Prescribing Information for Prenoxad (naloxone hydrochloride) 1mg/ml Solution for Injection in a prefilled syringe
Please refer to the Summary of Product Characteristics (SmPC) before prescribing.

Presentation: A sterile, clear and colourless liquid in a 2ml prefilled syringe, each 1 ml of solution contains 1 mg of naloxone hydrochloride. **Indications:** Prenoxad Injection is intended for emergency use in the home or other non-medical setting by appropriate individuals or in a health facility setting for the complete or partial reversal of respiratory depression induced by natural and synthetic opioids, including methadone and certain other opioids such as dextropropoxyphene and certain mixed agonist/antagonist analgesics: nalbuphine and pentazocine. Prenoxad Injection should be carried by persons at risk of such events. It may also be used for the diagnosis of suspected acute opioid overdose. **Dosage and Administration: Prenoxad Injection is for administration by intramuscular injection.** Prenoxad Injection may only be made available once the prescriber has assessed the suitability and competence of a client or representative to administer naloxone in the appropriate circumstances. Prenoxad Injection is administered as a part of a resuscitation intervention in suspected overdose casualties, where opioid drugs may be involved or suspected. It may need to be used in a non-medical setting. The prescriber should take appropriate steps to ensure that the patient thoroughly understands the indications and use of Prenoxad Injection. The prescriber should review with the patient or any other person who might be in a position to administer Prenoxad Injection to a patient experiencing a suspected opioid overdose event. **In patients where breathing does not appear to be normal:** Administration of Prenoxad Injection should be preceded by calling emergency services and requesting an ambulance. Following this, 30 chest compressions and if possible 2 rescue breaths (Basic Life Support SINGLE CYCLE) should be given; 0.4ml Prenoxad Injection solution should then be administered by intramuscular injection into the outer thigh muscle or muscles of the upper arm, through clothing if necessary. A further 3 cycles of chest compressions and rescue breaths should then be given followed by administration of 0.4ml Prenoxad Injection. Three cycles of chest compression and rescue breaths should take approximately 2 minutes. This should be repeated until an ambulance arrives or the patient begins breathing normally / regains consciousness. The patient when breathing normally or has regained consciousness should be placed in the recovery position (lying on their side, mouth open pointing towards the ground) and observed continuously. **In patients where breathing is normal but the patient is unrousable or suspected to be unconscious**: Patient should be placed in the recovery position (lying on their side, mouth open pointing towards the ground). 0.4ml Prenoxad Injection solution should be administered by intramuscular injection into the outer thigh muscle or muscles of the upper arm, through clothing if necessary, and an ambulance should be called, 0.4ml Prenoxad Injection solution should then be administered every 2-3 minutes and continued until the ambulance arrives and or the patient regains consciousness. The patient should be continuously observed but particularly their breathing. If there is a decrease in breathing it is important that 0.4ml Prenoxad Injection solution is given every 2 -3 minutes. Parenteral drug products should be inspected visually for particulate matter and discolouration prior to administration whenever solution and container permit. **Adults: Opioid overdosage (known or suspected). Use by individuals in the community.** 400 micrograms or 0.4ml of Prenoxad Injection solution by intramuscular injection into the outer thigh or muscles of the upper arm as part of the resuscitation intervention. The dose of 0.4ml can be repeated every 2-3 minutes in subsequent resuscitation cycles until the contents of a syringe are used up. The duration of action of certain opioids can outlast that of an IV bolus of Naloxone, e.g. 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. **Children:** The Prenoxad Injection presentation is not intended to be used for children in the home setting other than by an appropriately trained healthcare professional. In the event of a child being given or taking an opioid inappropriately an ambulance should be called and resuscitation started if required. **Neonatal Use:** Naloxone should only be used in Neonates under medical supervision. **Elderly:** Use as for adults. **Consult SmPC for further information. Contra-Indications:** Known hypersensitivity to Naloxone or any of the excipients. **Warnings and Precautions:** Patients must be instructed in the proper use of Prenoxad Injection (see above). Prenoxad Injection is intended as an emergency treatment and the patient should be advised to seek medical help immediately. It should be administered cautiously to patients who have received large doses of opioids or to those physically dependent on opioids since too rapid reversal of opioid effects by Prenoxad may precipitate an acute withdrawal syndrome in such patients. The same caution is needed when giving Prenoxad to neonates delivered to such patients. Hypertension, cardiac arrhythmias, pulmonary oedema and cardiac arrest have been described. For signs and symptoms of opioid withdrawal in a patient physically dependent on opioids please see SmPC. Patients who have responded satisfactorily to Prenoxad should be kept under medical observation for at least 2 hours. Repeated doses of Prenoxad may be necessary since the duration of

action of some opioids may exceed that of Prenoxad Injection. Prenoxad Injection 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 sequel of these events. Although a direct cause and effect relationship has not been established, Prenoxad should be used with caution in patients with pre-existing cardiac disease and in those receiving medications with potential adverse cardiovascular effects e.g. hypotension, ventricular tachycardia or fibrillation and pulmonary oedema. Caution should be exercised and patients monitored when Prenoxad Injection is administered to patients with renal insufficiency/failure or liver disease. 1 ml of naloxone hydrochloride contains 3.497 mg of sodium which is 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. The potential risk for humans is unknown, therefore, Prenoxad 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 Prenoxad Injection 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*: Prenoxad 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 Prenoxad Injection is administered to a nursing mother. Therefore, breast-feeding should be avoided in the first 24 hours after treatment. **Effects on ability to drive and use machines:** Patients who have received Prenoxad 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: Consult SmPC for the full list of undesirable effects.** *Very common (≥1/10):* nausea. *Common (≥1/100 to <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. **Overdose:** There is limited clinical experience with Naloxone overdosage in humans. Consult SmPC for management guidance. **Product Licence Number:** PL 12064/0125 **Product Licence Holder:** Aurum Pharmaceuticals Ltd, Bampton Road, Harold Hill, Romford, Essex RM3 8UG. **Basic NHS Price:** £18.00 **Legal Category:** POM. **Further information:** Martindale Pharma, Bampton Road, Romford, RM3 8UG. Tel: 01277 266 600. **Date of Preparation:** April 2023. **Job Bag Number:** UK-PREN-47

Adverse events should be reported. Reporting forms and information can be found at https://yellowcard.mhra.gov.uk/ or search for MHRA Yellow Card in the Google Play or Apple App Store.
Adverse events should also be reported to Martindale Pharma, an Ethypharm Group Company. Tel: 01277 266 600. e-mail: drugsafety.uk@ethypharm.com