

## KAP Keys Based on TIP 40

Clinical Guidelines for the Use of  
Buprenorphine in the Treatment  
of Opioid Addiction

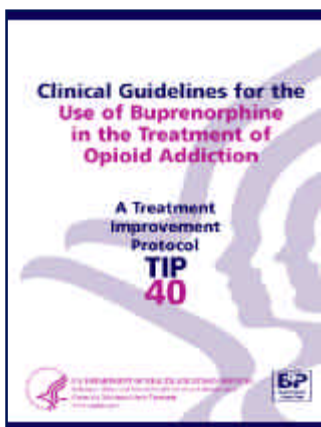
Knowledge Application Program

# KAP Keys

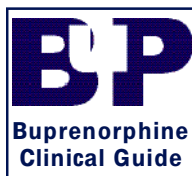
*For Physicians*

## Based on TIP 40

*Clinical Guidelines for the  
Use of Buprenorphine*



*in the  
Treatment  
of Opioid  
Addiction*



U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES  
Substance Abuse and Mental Health Services Administration  
Center for Substance Abuse Treatment  
[www.samhsa.gov](http://www.samhsa.gov)

## KAP Keys Based on TIP 40 Clinical Guidelines for the Use of Buprenorphine in the Treatment of Opioid Addiction

### Introduction

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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. These KAP Keys are based entirely on TIP 40 and are designed to meet the needs of the busy physician for concise, easily accessed “how-to” information.

For more information on the topics in these KAP Keys, readers are referred to TIP 40.

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

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**TIP 16:** *Alcohol and Other Drug Screening of Hospitalized Trauma Patients* (1995) **BKD164**

**TIP 24:** *A Guide to Substance Abuse Services for Primary Care Clinicians* (1997) **BKD234**

**TIP 28:** *Naltrexone and Alcoholism Treatment* (1998) **BKD268**

**TIP 43:** *Medication-Assisted Treatment for Opioid Addiction in Opioid Treatment Programs* (2005) **BKD524**

## Dosage Forms of Buprenorphine Available 1 in the United States (as of July 2004)

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Clinical Guidelines for the Use of Buprenorphine  
in the Treatment of Opioid Addiction

Medication	Trade Name	Dosage Form(s)	Indication	Company	FDA Approved for Opioid Addiction Treatment
Buprenorphine	Subutex®	2- or 8-mg sublingual tablets	Opioid addiction	Reckitt Benckiser	Yes
Buprenorphine/ naloxone combination	Suboxone®	2- or 8-mg sublingual tablets with buprenorphine/ naloxone in 4:1 ratio	Opioid addiction	Reckitt Benckiser	Yes
Buprenorphine	Buprenex®	Injectable ampules	Moderate-to-severe pain	Reckitt Benckiser	No
Buprenorphine	Buprenorphine injectable (generic)	Injectable ampules	Moderate-to-severe pain	Abbott Laboratories	No

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#### **Benzodiazepines and Other Sedative Drugs**

- Buprenorphine plus sedative-hypnotics (*including alcohol*) may cause serious depression of the central nervous system.
- If simultaneous treatment with buprenorphine and sedative-hypnotics is necessary, the doses of both medications may need to be lowered.

#### **Medications Metabolized by Cytochrome P450 3A4**

- Buprenorphine is metabolized by the cytochrome P450 3A4 enzyme system.
- Other medications that interact with this enzyme system should be used with caution in patients taking buprenorphine.
- A continuously updated list of cytochrome P450 3A4 drug interactions is available at [medicine.iupui.edu/flockhart/table.htm](http://medicine.iupui.edu/flockhart/table.htm).

#### **Opioid Antagonists**

- Buprenorphine treatment should not be combined with opioid antagonists (e.g., naltrexone).
- Naltrexone can precipitate an opioid withdrawal syndrome in patients maintained on buprenorphine.

