral solution	Sublingual tablet	Sublingual tablet	Oral tablet
Receptor Pharmacology	Full mu opioid agonist	Full mu opioid agonist	Partial mu opioid agonist	Partial mu opioid agonist/mu antagonist	Mu opioid antagonist
FDA Approval	Never formally approved by FDA	1993	2002	2002	1984
DEA Schedule	II	II	III	III	Not scheduled
Treatment Settings	OTP	OTP	Physician's office, OTP, or other health care setting	Physician's office, OTP, or other health care setting	Physician's office, OTP, or any substance abuse treatment program

See TIP 43, pages 26–32.

Possible Side Effects of Opioid Agonist and Partial Agonist Therapy

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Whole Body Effects

- Weakness, loss of energy (asthenia)
- Back pain, chills
- Fluid accumulation (edema)
- Hot flashes
- Flu syndrome and malaise
- Weight gain

Gastrointestinal Effects

- Constipation
- Dry mouth
- Nausea and vomiting
- Abdominal pain

Musculoskeletal Effects

- Joint pain (arthralgia)
- Muscle pain (myalgia)

Nervous System Effects

- Abnormal dreams
- Anxiety
- Decreased sex drive
- Depression
- Euphoria
- Headache
- Decreased sensitivity to tactile stimulation (hypesthesia)
- Insomnia
- Nervousness
- Somnolence

Respiratory Effects

- Cough
- Rhinitis
- Yawning

Cardiac Effects

- Electrocardiogram changes (possible QT prolongation with LAAM or high doses of methadone)
- Postural hypotension
- Slowed heart rate (bradycardia)

Hepatic Effects

- Abnormal liver function tests

Endocrine Effects

- Hyperprolactinemia
- Absence of menstrual periods (amenorrhea)

Skin and Appendage Effects

- Sweating
- Rash

Special Sensory Effects

- Blurred vision

Urogenital Effects

- Difficult ejaculation
- Impotence

See TIP 43, pages 33–36.

Reported Drug Interactions With Methadone

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Agent	Effect on Methadone
Amitriptyline	Decreased clearance
Amprenavir	Decreased serum levels; possible decreased opioid effects
Amylobarbitone	Increased clearance
Ciprofloxacin	Increased opioid effects
Diazepam	Increased opioid effects
Efavirenz	Decreased plasma levels and opioid effects
Ethanol	Increased opioid effects and added sedation
Fluconazole	Decreased methadone clearance and increased SMLs*
Fluoxetine	Increased SMLs
Fluvoxamine	Increased SMLs and increased opioid effects
Fusidic acid	Decreased opioid effects
Moclobemide	Increased opioid effects
Nelfinavir	Decreased SMLs
Nevirapine	Decreased SMLs and opioid effects
Paroxetine	Increased SMLs
Phenobarbital	Decreased SMLs and opioid effects
Phenytoin	Decreased SMLs and opioid effects
Rifampin	Decreased SMLs and opioid effects
Ritonavir	Decreased SMLs and opioid effects
Sertraline	Increased SMLs
Spironolactone	Increased clearance

*Serum methadone levels

See over for strategies to prevent harmful drug interactions.
See TIP 43, pages 36–40.

Strategies To Prevent or Minimize Harmful Drug Interactions in MAT

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- Obtain a thorough drug and medication history, including results of drug and other laboratory tests.
- When adding any drugs to a therapeutic regimen, start with low doses, increase slowly, and monitor patient reactions closely.
- Educate patient about the risks of drug interactions, potentially lethal drugs or medications during agonist-based pharmacotherapy, possible cardiovascular risks, and possible effects of deviating from dosage schedules and amounts.
- Substitute alternative medications that do not interact with opioid treatment medications or have the least potential for interaction.
- Consider whether administering other medications with or without food or altering dosing schedules might reduce the risk of drug interactions.
- Simplify the medication regimen to make it easier for patient to adhere to it.
- Adjust opioid medication dosage based on patient response to avoid drug interaction, but be vigilant for signs of withdrawal or sedation.
- Increase drug testing and monitoring of drug serum levels. Advise patient of the physical signs of adverse interactions, and explain what to do if these occur.
- Be aware of concomitant diseases (e.g., liver disease) that might influence the potential for adverse drug interactions.

