

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Naloxone Hydrochloride 20 micrograms/ml solution for injection

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 2ml ampoule contains 40 micrograms of naloxone hydrochloride (as dihydrate) equivalent to 20 micrograms per ml. Excipient: sodium 9 mg/ml.

For full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for injection

Clear, colourless, aqueous solution.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

1. Treatment of respiratory depression induced by synthetic and natural opiates.
2. Treatment of respiratory depression induced by partial opiate antagonists.
3. Diagnosis of suspected acute opiate overdose.
4. Treatment of asphyxia resulting from administration of opiates during labour.

4.2 Posology and method of administration

Children

Overdosage of narcotics: Known or suspected: 10mcg/kg body weight intravenously. If the desired degree of clinical improvement is not seen, a subsequent dose of 100mcg/kg may be given. Naloxone can be diluted with sterile Water for Injection BP. If I.V. route is not available, Naloxone may be administered by I.M. or subcutaneous routes.

Postoperative respiratory depression: In children the initial dose of Naloxone for the reversal of respiratory depression should be in increments of 5-10 micrograms (0.25-0.5ml) of 20 micrograms/ml strength intravenously at 2-3 minute intervals, to the required degree of reversal.

Neonates

Narcotic induced depression: 10 micrograms/kg body weight administered intravenously or alternatively, by I.M. or subcutaneous injection. This dose may be repeated at 2-3 minutes intervals, to the required degree of reversal.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Warnings: Naloxone should be given with caution to patients known or suspected to be physically dependent on opiates (including neonates born to women who are opiate dependent), because the drug may precipitate severe withdrawal symptoms.

Patients who have satisfactorily responded to Naloxone should be carefully monitored since the duration of action of some opiates may exceed that of Naloxone. Repeated doses of Naloxone should be administered when necessary.

Naloxone is not effective against respiratory depression not due to opioid drugs.

When Naloxone is used in the management of acute opioid overdose, other resuscitative measures such as maintenance of a free airway, artificial ventilation, cardiac massage and vasopressor agents should be readily available and used when necessary.

Precautions: Naloxone should be used with caution in patients with pre-existing cardiovascular disease or in those receiving potentially cardiotoxic drugs, since serious adverse cardiovascular effects (e.g. ventricular tachycardia and fibrillation) have occurred in postoperative patients following Naloxone administration.

Excessive dosage of Naloxone following the use of opiates in surgery should be avoided because it may result in excitement, increased blood pressure and clinically important reversal of analgesia. Too rapid reversal of opiate effects may induce nausea, vomiting, sweating or tachycardia.

4.5 Interaction with other medicinal products and other forms of interaction

No drugs should be added to solutions containing naloxone unless compatibility is known. Naloxone should not be mixed with preparations containing bisulphate, metabisulphate, long chain or high molecular weight anions or those with an alkaline pH.

4.6 Fertility, pregnancy and lactation

There are no or limited amount of data from the use of Naloxone in pregnant women.

Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity (see section 5.3). As a precautionary measure, it is preferable to avoid the use of Naloxone during pregnancy.

It is not known whether Naloxone is excreted in human milk. A risk to the newborns/infants cannot be excluded.

A decision must be made whether to discontinue breast-feeding or to discontinue Naloxone therapy taking into account the benefit of breast feeding for the child and the benefit of therapy for the woman.

4.7 Effects on ability to drive and use machines

Naloxone has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

The following undesirable effects are ranked according to system organ class and to their frequency. Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

The following frequency terminology is used:

Very common: $\geq 1/10$;

Common: $\geq 1/100$, $< 1/10$;

Uncommon: $\geq 1/1,000$, $< 1/100$;

Rare: $\geq 1/10,000$, $< 1/1,000$;

Very rare: $< 1/10,000$;

Not known (cannot be estimated from the available data)

In postoperative patients excessive dosage of Naloxone may result in excitement, increased blood pressure and significant reversal of analgesia.

Nervous system disorders:

Uncommon: Tremor

Rare: Seizures have occurred rarely following administration of Naloxone, however, a causal relationship has not been established.