#### **Opioid Agonists**

- Full agonists may not provide adequate analgesia in patients stabilized on maintenance buprenorphine.
- If use of a full mu agonist is needed for pain relief in a patient maintained on buprenorphine, the buprenorphine should be discontinued until the pain can be controlled without the use of opioid pain medications.

## Components of a Complete Substance Abuse Assessment

3

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- **Substance use history** (e.g., age of first use; substances used; change in effects over time; history of tolerance, overdose, withdrawal; attempts to quit; current problems with compulsivity or cravings)
- **Addiction treatment history** (e.g., previous treatments for addiction, types of treatments tried, outcomes of treatment attempts)
- **Psychiatric history** (e.g., patient's diagnoses, psychiatric treatments recommended/attempted, outcomes of treatments)
- **Family history** (e.g., substance use disorders in family, family medical and psychiatric histories)
- **Medical history** (e.g., detailed review of systems, past medical/surgical history, sexual history [for women, likelihood of pregnancy], current and past medications, pain history)
- **Social history** (e.g., quality of recovery environment, family/living environment, substance use by members of support network)
- **Readiness to change** (e.g., patient's understanding of his or her substance use problem, patient's interest in treatment now, whether treatment is coerced or voluntary)

## **Recommended Baseline Laboratory Evaluation 4 of Patients Who Are Addicted to Opioids**

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Clinical Guidelines for the Use of Buprenorphine  
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- Serum electrolytes
- BUN and creatinine
- CBC with differential and platelet count
- Liver function tests (GGT, AST, ALT, PT or INR, albumin)
- Lipid profile
- Urinalysis
- Pregnancy test (for women of childbearing age)
- Toxicology tests for drugs of abuse
- Blood alcohol level (using a breath-testing instrument or a blood sample)
- HIV antibody testing
- Hepatitis B virus (HBV) and hepatitis C virus (HCV) screens
- Serology test for syphilis—Venereal Disease Research Laboratories (VDRL)
- Purified protein derivative (PPD) test for tuberculosis, preferably with control skin tests

## Signs of Opioid Intoxication and Withdrawal

5

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Syndrome	Physical Findings
Opioid intoxication	Conscious Sedated, drowsy Slurred speech “Nodding” or intermittently dozing Memory impairment Mood normal to euphoric Pupillary constriction
Opioid overdose	Unconscious Pinpoint pupils Slow, shallow respirations (respirations below 10 per minute) Pulse rate below 40 per minute Overdose triad: apnea, coma, pinpoint pupils (with terminal anoxia: fixed and dilated pupils)

## Staging and Grading Opioid Withdrawal

6

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in the Treatment of Opioid Addiction

Stage of Withdrawal	Grade	Physical Signs/Symptoms
Early withdrawal (8–24 hours after last use)	1	Lacrimation and/or rhinorrhea Diaphoresis Yawning Restlessness Insomnia
	2	Dilated pupils Piloerection Muscle twitching Myalgia Arthralgia Abdominal pain
Fully developed withdrawal (1–3 days after last use)	3	Tachycardia Hypertension Tachypnea Fever Anorexia or nausea Extreme restlessness
	4	Diarrhea and/or vomiting Dehydration Hyperglycemia Hypotension Curled-up position



## Assessing Appropriateness for Buprenorphine Treatment

7

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#### **Before a candidate is approved for buprenorphine treatment for opioid addiction, he or she should, at a minimum,**

- Have an objectively ascertained diagnosis of opioid addiction (compulsive use of opioids despite harm), otherwise known as opioid dependence as defined in the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision*
- Be interested in treatment for opioid addiction
- Have no absolute contraindication (i.e., known hypersensitivity) to buprenorphine (or to naloxone if treating with the buprenorphine/naloxone combination)
- Be expected to be reasonably compliant with buprenorphine treatment
- Understand the risks and benefits of buprenorphine treatment
- Be willing to follow safety precautions for buprenorphine treatment
- Agree to buprenorphine treatment after a review of treatment options