See TIP 43, pages 40–42.

Medications/Substances That Alter Opioid Medication Levels in the Body

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Expected To Reduce Opioid Medication Level

Carbamazepine	Ethosuximide	Rifabutin
Dexamethasone	Primidone	Troglitazone

Expected To Increase Opioid Medication Levels*

Amiodarone	Itraconazole	Norfloxacin
Cannabinoids	Ketoconazole	Omeprazole (slight)
Clarithromycin	Metronidazole	Quinine
Erythromycin	Mibefradil	Saquinavir
Grapefruit juice	Miconazole	Troleandomycin
Indinavir	Nefazodone	Zafirlukast

*Although clarithromycin and erythromycin increase opioid medication levels, azithromycin does not.

Adapted from *Pharmacotherapy* (Michalets 1998) with permission; with additional information from Gourevitch and Friedland 2000 and McCance-Katz et al. 2000.

See TIP 43, page 40.

Criteria for Take-Home Medications and Maximum Take-Home Dose

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SAMHSA Criteria To Allow Take-Home Medication Privileges

- Absence of recent drug and alcohol abuse, behavioral problems, criminal activity
- Regular OTP attendance
- Stable home environment and social relationships
- Acceptable time in comprehensive maintenance treatment
- Assurance of safe storage of medication
- Benefits of decreased OTP attendance clearly outweigh risks of diversion

Source: 42 Code of Federal Regulations, Part 8 § 12(i).

Continuous Time in Treatment	Maximum Doses of Take-Home Medication Allowed
First 90 days (months 1–3)	1 dose per week
Second 90 days (months 4–6)	2 doses per week
Third 90 days (months 7–9)	3 doses per week
Fourth 90 days (months 10–12)	6 days' supply per week
After 1 year of treatment	2 weeks' supply
After 2 years of treatment	1 month's supply (monthly OTP visits are still required)

- Any patient may receive take-home medication for days when treatment facilities are closed, including Sundays and holidays.
- State requirements may vary.
- No patient in short-term detoxification or interim maintenance may receive take-home maintenance medication.

Source: 42 Code of Federal Regulations, Part 8 § 12(i).

See TIP 43, pages 81–85.

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Recommended Focuses

- Providing support and guidance, especially to eliminate substance abuse
- Monitoring other problem behaviors
- Helping patients comply with OTP rules
- Identifying problems needing referral and extended services
- Identifying and removing treatment barriers
- Providing motivational enhancement

Standard Components

- Identification of problems needing immediate attention (e.g., homelessness)
- Help locating and joining mutual-help groups (e.g., Narcotics Anonymous, Methadone Anonymous)
- Education about addiction and effects of substance abuse
- Education about relapse prevention strategies
- Information about stress- and time-management techniques
- Assistance in developing a healthy lifestyle (e.g., exercise, good nutrition, smoking cessation, avoidance of risky sexual behaviors)
- Assistance in joining socially constructive groups (e.g., community and faith-based organizations)
- Continuing education on health issues (e.g., HIV/AIDS, hepatitis)

Types of Group Counseling in MAT

- Psychoeducational groups
- Skill development groups (e.g., relapse prevention, stress management, substance use cessation)
- Cognitive-behavioral groups
- Interpersonal-process groups
- Support groups

Common Topics for Patient Educational Sessions in MAT 10

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- Physical and psychological effects of opioid and other substance abuse
- Health information, including medical problems related to addiction, smoking cessation, improving nutritional habits (including special needs of persons with HIV), and exercise, including aerobic and meditative exercises (e.g., yoga)
- Effects of drug use on family and other relationships
- Introduction to mutual-help groups such as Methadone Anonymous
- Effects and side effects of addiction treatment medications and interactions with other drugs
- Symptoms of co-occurring disorders
- Compulsive behaviors besides substance abuse (e.g., gambling, sexual behaviors)
- Skills to attain and sustain abstinence, such as anger management and coping with cravings
- Developing non-drug-related leisure activities
- Stress management and relaxation
- Communication skills and assertiveness training
- Time management
- Parenting skills
- Avoidance of sexually transmitted diseases and promotion of responsible sexual behavior
- Vocational planning and employment (sometimes linked with cognitive testing and conducted with vocational agencies)

See TIP 43, pages 124–133.

