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Guideline to Promote Prescription Safety of Sedative-Hypnotics for CBHS clients.

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OVERVIEW

GOAL

Promote prescription safety of sedative-hypnotics for CBHS clients. Sedative-hypnotics include the following:

- Benzodiazepines: alprazolam, chlordiazepoxide, clonazepam, diazepam, estazolam, oxazepam, lorazepam, temazepam, triazolam.
- Non-benzodiazepine hypnotics: zolpidem, zaleplon, eszopiclone.

CBHS approach to medication use: CBHS prescribers promote safe, patient-centered, effective prescribing practice in an equitable manner across our system. CBHS prescribers develop a trusting relationship that takes into account clients' values and progress in treatment, and enhances clients' ability to participate in shared decisions about care.

NEED FOR A GUIDELINE

Sedative-hypnotics are frequently used in our system.ⁱ Although DPH promotes integration of care across disciplines, CBHS prescribers may not be aware of clients' other prescriptions, overdose history or substance use history. Prescription poisoning accidents in San Francisco include opioids, benzodiazepines and other sedative-hypnotics.ⁱⁱ Discontinuation of inappropriate benzodiazepines is difficult to implement. The Medication Use Improvement Committee believes that guidelines can be useful in promoting effective and safe use of sedative-hypnotics and other medications across our system.

CLIENT-SPECIFIC RISKS

There are clinical characteristics that increase risk of side effects related to sedative-hypnotics. Current or past substance use history marks susceptibility to developing benzodiazepine use disorder.ⁱⁱⁱ Clients may then pose difficult behaviors, with early refills and requests for higher doses as the medication becomes ineffective at original doses. Presence of opioids or other sedatives such as alcohol can create synergistic sedation with dangerous respiratory depression. History of previous overdose marks high risk of recurrent overdose. Multiple prescription sources or unusually high doses from a single

source raise likelihood of stockpiling or possibility of illicit diversion which elevates community risk. Even patients who have been taking sedative-hypnotics for years might experience increase in risk if new medications are prescribed, if they develop lung disease, or in cases of intercurrent illness or surgery, or with increasing age. Inability to adhere to dosing instructions - for example in dementia or confusion - increases risk.

CBHS POPULATION

Most of CBHS clients have severe and persistent mental illness, and are indigent with respect to finances, housing, and other social resources. Persons with psychiatric conditions are more likely to be diagnosed with pain and more likely to receive opioid prescriptions.^{iv} Community mental health psychiatrists are consulted by primary care physicians for expert opinion and prescribing of sedative-hypnotics, in particular in their patients who are also on chronic long-term opioids. Many CBHS clients are homeless and otherwise disenfranchised, and engagement in care at CBHS clinics is important to maintain. Persons who are homeless and persons with psychiatric disorders have higher risk of overdose death.^v Some CBHS clients are vulnerable elders. The co-occurrence of substance use disorders and complex medical conditions is high. In such marginalized population the need for risk reduction is high. These client characteristics are taken into account by the Medication Use Improvement Committee in the guideline.

GUIDELINE

GENERAL STATEMENT OF GUIDELINE

Safety analysis is done in cases where sedative-hypnotics are under consideration by prescribers. Sedative-hypnotics are not started or re-started for clients with known risk factors. Sedative-hypnotics used acutely - for example in hospital settings to manage symptoms, or used for alcohol detoxification - are not continued after discharge. Sedative-hypnotic use is re-evaluated for clients with ongoing prescriptions who have or who develop risk factors. Exceptions to the above include clear documentation of ongoing benefit that outweighs known risk, along with review by prescriber colleagues in some cases.

SPECIFICS OF GUIDELINE

- I. Recommendations for all clients for whom sedative-hypnotics are considered or prescribed:
 - a. Assess and document risk of misuse, overdose or sedation. Include the following:
 - i. CURES report to show other prescribed scheduled substances
 - ii. Current or previous substance or alcohol use disorder
 - iii. History of overdose
 - iv. Fall risk (age, medical fragility)^{vi}
 - v. Memory problems^{vii}
 - vi. Sleep apnea.^{viii}
 - b. Use non-medical and/or non-addictive anxiolytics as the first approach in treating anxiety.

- c. Whenever sedative-hypnotics are prescribed, provide informed consent regarding dangers.
 - d. Limit initial sedative-hypnotic prescriptions in quantity and dose.
- II. Recommendations for clients who have ongoing prescriptions of sedative-hypnotics (longer than two weeks):
- a. Document justification for use of sedative-hypnotics, and periodically re-assess and document risks.
 - b. Develop formalized treatment agreement with the client, and consider short, more frequent visits and pill counts.
 - c. Offer client transfer to non-medical and/or non-addictive anxiolytic treatments when indicated.
 - d. If taper decision is made, offer psychosocial support and education during taper process.
- III. Recommendations for clients who are known to be on opioids, and for whom prescription of sedative-hypnotics are being considered:
- a. Treatment with sedative-hypnotics is extremely rare. Include clearly documented justification and evaluation of risk, and sign off by prescriber colleagues.
 - b. Prescribe or provide naloxone rescue kit and instructions.
 - c. Provide education about risk of respiratory depression and sedation.
 - d. Coordinate care with opioid prescriber. (In the case of methadone maintenance this requires written consent from the client.)

