DEPARTMENT OF HEALTH & HUMAN SERVICES

Substance Abuse and Mental Health Services Administration

Center for Mental Health Services
Center for Substance Abuse Prevention
Center for Substance Abuse Treatment
Rockville MD 20857

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Dear Colleague:

The purpose of this letter is to advise all opioid treatment programs (OTPs) of concerns the Center for Substance Abuse Treatment (CSAT) has relative to methadone admission, dosing and induction practices. CSAT has obtained information from OTP inspections and published literature (Maxwell, 2005) that programs are relatively unaware of the risks associated with initial methadone dosing and the two-week induction process. Many programs appear to believe that the initial dose of methadone for all patients is 30 milligrams. In addition, some OTPs have incorporated "Standing Orders" that include automatic daily dose increases of methadone during patient induction to opioid dependency treatment.

SAMHSA cannot emphasize strongly enough that determining the admitting diagnosis, admitting the patient, and setting the initial dose must only be done by the OTP physician who possesses the demonstrated competency to diagnose and treat patients with opioid intoxication, dependency, and withdrawal, as well as opioid-related medical and psychiatric conditions. In determining the initial dose for each individual patient, the physician should consider factors such as body weight, size, other substance use and abuse, diet, co-occurring disorders (check for prescribed SSRIs, benzodiazepines, HIV medications, anti-seizure medication, etc.) and medical diseases, genetic factors, and tolerance. The drug labeling states that "methadone's pharmacokinetic properties, coupled with high inter-patient variability in its absorption, metabolism, and relative analgesic potency, necessitate a cautious and highly individualized approach to prescribing." Even though the Treatment Improvement Protocol (TIP #43) and drug labeling state that a typical first dose of methadone for a patient actively abusing opioids is 20 to 30 milligrams, some patients may require a much lower dose. According to 42 CFR 8.12 (h) (3) (ii), "...the initial dose of methadone **shall not exceed** 30 milligrams and the total dose for the first day shall not exceed 40 milligrams...." (emphasis added). The initial methadone dose should be appropriate for the individual patient, with the maximum initial dose being 30 mg. Clearly, a 30-mg dose should not be the initial dose for all patients.

Of note, there has been a rapid increase in the abuse of the opioid-type pain relieving medications. Typically, hydrocodone and oxycodone are the drugs of choice, and the resulting addiction is treated by the OTPs. These are short-acting opioids with a half-life of 2 to 4 hours. However, methadone has an elimination half-life that can vary from 8 to 59 hours depending on the individual being treated. Thus, methadone induction must be approached cautiously.

Because methadone overdose deaths have occurred in early treatment due to the drug's cumulative effects of the first several days, it is also important to be cautious when adjusting the dose. According to the drug labeling, the peak respiratory depressant effects of methadone typically occur later and persist longer than its peak analgesic

effects, which can contribute to cases of iatrogenic overdose, particularly during treatment initiation and dose titration. With repeated dosing, "methadone may be retained in the liver and released slowly, prolonging the duration of action despite low plasma concentrations." The drug labeling also states that "**steady-state concentrations are not usually attained until 3 to 5 days of dosing,**" and that doses "**will 'hold' for a longer period of time as tissue stores of methadone accumulate.**" Therefore, patients should be closely monitored during the induction phase, and the increase in dose should be under the close supervision of a physician as stated in 42 CFR 8.12 (h)(4), "Dosing and administration decisions shall be made by a program physician familiar with the most up-to-date product labeling."

For additional information or questions, please contact Jennifer Fan, Pharm.D., J.D., Public Health Advisor, at (240) 276-1759 or by e-mail at Jennifer.fan@samhsa.hhs.gov.

Sincerely,

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