Treatment Plan

- Is based on a thorough patient history and assessment
- Is tailored to each patient's needs
- Has short- and long-term goals that reflect awareness of the patient's abilities and limitations
- Describes actions needed to reach goals
- Indicates which goals require referral and followup
- Includes specific, measurable objectives
- Incorporates strategies for building therapeutic relationships with patients
- Uses motivational enhancement to involve patients
- Is written in the patient's own words
- Describes the patient's strengths, abilities, and challenges
- Includes assessment of linguistic or cultural factors that affect treatment

Multidisciplinary Team

- A physician trained in addiction psychiatry
- Nonphysician medical staff members (e.g., registered nurse, nurse practitioner, physician's assistant)
- A pharmacist or pharmacy assistant
- Nonmedical professional staff members (e.g., case coordinator, social worker, psychologist, vocational and educational specialist)
- A certified or licensed addiction specialist or drug counselor
- Nontreatment and administrative staff members (e.g., office manager, clerical staff, receptionist, secretary)
- Security personnel who ensure the safety and well-being of patients and staff on site

See TIP 43, pages 95–100.

**KAP Keys Based on TIP 43
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- Endocarditis
- Soft-tissue infections (e.g., cellulitis, abscesses)
- Necrotizing fasciitis
- Wound botulism

Infectious Diseases

- TB
- Syphilis
- Genital chlamydia
- Gonococcus infections
- Hepatitis A, B, and C
- HIV/AIDS

Chronic Diseases

- Diabetes
- Asthma
- Hypertension
- Chronic obstructive pulmonary disease
- Coronary artery disease

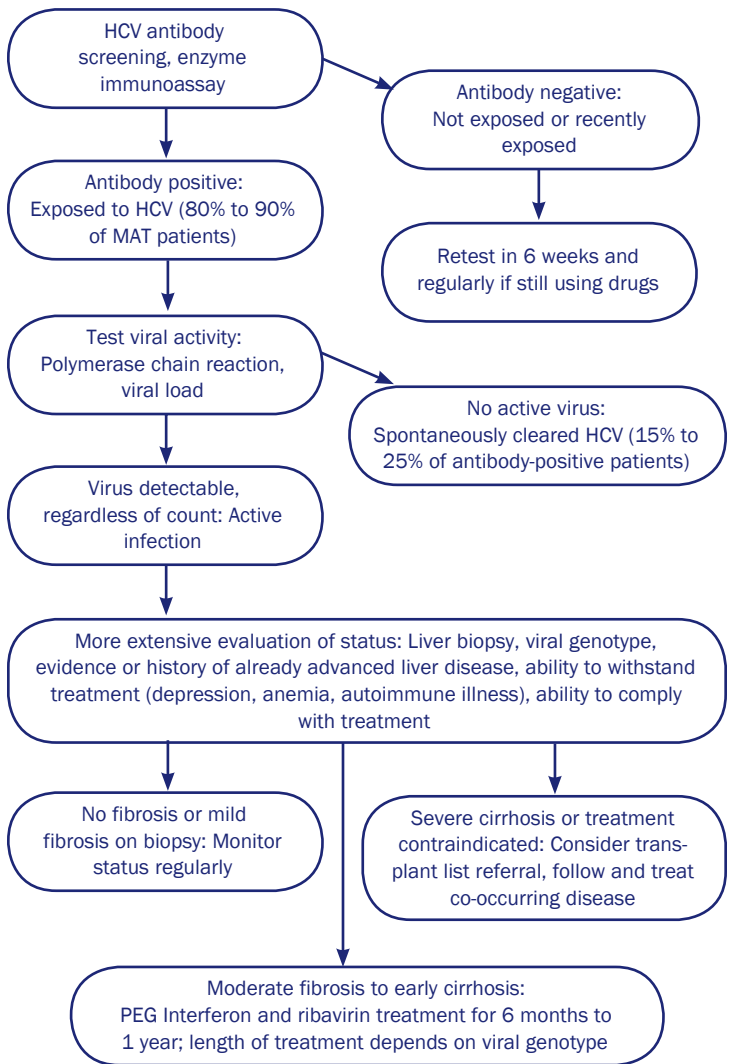
Pain

- Acute (e.g., associated with traumatic injury, labor and delivery)
- Chronic (e.g., associated with cancer, arthritis, disc disease)

See KAP Key 13 for hepatitis C evaluation flowchart.

