Naloxone hydrochloride 1mg/ml solution for injection
Prescribing Information

Please refer to the Summary of Product Characteristics (SmPC) before prescribing.
Presentation: Sterile, isotonic solution for injection in a glass prefilled syringe, containing 1mg of naloxone hydrochloride per ml of solution. **Indications:** The complete or partial reversal of opioid depression, including mild to severe respiratory depression induced by natural and synthetic opioids, including dextropropoxyphene, methadone and certain mixed agonist/antagonist analgesics: nalbuphine and pentazocine. It may also be used for the diagnosis of suspected acute opioid overdosage. To counteract respiratory and other CNS depression in the new-born resulting from the administration of analgesics to the mother during childbirth. **Dosage and administration:** Intravenous, intramuscular or subcutaneous injection, or intravenous infusion. Intravenous infusion: naloxone may be diluted for intravenous infusion in normal saline (0.9%) or 5% dextrose in water or saline. The rate of administration should be titrated in accordance with the patient's response to both naloxone infusion and to any previous bolus doses administered. *Adults - Opioid overdose (known or suspected):* Initially 400 to 2000 micrograms IV. The dose may be repeated at 2 to 3 minute intervals if the desired degree of counteraction and improvement in respiratory function is not obtained. If no response is observed after 10mg, then the diagnosis should be questioned. Give IM or SC if the IV route is not feasible. The duration of action of certain opioids can outlast that of an IV bolus of naloxone (eg, dextropropoxyphene, dihydrocodeine and methadone); in situations where one of these opioids is known or suspected, it is recommended that an infusion of naloxone be used to produce sustained antagonism to the opioid without repeated injection. *Post-operative use:* Titrate dose according to respiratory response. 100-200micrograms IV (approximately 1.5-3 micrograms/kg body weight) is usually sufficient, however a full two minutes should be allowed between each 100 micrograms increment of naloxone administered. Further intramuscular doses may be needed within one to two hours. Alternatively, give naloxone as an IV infusion. *Paediatric population:* The usual initial dose in children is 10 micrograms/kg body weight given IV. If this dose does not result in the desired degree of clinical improvement, a subsequent dose of 100 micrograms/kg of bodyweight may be administered. Naloxone may be required by infusion as described above. If an IV route of administration is not feasible, naloxone may be administered IM or SC in divided doses. *Neonates:* Prior to administration, an adequate airway should be established. Administer 10 micrograms/kg bodyweight IV, IM or SC; if required, repeat dose at 2 to 3 minute intervals. Alternatively, give a single dose of 200 micrograms, approximately 60micrograms/kg bodyweight IM at birth. The onset of action is slower following IM injection, and care should be taken for those neonates needing naloxone infusion in saline to avoid excessive sodium intake. *Elderly:* No specific studies. **Contra-Indications:** Hypersensitivity to the drug or to any of the excipients. **Warnings and precautions:** Administer cautiously to patients who have received large doses of opioids or to those physically dependent on opioids, since rapid reversal of opioid effects by naloxone may precipitate an acute withdrawal syndrome. The same caution is needed when giving naloxone to neonates delivered of such patients. Hypertension, cardiac arrhythmias, pulmonary oedema and cardiac arrest have been described. Signs and symptoms of opioid withdrawal in physically dependent patients may occur, as well as in neonates. Patients who have responded satisfactorily to naloxone should be kept under observation. Repeated doses of naloxone may be necessary since the duration of action of some opioids may exceed that of naloxone. Naloxone is not effective against respiratory depression caused by non-opioid drugs. Reversal of buprenorphine-induced respiratory depression may be incomplete. If an incomplete response occurs, respiration should be mechanically assisted. Abrupt postoperative reversal of opioid depression may result in nausea, vomiting, sweating, tremulousness, tachycardia, increased blood pressure, seizures, ventricular tachycardia and fibrillation, pulmonary oedema and cardiac arrest which may result in death. Several instances of hypotension, hypertension, ventricular tachycardia and fibrillation, pulmonary oedema and cardiac arrest have been reported in postoperative patients. Death, coma and encephalopathy have been reported as sequelae of these events. Although a direct cause and effect relationship has not been established, naloxone should be used with caution in patients with pre-