#### **A candidate for buprenorphine treatment for opioid addiction should *not* have**

- Comorbid dependence on high doses of benzodiazepines or other central nervous system depressants (including alcohol)
- Significant untreated psychiatric comorbidity
- Active or chronic suicidal or homicidal ideation or attempts
- Multiple previous treatments for drug abuse with frequent relapses (except that multiple previous attempts at detoxification with subsequent relapse may be a strong indication for long-term maintenance treatment)
- Poor response to previous well-conducted attempts at buprenorphine treatment
- Significant medical complications
- Conditions that are outside the treating physician's expertise

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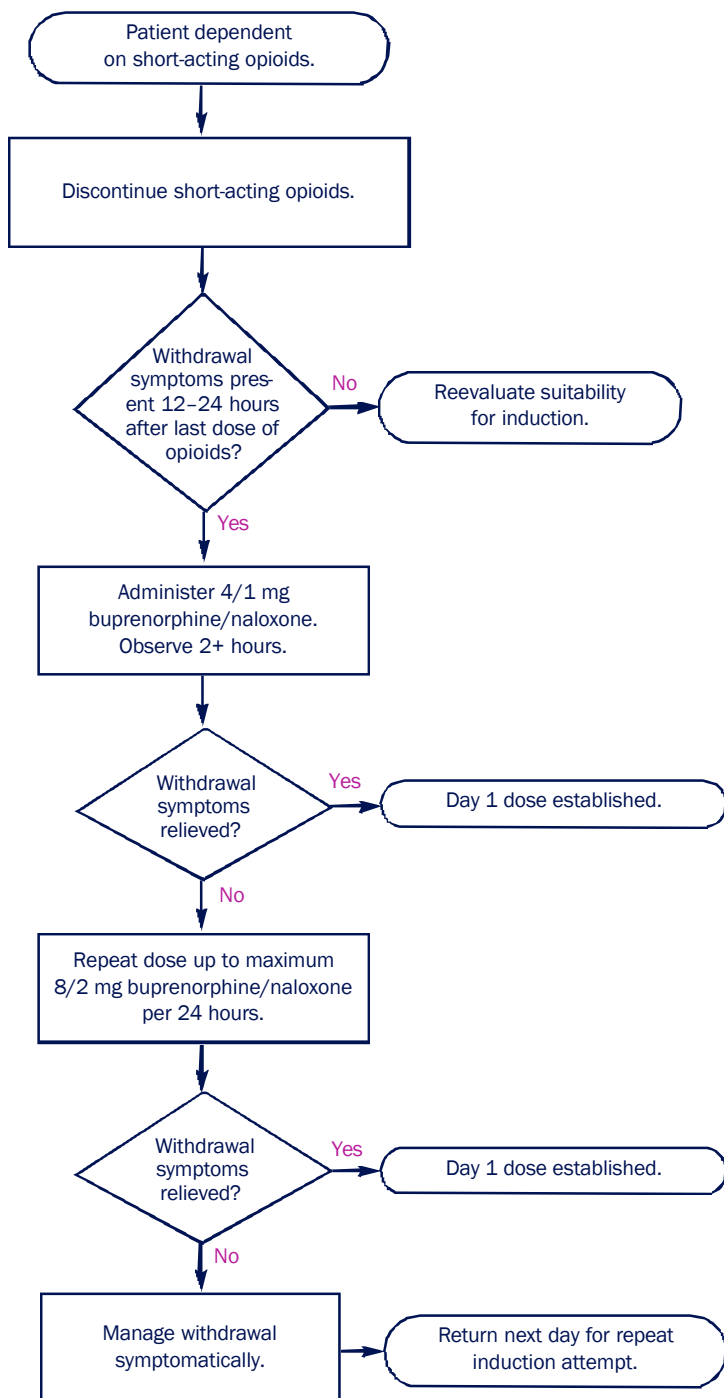
**Buprenorphine should be used with caution with patients who**