See TIP 43, pages 163–173.

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See TIP 43, pages 167–171.

Cutoff Concentrations and Detection Times for Substances of Abuse

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Drug	Cutoff Concentrations (ng/mL*)		Analytes Tested in Confirmation	Urine Detection Time (Days)
	Initial Testing	Confirmation		
Amphetamine	1,000	500	Amphetamine	2–4
Barbiturates	200	200	Amobarbital, secobarbital, other barbiturates	2–4 for short acting; up to 30 for long acting
Benzodiazepines	200	200	Oxazepam, diazepam, others	Up to 30 for long acting
Cocaine	300	150	Benzoyllecgonine	1–3 for sporadic use; up to 12 for chronic use
Codeine	300	300, 300	Codeine, morphine	1–3
Heroin	300	300, 10	Morphine, 6-acetylmorphine	1–3
Marijuana	100, 50, 20	15	Tetra-hydrocannabinol (THC)	1–3 for casual use; up to 30 for chronic use
Methadone	300	300	Methadone	2–4
Methamphetamine	1,000	500, 200	Methamphetamine, amphetamine	2–4
Phencyclidine	25	25	Phencyclidine	2–7 for casual use; up to 30 for chronic use

*ng/mL: nanograms per milliliter

Adapted from Cone 1997.

See TIP 43, pages 144–146.

**KAP Keys Based on TIP 43
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- Perform specimen collection in a therapeutic, humane environment.
- Clean bathrooms frequently, and supply with soap and toilet articles.
- Inform patients at admission of testing and collection procedures, including whether and when observed dosing may be used, and their responsibility.
- Use clinical judgment about need for direct observation of specimen collection (vs. temperature strips, adulterant checks, ambient-temperature guns, substitution of oral swabs) unless mandated by State.
- Put testing policies and procedures in writing, and give each patient a copy.
- Protect patients' dignity and privacy.
- Minimize opportunities for falsification (monitor bathrooms, have patients leave parcels outside, allow only one patient in bathroom at a time).
- Ensure confidentiality by storing specimens and records so only authorized personnel can access them.
- Maintain universal safety precautions when handling specimens.

Specific Procedures

- Staff member greets patient and decides whether a specimen is required (based on judgment or random list) before patient receives medication.
- Patient is sent to bathroom with a labeled container to provide specimen.
- Staff member receives container and ensures a valid specimen (checks warmth or uses temperature strips, adulterant checks, ambient-temperature guns).
- Staff member packages specimen and sends it to the lab.

See TIP 43, pages 146–149.

Common Immunoassays Used in Drug Testing

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Assay	Brand Name(s)	Maker(s)	Comments
EIA	EMIT, CEDIA	Syva, Boehringer Mannheim/Microgenics	Used widely; inexpensive; equipment available for automated, high-volume rapid analysis; sensitive to some adulterants
Fluorescence polarization	ADx, TDx	Abbott Diagnostics	Resistant to several adulterants; reasonably good quantitative estimates of concentrations; slower and more expensive than EIA and KIMS
Kinetic interaction of microparticles (KIMS)	OnTrak, TesTcup, OnLine	Roche Diagnostics	Equipment available for automated, high-volume rapid analysis; used by some large laboratories
Colloidal metal (CMI)	Triage	Biosite Diagnostics	Used in onsite testing
RIA	Abu-screen	Roche Diagnostics	Labor intensive; resistant to several adulterants; not used widely

Adapted from Swotinsky and Smith 1999, with permission of Medical Review Officer Certification Council.

See TIP 43, pages 149–151.

