STANDING ORDERS

Naloxone is indicated for reversal of opioid overdose in the setting of respiratory depression or unresponsiveness. It may be delivered intranasally with the use of a mucosal atomizer device or intramuscularly with a syringe. This standing order is current as of August 2011. All standing orders should be reviewed carefully against the most current recommendations and may be revised by the clinician signing them. Naloxone is indicated for treatment/reversal of opioid overdose.

1. This standing order authorizes the DOPE Project to maintain supplies of Injectable naloxone kits for the purposes of distributing them as part of this collaboration with SDPH.

2. This standing order authorizes DOPE Project Overdose Prevention Educators to possess and distribute naloxone to Opioid Overdose Responders who have completed an overdose training and required documentation.

3. This standing order authorizes Opioid Overdose Responders, trained by DOPE Project Overdose Prevention Educators, who are trained employees of the DOPE Project, to possess and administer naloxone to a person who is experiencing an opioid overdose.

Naloxone - Clinical Pharmacology:

Complete or Partial Reversal of Opioid Depression

Naloxone prevents or reverses the effects of opioids including respiratory depression, sedation and hypotension. Also, Naloxone can reverse the psychotomimetic and dysphoric effects of agonist-antagonists such as pentazocine. Naloxone is an essentially pure opioid antagonist, i.e., it does not possess the “agonistic” or morphine-like properties characteristic of other opioid antagonists. When administered in usual doses and in the absence of opioids or agonistic effects of other opioid antagonists, it exhibits essentially no pharmacologic activity.

Naloxone has not been shown to produce tolerance or cause physical or psychological dependence. In the presence of physical dependence on opioids, Naloxone will produce withdrawal symptoms. However, in the presence of opioid dependence, opioid withdrawal symptoms may appear within minutes of Naloxone administration and subside in about 2 hours. The severity and duration of the withdrawal syndrome are related to the dose of Naloxone and to the degree and type of opioid dependence. While the mechanism of action of Naloxone is not fully understood, in vitro evidence suggests that Naloxone antagonizes opioid effects by competing for the μ, κ and σ opioid receptor sites in the CNS, with the greatest affinity for the μ receptor.

Indications and Usage for Naloxone

Naloxone is indicated for the complete or partial reversal of opioid depression, including respiratory depression, induced by natural and synthetic opioids, including propoxyphene, methadone and certain mixed agonist-antagonist analgesics: nalbuphine, pentazocine, butorphanol, and cyclazocine. Naloxone is also indicated for diagnosis of suspected or known acute opioid overdosage.

Contraindications:

Naloxone is contraindicated in patients known to be hypersensitive to naloxone hydrochloride or to any of the other ingredients in Naloxone.

Warnings:

Repeat Administration

The patient who has satisfactorily responded to Naloxone should be kept under continued surveillance and repeated doses of Naloxone should be administered, as necessary, since the duration of action of some opioids may exceed that of Naloxone.

Respiratory Depression due to Other Drugs

Naloxone is not effective against respiratory depression due to non-opioid drugs and in the management of acute toxicity caused by levopropoxyphene. Reversal of respiratory depression by partial agonists or mixed agonist/antagonists, such as buprenorphine and pentazocine, may be incomplete or require higher doses of naloxone. If an incomplete response occurs, respirations should be mechanically assisted as clinically indicated.
**Precautions:**

**General**
In addition to Naloxone, other resuscitative measures such as maintenance of a free airway, artificial ventilation, cardiac massage, and vasopressor agents should be available and employed when necessary to counteract acute opioid poisoning.

**Drug Interactions**
Large doses of naloxone are required to antagonize buprenorphine since the latter has a long duration of action due to its slow rate of binding and subsequent slow dissociation from the opioid receptor. Buprenorphine antagonism is characterized by a gradual onset of the reversal effects and a decreased duration of action of the normally prolonged respiratory depression. The barbiturate methohexital appears to block the acute onset of withdrawal symptoms induced by naloxone in opioid users.

**Carcinogenesis, Mutagenesis, Impairment of Fertility**
Studies in animals to assess the carcinogenic potential of Naloxone have not been conducted. Naloxone was weakly positive in the Ames mutagenicity and in the in vitro human lymphocyte chromosome aberration test but was negative in the in vitro Chinese hamster V79 cell HGPRT mutagenicity assay and in the in vivo rat bone marrow chromosome aberration study. Reproduction studies conducted in mice and rats at doses 4-times and 8-times, respectively, the dose of a 50 kg human given 10 mg/day (when based on surface area or mg/m2), demonstrated no embryotoxic or teratogenic effects due to Naloxone.

**Use in Pregnancy:**

**Teratogenic Effects: Pregnancy Category C**
Teratology studies conducted in mice and rats at doses 4-times and 8-times, respectively, the dose of a 50 kg human given 10 mg/day (when based on surface area or mg/m2), demonstrated no embryotoxic or teratogenic effects due to Naloxone. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, Naloxone should be used during pregnancy only if clearly needed.