- Are being treated for seizure disorders
- Are taking HIV antiretroviral medications
- Have hepatitis or otherwise impaired hepatic function
- Are pregnant
- Are dependent on or abusing alcohol or drugs other than opioids

## Treatment Protocols Induction Days 1–2: Short-Acting Opioids

8

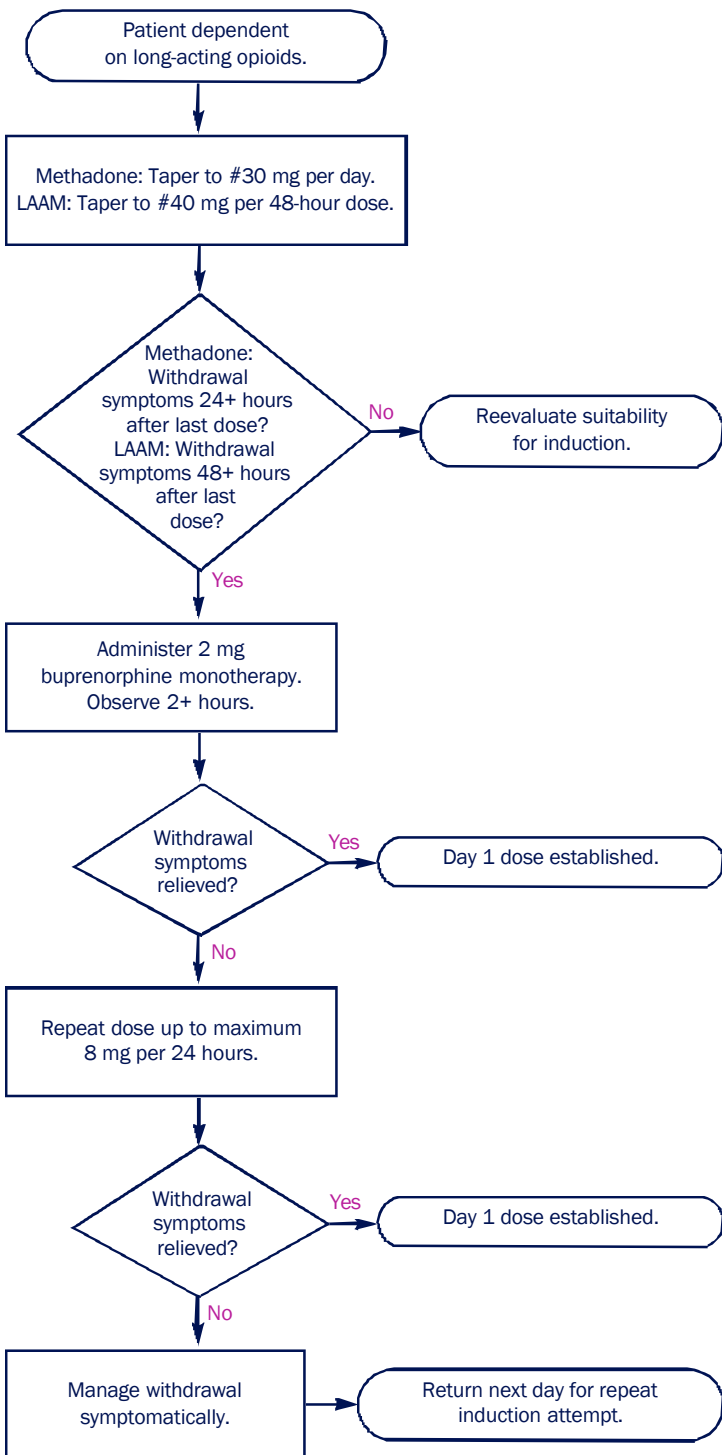
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## Induction Days 1–2: Long-Acting Opioids

