



Knoa Pharma Medical Affairs Request for Proposal

Knoa Pharma seeks proposals for Investigator Initiated Research (IIR) examining injectable nalmefene as an alternative for continuous naloxone infusions in hospital settings

Background	The FDA approval of Nalmefene HCl Injection has given healthcare professionals an additional treatment option for the management of known or suspected opioid overdose. In the current fentanyl-driven overdose landscape, recurrent or refractory respiratory depression may outlast bolus naloxone, prompting use of continuous naloxone infusion (CNI) in hospital settings despite limited real-world evidence and potential association with greater healthcare resource utilization.¹ Nalmefene HCl injection, with a long duration of action, may be a suitable alternative to CNI when treating opioid toxicity in selected patients.¹
Study Objectives	To evaluate the use of Nalmefene HCl Injection as an alternative or in comparison to the use of continuous naloxone infusion for the treatment of opioid toxicity in hospital settings. Studies that examine patient outcomes, treatment characteristics, safety, hospital admission rates and resource utilization are of particular interest.
Instructions for submitting a research proposal	Sponsor investigator applicants must submit their CV and a brief Letter of Intent (i.e., 1-2 pages) outlining the study concept via email to iirprogram@pharma.com by 5:00 PM ET October 30, 2026. The Letter of Intent should include: » Sponsor/investigator CV » Institutional affiliation/Study Sites » Research Objectives » Study design, methods, target populations, endpoints and intended analyses » Estimated study duration and preliminary budget requirements » Anticipated drug supply required and any funding request
Proposal Review and Response	Applicant proposals will be evaluated by a medical and scientific review committee. Selection of proposals will be based on scientific merit, feasibility, and investigator/site qualifications along with a focus on care innovation, cost-efficiency, and translatability to medical practice. Following the initial Letter of Intent, a full study proposal will be requested from selected applicants for final review, which must include a line-item budget reflective of the fair market costs for executing the proposed research. Financial support and/or drug supply will be issued based upon a fully executed agreement. All approved projects are expected to result in publication of findings in a peer-reviewed journal. Sponsor Investigators must be willing to assume regulatory responsibility for the research including obtaining an IND or exemptions granted by FDA, as applicable.

Please see Nalmefene HCl Injection Important Safety Information below and Full Prescribing Information [Here](#)

IMPORTANT SAFETY INFORMATION AND INDICATION ABOUT NALMEFENE HCL INJECTION²

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%).

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.

Please consult the Nalmefene HCl Injection [Full Prescribing Information](#) for complete product information.

References:1. Seltzer J, Moriguchi R, Lucarelli S, Stevens CA. Naloxone Infusions for Opioid Overdose: A 10-Year Retrospective Analysis. *J Emerg Med.*2026;86, 45-51.; 2. Nalmefene HCl Injection [Full Prescribing Information]. Stamford, CT: Knoa Pharma LLC.

Please see Nalmefene HCl Injection Full Prescribing Information [Here](#)

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