IMPORTANT SAFETY INFORMATION

INDICATIONS AND USAGE

Nalmefene Hydrochloride Injection is indicated for the complete or partial reversal of opioid drug effects, including respiratory depression, induced by either natural or synthetic opioids.

Nalmefene Hydrochloride Injection is indicated in the management of known or suspected opioid overdose.

CONTRAINDICATION

Nalmefene Hydrochloride injection is contraindicated in patients with a known hypersensitivity to the product.

WARNINGS AND PRECAUTIONS

Use of Nalmefene Hydrochloride injection in Emergencies
Nalmefene Hydrochloride injection, like all drugs in this class, is not the primary treatment for ventilatory failure. In most emergency settings, treatment with Nalmefene Hydrochloride injection should follow, not precede, the establishment of a patent airway, ventilatory assistance, administration of oxygen, and establishment of circulatory access.

Risk of Recurrent Respiratory Depression
Accidental overdose with long acting opioids [such as methadone and *levo*-alpha-acetylmethadol (LAAM)] may result in prolonged respiratory depression. Respiratory depression in both the postoperative and overdose setting may be complex and involve the effects of anesthetic agents, neuromuscular blockers, and other drugs. While Nalmefene Hydrochloride injection has a longer duration of action than naloxone in fully reversing doses, the physician should be aware that a recurrence of respiratory depression is possible, even after an apparently adequate initial response to Nalmefene Hydrochloride injection treatment.

Patients treated with Nalmefene Hydrochloride injection should be observed until, in the opinion of the physician, there is no reasonable risk of recurrent respiratory depression.

Cardiovascular Risks with Narcotic Antagonists
Pulmonary edema, cardiovascular instability, hypotension, hypertension, ventricular tachycardia, and ventricular fibrillation have been reported in connection with opioid reversal in both postoperative and emergency department settings. In many cases, these effects appear to be the result of abrupt reversal of opioid effects.

Although Nalmefene Hydrochloride injection has been used safely in patients with pre-existing cardiac disease, all drugs of this class should be used with caution in patients at high cardiovascular risk or who have received potentially cardiotoxic drugs

Risk of Precipitated Withdrawal
Nalmefene Hydrochloride injection, like other opioid antagonists, is known to produce acute withdrawal symptoms and, therefore, should be used with extreme caution in patients with known physical dependence on opioids or following surgery involving high doses of opioids. Imprudent use or excessive doses of opioid antagonists in the postoperative setting has been

associated with hypertension, tachycardia, and excessive mortality in patients at high risk for cardiovascular complications.

Incomplete Reversal of Buprenorphine
Preclinical studies have shown that nalmefene at doses up to 10 mg/kg (437 times the maximum recommended human dose) produced incomplete reversal of buprenorphine-induced analgesia in animal models. This appears to be a consequence of a high affinity and slow displacement of buprenorphine from the opioid receptors. Hence, Nalmefene Hydrochloride injection may not completely reverse buprenorphine-induced respiratory depression.

Use in Pediatric Patients

Safety and effectiveness of nalmefene hydrochloride injection in pediatric patients have not been established.

ADVERSE REACTIONS

The most common adverse reactions (>1%) reported in clinical trials with nalmefene injection were nausea (18%), vomiting (9%), tachycardia (5%), hypertension (5%), postoperative pain (4%), fever (3%), and dizziness (3%).

To report SUSPECTED ADVERSE REACTIONS, contact Purdue Pharma L.P. at 1-888-726-7535 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Please read Prescribing Information available at: https://www.accessdata.fda.gov/spl/data/d4bb0797-a4ed-4ed4-9904-604433eea4ff/d4bb0797-a4ed-4ed4-9904-604433eea4ff.xml