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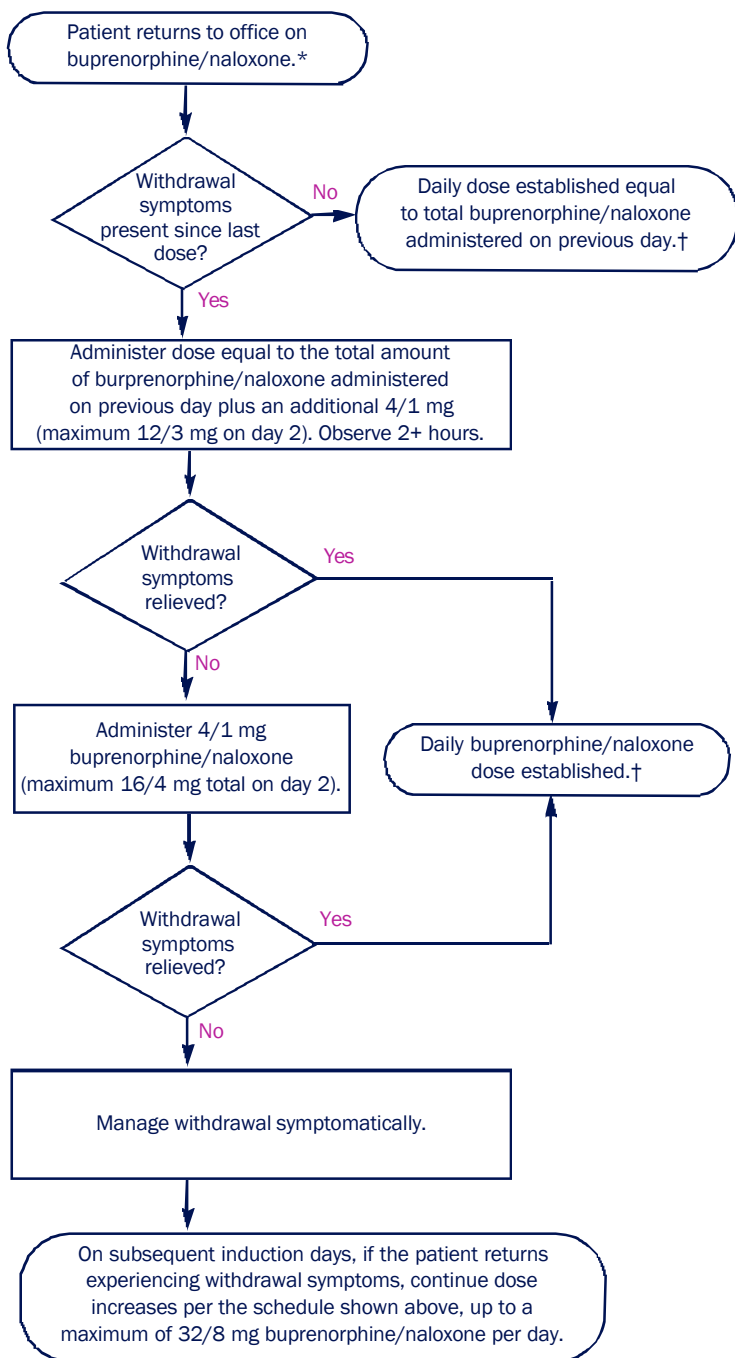
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## Treatment Protocols Induction Day 2 Forward