existing cardiac disease or patients who have received medications with potential adverse cardiovascular effects, such as hypotension, ventricular tachycardia or fibrillation and pulmonary oedema. 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 poisoning. *Renal Insufficiency/Failure***:** Caution should be exercised, and patients monitored when naloxone is administered to this patient population. *Liver disease:* Caution should be exercised when naloxone is administered to a patient with liver disease. This medicinal product contains less than 1 mmol sodium (23 mg) per dose, i.e. essentially 'sodium- free'. **Consult SmPC for further information. Interactions:** The effect of naloxone hydrochloride is due to the interaction with opioids and opioid agonists. When administered to subjects dependent on opioids, in some subjects the administration of naloxone hydrochloride can cause pronounced withdrawal symptoms. Hypertension, cardiac arrhythmias, pulmonary oedema and cardiac arrest have been described. With a standard naloxone hydrochloride dose there is no interaction with barbiturates and tranquillizers. Data on interaction with alcohol are not unanimous. In patients with multi intoxication as a result of opioids and sedatives or alcohol, depending on the cause of the intoxication, one may possibly observe a less rapid result after administration of naloxone hydrochloride. When administering naloxone hydrochloride to patients who have received buprenorphine as an analgesic complete analgesia may be restored. It is thought that this effect is a result of the arch-shaped dose-response curve of buprenorphine with decreasing analgesia in the event of high doses. However, reversal of respiratory depression caused by buprenorphine is limited. Severe hypertension has been reported on administration of naloxone hydrochloride in cases of coma due to a clonidine overdose. **Pregnancy and lactation:** *Pregnancy***:** The safety of this medicinal product for use in human pregnancy has not been established. Animal studies have shown reproductive toxicity (see section 5.3). The potential risk for humans is unknown. The medicinal product should not be used during pregnancy unless clearly necessary. In a pregnant woman who is known or suspected to be opioid-dependent, risk benefit must be considered before naloxone is administered, since maternal dependence may be accompanied by foetal dependence. In this type of circumstance, the neonate should be monitored for respiratory rate and signs of opioid withdrawal. *Use in Labour and Delivery*: naloxone may be administered to mothers during the second stage of labour to correct respiratory depression caused by opioids used to provide obstetrical analgesia. It is not known if naloxone affects the duration of labour and/or delivery. *Breast-feeding*: 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 mother. Therefore, breast-feeding should be avoided for 24 hours after treatment. **Effects on ability to drive and use machines**: Patients who have received naloxone hydrochloride to reverse the effects of opioids should be warned to avoid road traffic, operate machinery or engage in other activities demanding physical or mental exertion for at least 24 hours, since the effect of the opioids may return. **Undesirable effects:** *Very common (≥ 1/10):* Nausea. *Common (≥ 1/100, < 1/10):* dizziness, headache. Tachycardia. Hypotension, hypertension and cardiac arrhythmia (including ventricular tachycardia and fibrillation) have also occurred with the postoperative use of naloxone hydrochloride, adverse cardiovascular effects have occurred most frequently in postoperative patients with a pre-existing cardiovascular disease or in those receiving other drugs that produce similar adverse cardiovascular effects. Vomiting. Postoperative pain. **Refer to the SmPC for the full list of side effects. Overdose**: refer to the SmPC for general information and patient management. **Product Licence Number:** PL 12064/0060. **Product Licence Holder:** Aurum Pharmaceuticals Ltd, Bampton Road, Romford, RM3 8UG. **Basic NHS Price:** £16.80. **Legal Category:** POM. **Further information:** Martindale Pharma, Bampton Road, Romford, RM3 8UG. Tel: 01277266600. **Date of Preparation:** October 2020.

Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard. Adverse events should also be reported to Martindale Pharma. Tel: 01277266600. e-mail. drugsafety.uk@ethypharm.com