CLIENT EDUCATION

CBHS clients are given information about risk of sedative-hypnotics, and the existence of the guidelines. The purpose of this information is to support shared decisions, and to keep the client engaged in helpful treatment.

GUIDELINE REVIEW

Benefit as well as unintended consequences of the guidelines are monitored by prescription reports, chart reviews and case conferences. Part of the purpose of review is to support prescribers who may be having difficulty implementing the guidelines.

UNSPECIFIED ELEMENTS

This guideline does not include specifics of the following recommendations:

- Dose or quantity limits,
- Prescriber colleague reviews,
- Psychosocial support given during tapers,
- Frequency of visits or periodic reviews of risks and benefits on ongoing treatment

ⁱ Clonazepam is the third most prescribed drug in CBHS clinics, after risperidone and trazodone. In December 2013, there were 1549 active clonazepam prescriptions in CBHS clinics, with an average daily dose of 1.72mg (Data reported from Infoscriber by James Gasper, CBHS Pharmacy)

ⁱⁱ Locally: Drug Abuse Warning Network (DAWN) reported 171 drug-related unintentional deaths in 2010 in San Francisco (Population 815, 266, rate 21/100,000). Among those deaths, 16% (28/171) were due to benzodiazepines, and 58% (99/171) to prescription opioids. Benzodiazepines were also mentioned as a contributing factor in 30% of the prescription opioid deaths. (SAMHSA, *Drug Abuse Warning Network, 2010: Area Profiles of Drug-Related Mortality*. HHS Publication No. (SMA) 12-4699, DAWN Series D-36. Rockville, MD: Substance Abuse and Mental Health Services Administration, 2012). Nationwide: Out of the 22,000 prescription drug overdose deaths in 2010, 75% involved opioid analgesics and 30% involved benzodiazepines. Furthermore, benzodiazepines were involved in 30% of the opioid analgesic deaths and opioid analgesics were involved in 77% of the benzodiazepine fatalities. Drug overdoses now account for more deaths than motor vehicle accidents in the United States. (Jones CM, et al. Pharmaceutical overdose deaths, United States. *JAMA* 309:657-659, 2013.)

ⁱⁱⁱ History of SUD, in particular opioids, alcohol or other sedative-hypnotics, even when not currently active is considered a “strong relative contraindication” to co-prescription of benzodiazepines and opioids, and if deemed absolutely necessary, dosage of each to be kept at a minimum to lower risk. (Reisfield GM, et al. Benzodiazepines in long term opioid therapy. *Pain Medicine* 14(10):1441-6, 2013)

^{iv} Depressive and anxiety disorders are more common and more strongly associated with prescribed opioid use than drug abuse disorders (Sullivan MD, et al. Regular use of prescribed opioids: association with common psychiatric disorders. *Pain* 119(1-3):95-103, 2005). After controlling for demographic and clinical factors, youth with pre-existing mental health diagnoses had a 2.4-fold increased risk of subsequently receiving chronic opioids versus no opioids (OR:2.36, 95% CI = 1.73–3.23) and a 1.8-fold increased likelihood of receiving chronic opioids versus some opioids (OR: 1.83, 95% CI= 1.34–2.50) (Richardson LP, et al. Mental health disorders and long-term opioid use among adolescents and young adults with chronic pain. *J Adolesc Health* 50(6):553–558, 2012).

^v Overdose and suicide mortality rates are higher in homeless and previously homeless adults, with overdose being the leading cause of death in this group (Baggett TP, et al. Mortality among homeless adults in Boston: shifts in causes of death over a 15-year period. *JAMA Intern Med* 173(3):189–195, 2013).

^{vi} Use of sedative-hypnotics may predispose to fractures and falls in those over 65 years of age. (Li L, et al. Opioid use for noncancer pain and risk of fracture in adults: a nested case-control study using the general practice research database. *Am J Epidemiol* 178: 559-69, 2013 and Nurminen J, et al., Opioids, antiepileptic and anticholinergic drugs and the risk of fractures in patients 65 years of age and older: a prospective population-based study. *Age Ageing* 42:318-24, 2013).

^{vii} Review of effects of sedative-hypnotics on memory (Chavant F, et al. Memory disorders associated with consumption of drugs: updating through a case/noncase study in the French Pharmacovigilance Database. *Br J Clin Pharmacol* 72:6,898–904.

^{viii} Snoring and obstructive apnea can be worsened with benzodiazepine as well as with opioids (Lu B, et al: Sedating medications and undiagnosed obstructive sleep apnea: physician determinants and patient consequences. *J Clin Sleep Med*. 15;1(4):367-71, 2005).