Frequently Used Substance Combinations 17 and Common Reasons for Use

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Combination	Reasons
Heroin plus alcohol	Enhance a high; create euphoria or sedation
Heroin followed by alcohol	Medicate opioid withdrawal; medicate cocaine overstimulation (e.g., anxiety, paranoia)
Heroin plus cocaine (“speedball”)	Enhance or alter cocaine euphoria
Heroin followed by cocaine	Medicate opioid withdrawal
Cocaine plus alcohol	Enhance high; reduce cocaine overstimulation (e.g., anxiety, paranoia)
Cocaine followed by heroin	Reduce cocaine overstimulation (e.g., anxiety, paranoia); modulate the cocaine “crash”
Methadone plus alcohol	Create a high; sedate
Methadone plus cocaine	Reduce cocaine overstimulation (e.g., anxiety, paranoia); moderate the cocaine “crash”
Methadone plus benzodiazepines	Create a high; sedate
Any opioid plus any nonbenzodiazepine sedative	Create a high; sedate
Any opioid followed by any nonbenzodiazepine sedative	Medicate opioid withdrawal
Any opioid plus amphetamine	Create a high

See TIP 43, pages 181–182.

Common Medical and Obstetrical Complications Among Pregnant Women

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Medical Complications

Anemia Bacteremia/septicemia Cardiac disease, especially endocarditis Cellulitis Depression and other mental disorders Edema Gestational diabetes Hepatitis (acute and chronic) Hypertension/tachycardia Phlebitis Pneumonia Poor dental hygiene	STDs Chlamydia Condyloma acuminatum Gonorrhea Herpes HIV/AIDS Syphilis Tetanus TB Urinary tract infections Cystitis Pyelonephritis Urethritis
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Adapted from Finnegan 1979.

Obstetrical Complications

Abruptio placentae Chorioamnionitis Intrauterine death Intrauterine growth retardation Intrauterine passage of meconium Low Apgar scores Placental insufficiency	Postpartum hemorrhage Preeclampsia Premature labor/delivery Premature rupture of membranes Septic thrombophlebitis Spontaneous abortion
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Reprinted from *Obstetrics and Gynecology Clinics of North America*, 25(1),
Kaltenbach et al., Opioid dependence during pregnancy. Effects and man-
agement, pp. 139–151, 1998, with permission from Elsevier.

See TIP 43, pages 212–215.

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- Complete blood count with differential and platelets
- SMA-12 chemistry screen
- Hepatic panel (liver function tests)
- Hepatitis B surface antigen (full panel if positive)
- Hepatitis C antibody
- Rubella titer
- Serology (Venereal Disease Research Laboratory or Rapid Plasma Reagin tests)
- Sickle prep (if appropriate)
- Blood type; Rh and indirect Coombs Varicella (if unsure of history)
- HIV (with counseling)
- Urine tests
 - Urinalysis—routine and microscopic
 - Urine culture and sensitivity
 - Urine drug screen
- Tuberculin skin test (Mantoux)
- Alpha-fetoprotein between 15 and 21 weeks' gestation (optimal, 16 to 18 weeks)
- 1-hour, 50 milligrams (mg) glucose challenge test at 24 to 28 weeks' gestation (at initial visit if risk factors)
- Repeat complete blood count and serology at 24 to 28 weeks' gestation
- Group B Strep vaginal-rectal culture at 35 to 37 weeks' gestation

Reprinted from *Obstetrics and Gynecology Clinics of North America*, 25(1), Kaltenebach et al., Opioid dependence during pregnancy. Effects and management, pp. 139–151, 1998, with permission from Elsevier.

See TIP 43, pages 214–215.



Ordering Information

TIP 43

Medication-Assisted Treatment for Opioid Addiction in Opioid Treatment Programs

Three Ways to Obtain Free Copies of All TIP Products

1. Call SAMHSA's National Clearinghouse for Alcohol and Drug Information (NCADI) at **800-729-6686**, TDD (hearing impaired) **800-487-4889**.
2. Visit NCADI's Web site at **www.ncadi.samhsa.gov**.
3. Access TIPs online at **www.kap.samhsa.gov**.

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