Cardiac disorders:

Common: Tachycardia

Uncommon: Atrial and ventricular arrhythmias

Very rare: Cardiac arrest

Vascular disorders:

Common: Hypertension

Respiratory, thoracic and mediastinal disorders:

Uncommon: Hyperventilation

Very rare: Pulmonary oedema

Gastrointestinal disorders:

Very common: Nausea

Common: Vomiting

Skin and subcutaneous tissue disorders:

Uncommon: Sweating

Abrupt reversal of narcotic depression has been reported to result in nausea, vomiting, sweating, tachycardia, tremor and hyperventilation.

Hypertension, pulmonary oedema, atrial and ventricular arrhythmias and cardiac arrest have been reported in certain patients, particularly those with pre-existing cardiac abnormalities.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via IMB Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.imb.ie; e-mail: imbpharmacovigilance@imb.ie.

4.9 Overdose

There is no clinical experience of Naloxone overdose in humans.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: antidotes, ATC code: V03AB15

Naloxone hydrochloride is essentially a pure opiate antagonist, it has little or no agonistic activity. Naloxone is thought to act as a competitive antagonist at μ (Mu) -, κ (Kappa) - and σ (Sigma) - opioid receptors in the CNS. Small doses (0.4mg to 0.8mg) of naloxone given intramuscularly or intravenously prevent or promptly reverse the effects of opioids. In patients with respiratory depression, there is an increase in respiratory rate within 1 or 2 minutes. Sedative effects are reversed and blood pressure, if depressed, returns to normal. Naloxone also

reverses the psychotomimetic and dysphoric effects of agonist-antagonists such as pentazocine, but higher doses (10-15mg) are required. One milligram of naloxone intravenously completely blocks the effects of 25mg of diacetylmorphine.

When administered in usual doses to patients who have not recently received opiates, naloxone exerts little or no pharmacological effect. Even extremely high doses (10 times the usual therapeutic dose) produce insignificant analgesia, only slight drowsiness, and no respiratory depression, psychotomimetic effects, circulatory changes, or miosis.

Naloxone does not produce tolerance or physical or psychological dependence.

Parenteral administration (S.C., I.M. or I.V.) of naloxone will produce withdrawal symptoms in patients physically dependent on opiates or pentazocine.

5.2 Pharmacokinetic properties

Naloxone has an onset of action within 1-2 minutes following I.V. administration and within 2-5 minutes following subcutaneous or I.M. administration. The duration of action depends on the dose and route of administration and is more prolonged following I.M. administration than after I.V. administration. Duration of action is reported up to several hours but practical duration probably 1 hour or less.

Following parenteral administration, naloxone is rapidly distributed into body tissues and fluids. It is rapidly metabolised in the liver, principally by conjugation with glucuronic acid, and is excreted in the urine. The plasma half-life of naloxone has been reported to be 60-90 minutes in adults and about 3 hours in neonates.

5.3 Preclinical safety data

Reproduction studies in mice and rats using naloxone hydrochloride in doses up to 1000 times the usual human dosage revealed no evidence of impaired fertility or harm to the foetus.

There is no other pre-clinical data of relevance to the prescriber which are additional to that already included in other sections of the SPC.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium Chloride
Water for Injections

6.2 Incompatibilities

No drugs should be added to solutions containing Naloxone unless compatibility is known. Naloxone should not be mixed with preparations containing bisulphate, metabisulphate, long chain or high molecular weight anions or those with an alkaline pH.

6.3 Shelf life

Unopened: 2 years.

Once opened the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2 to 8°C, unless reconstitution / dilution (etc) has taken place in controlled and validated aseptic conditions.

6.4 Special precautions for storage

Do not store above 25°C. Keep blister-packed ampoule in outer carton in order to protect from light.

6.5 Nature and contents of container

Clear Type I glass ampoule containing 2 ml of solution.

Cartons containing 5 ampoules, blister packed in perforated strips.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Hospira UK Limited
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Warwickshire CV31 3RW
United Kingdom

8 MARKETING AUTHORISATION NUMBER

PA 0437/024/002

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 31 May 1991

Date of last renewal: 31 May 2006

10 DATE OF REVISION OF THE TEXT

May 2014