10

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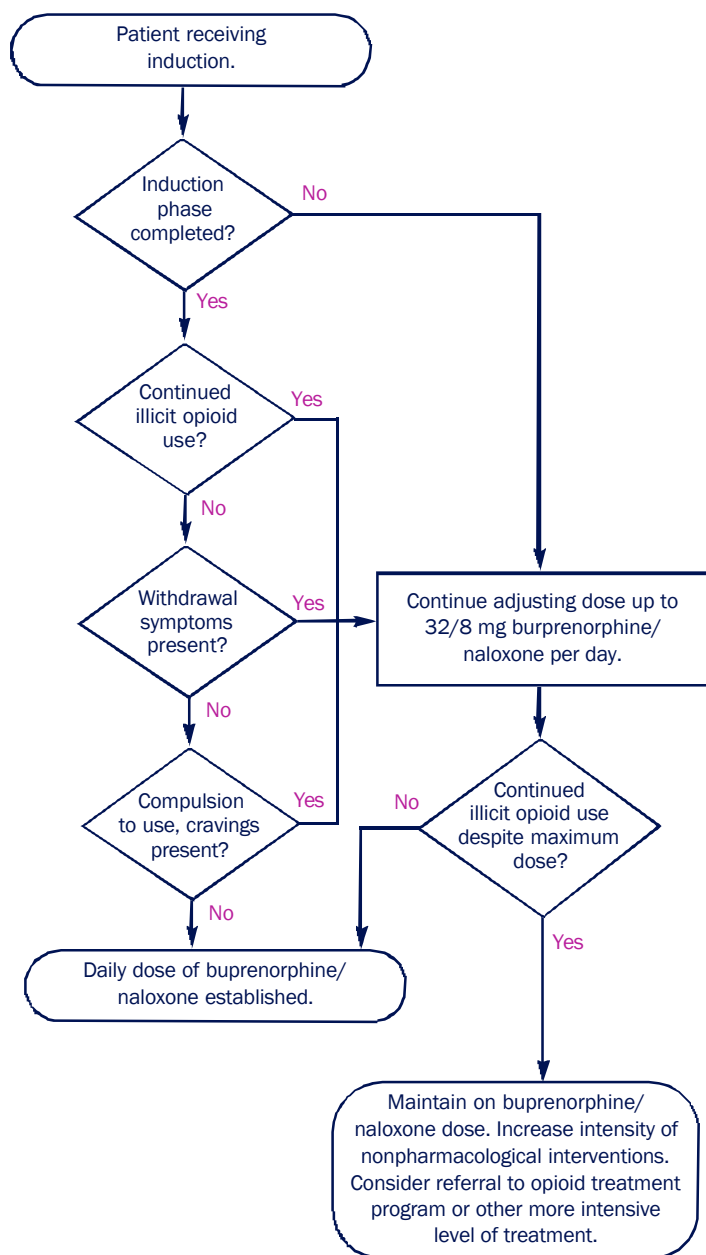


\*If buprenorphine monotherapy was administered on day 1, switch to burprenorphine/naloxone on day 2 (for a patient who is not pregnant).  
†Dose may be increased by 2/0.5–4/1 mg increments on subsequent days as needed for symptom relief. Target dose is 12/3–16/4 mg buprenorphine/naloxone per day by the end of the first week.

## Treatment Protocols Stabilization Phase

11

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Clinical Guidelines for the Use of Buprenorphine  
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Pharmacotherapy alone is rarely sufficient treatment for substance use disorders. Treatment outcome literature demonstrates that adding psychosocial treatment to buprenorphine treatment is correlated with better patient outcomes.

**Physicians considering making buprenorphine available to their patients should**

- Ensure that they are capable of providing psychosocial services, either in their own practices or through referrals to reputable behavioral health practitioners in their communities
- Consider providing office staff training in brief treatment interventions and motivational interviewing; this information could also enhance the effectiveness of treatment for other medical problems
- Be able to determine the intensity of services needed by individual patients and when those needs exceed what the physician can offer
- Work with qualified behavioral health practitioners to determine the intensity of services needed beyond the medical services
- Establish contingency plans for patients who do not follow through with referrals to psychosocial treatments



## Ordering Information

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### **TIP 40**

#### *Clinical Guidelines for the Use of Buprenorphine in the Treatment of Opioid Addiction*

### **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](http://www.ncadi.samhsa.gov)**.
3. Access TIPs online at **[www.kap.samhsa.gov](http://www.kap.samhsa.gov)**.

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