**Non-teratogenic Effects**
Risk-benefit must be considered before Naloxone is administered to a pregnant woman who is known or suspected to be opioid-dependent since maternal dependence may often be accompanied by fetal dependence. Naloxone crosses the placenta, and may precipitate withdrawal in the fetus as well as in the mother. Patients with mild to moderate hypertension who receive naloxone during labor should be carefully monitored as severe hypertension may occur.

**Nursing Mothers**
It is not known whether Naloxone is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Naloxone is administered to a nursing woman.

**Geriatric Use**
Clinical studies of Naloxone did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

**Adverse Reactions:**

**Opioid Dependence:**
Abrupt reversal of opioid effects in persons who are physically dependent on opioids may precipitate an acute withdrawal syndrome which may include, but is not limited to, the following signs and symptoms: body aches, fever, sweating, runny nose, sneezing, piloerection, yawning, weakness, shivering or trembling, nervousness, restlessness or irritability, diarrhea, nausea or vomiting, abdominal cramps, increased blood pressure, tachycardia.

**Drug Abuse and Dependence:**
Naloxone is an opioid antagonist. Physical dependence associated with the use of Naloxone has not been reported. Tolerance to the opioid antagonist effect of Naloxone is not known to occur.
**Naloxone Dosage and Administration:**

Through a collaboration with the San Francisco Department of Public Health, Housing and Urban Health Clinic, the Drug Overdose Prevention and Education (DOPE) Project will train opioid users and their contacts in the use of Naloxone for the reversal of opioid overdose.

Program participants must meet all of the following criteria:
- Current opioid users, individuals with a history of opioid use, or someone with frequent contact with opioid users;
- Risk for overdose or likelihood of contact with someone at risk, by report or history;
- Able to understand and willing to learn the essential components of Overdose Prevention and Response and Naloxone administration.

A trained opioid Overdose Prevention Educator from the DOPE Project will complete a Registration form and review it with the prospective program participant to make a determination about the individual’s eligibility for the program using the above mentioned criteria. The trainer will then engage the participant in a brief educational program about overdose prevention and response.

The educational program components will include:
- Overdose prevention techniques
- Recognizing signs and symptoms of overdose
- Calling 911
- Airway and breathing assessment
- Rescue breathing
- Naloxone storage, carrying, and administration
- Post-overdose follow-up and care

Upon completion of the program, the participant will be assessed by the trainer on their understanding of the information and their comfort with the basic components of overdose response. Naloxone will be dispensed to trained program participants who will carry and use Naloxone to treat individuals experiencing an opioid overdose. The Medical Director will review completed forms at least every other month.

**Order to dispense:**

Upon participant completion of Overdose Prevention Training Program and documentation of competency,

**Dispense for use by a trained program participant:**

Two 1cc Naloxone Hydrochloride (concentration .4mg/ml) vials and two 3ml syringes with 25g 1” needles.

**Injectable Naloxone kits** contain the following at a minimum:
- Two 1cc Naloxone Hydrochloride (concentration .4mg/ml)
- Two 3ml syringes with 25g 1” needles.
- Overdose prevention pamphlet
- Step-by-step instructions for administration of naloxone

**Directions for administration of injectable naloxone:** Administer naloxone to a person suspected of an opioid overdose with respiratory depression or unresponsiveness as follows:

1. Pop off the orange cap from the vial of naloxone, exposing the rubber seal.
2. Open one intramuscular syringe with needle and twist the needle component to secure it to the syringe.
3. Draw the entire contents of the 1cc vial of naloxone into the syringe.
4. Inject the naloxone into the muscle of the upper arm, upper thigh, or upper, outer quadrant of the buttocks.
5. Resume rescue breathing until the overdosing person begins to breathe on their own and shows signs of responsiveness.
6. Administer second dose (1cc) of naloxone if there is no response after approximately 2-3 minutes.
7. Remain with the person until he or she is under care of a medical professional, like a physician, nurse or emergency medical technician.
8. Do not administer naloxone to a person with known hypersensitivity to naloxone.
**Refills**: to be provided to registered participants upon completion of follow-up assessment by program staff of the Drug Overdose Prevention and Education Project.

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**Physician’s Signature and License No.**

**Date**

**Physician’s Name (Print)**

**Order Expiration Date**

**Definitions** (for further detail about the program, see DOPE Project Program Guidelines)

**The DOPE Project**: A program contracted with the San Francisco Department of Public Health’s Community Behavioral Health Services to provide overdose prevention and response education in the community and train opioid overdose responders in accordance with these guidelines.

**DOPE Project Overdose Prevention Educator**: A person trained by the DOPE Project Manager, under the supervision of the Medical Director, to conduct Opioid Overdose Responder trainings.

**Opioid Overdose Responder**: A person, who successfully completed an Opioid Overdose Prevention Training within the past two years, provided the training was presented by an approved DOPE Project Overdose Prevention Educator.

**Medical Director**: A physician licensed by the State of California and who holds a valid DEA license and who is assigned responsibility by the Department of Public Health to provide medical oversight to the public health program in general, including clinical oversight to the DOPE Project, review and approval of the curriculum and distribution of naloxone to the DOPE Project Manager and Overdose Prevention Educators.

**References**:


30. Take-home naloxone to reduce heroin death 1831© 2005 Society for the Study of Addiction Addiction, 100, 1823–1831