SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Naloxone 400 micrograms/ml Solution for Injection or Infusion

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1ml contains naloxone hydrochloride (dihydrate) 0.44mg

This is equivalent to 0.40mg/ml of anhydrous naloxone hydrochloride

For excipients see 6.1

3 PHARMACEUTICAL FORM

Solution for injection or Infusion (injection)

A clear, colourless solution free from particulate matter.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Naloxone is indicated for the treatment of respiratory depression induced by natural and synthetic opioids. It may also be used for the diagnosis of suspected acute opioid overdosage.

4.2 Posology and method of administration

Naloxone injection is for intravenous (iv), intramuscular (im) or subcutaneous (sc) injection.

Opioid overdosage (known or suspected)

Adults:

An initial dose of 400 micrograms to 2mg of naloxone may be administered intravenously. If the desired degree of counteraction and improvement in

respiratory function is not obtained it may be repeated at two to three minute intervals. If no response is observed after 10mg of naloxone being administered the diagnosis of opioid-induced or partial opioid induced toxicity should be questioned. Intramuscular or subcutaneous administration may be necessary if dosing by the intravenous route is not feasible.

Post-operative Use:

When naloxone is used post-operatively, the dose should be titrated for each patient in order to obtain respiratory response while maintaining analgesia. An intravenous dose of 1.5 - 3.0 micrograms/kg body weight is usually sufficient, but a full two minutes should be allowed between each 100 microgram increment of naloxone administered. Further intramuscular doses may be needed within one to two hours, depending on the interval since the last opioid administration and the amount and type (i.e. long or short acting) of drug used. Alternatively, naloxone may be administered as an intravenous infusion (see below).

Children:

The usual initial dose in children is 5-10 micrograms per kg body-weight given intravenously. If this does not result in the desired degree of clinical improvement, a subsequent dose of 100 micrograms per body weight may be administered. Naloxone may be administered intramuscularly or subcutaneously in divided doses.

Intravenous Infusion (iv)

In situations where one of the longer acting opioids is known or suspected to be the cause of the symptoms, IV infusion of naloxone is recommended to produce sustained antagonism to the opioid (without antagonism of pain relief) rather than repeated injection.

Naloxone may be diluted for intravenous infusion in normal saline (0.9%) or 5% dextrose in water or saline.

Mixtures should be used within 24 hours. Any remaining unused solution must then be discarded. The rate of administration should be titrated in accordance with the patient's response.

4.3 Contraindications

Naloxone should not be given to patients who are known to be hypersensitive to it.

4.4 Special warnings and precautions for use

Patients who have responded satisfactorily to naloxone should be kept under observation. Repeated doses 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.

Cautions: cardiovascular disease or concomitant cardiotoxic drugs as serious adverse cardiovascular effects have been reported (see section 4.8 Undesirable effects); physical dependence on opioids (including patients being treated with methadone), or after large doses of opioids, as naloxone may precipitate acute withdrawal syndrome (see section 4.8 Undesirable effects).

Naloxone may antagonise the analgesic effects of the opioids in the control of postoperative pain.

4.5 Interaction with other medicinal products and other forms of interaction

Naloxone should be used with caution in patients who are opioid dependent (including patients being treated with methadone), as it may precipitate an acute withdrawal syndrome.

Naloxone reverses the analgesic effects of opioid analgesics (e.g. nalbupine, pentazocine) and opioid agonist analgesics (e.g. alfentanil, fentanyl, remifentanil).

4.6 Pregnancy and lactation

Naloxone crosses the placenta; adequate and well-controlled studies in humans have not been done, therefore naloxone, like all drugs, should be used with caution during pregnancy. Risk-benefit must be considered before naloxone is administered to a pregnant woman who is known or suspected to be opioid dependent because naloxone may precipitate withdrawal in the foetus as well as the mother.

It is not generally advisable to give naloxone just prior to delivery as blocking endogenous endorphins may affect the ability of the foetus to withstand the stress of delivery.

It is not known if naloxone is distributed into breast milk Problems in humans have not been documented.

4.7 Effects on ability to drive and use machines

None known.

4.8 Undesirable effects

Cardiac disorders: atrial and ventricular dysrhythmias, including atrial premature contractures, ventricular tachycardia and fibrillation, asystole, hypotension, hypertension, left ventricular failure and cardiac arrest.

Gastrointestinal disorders: Nausea and vomiting.

General disorders and administration site conditions: Opioid withdrawal symptoms- sweating, yawning, rhinorrhoea, sneezing, muscle tremor, weakness, anxiety, irritability, restlessness, nausea, vomiting, diarrhoea, abdominal and muscle cramps, piloerection, increases in heart rate (tachycardia), blood pressure and temperature (fever). Acute withdrawal syndrome may include, but is not limited to the above listed signs and symptoms. Acute withdrawal effects after naloxone have only been reported in individuals physically dependent on opioids or after large doses of opioids.

Nervous system disorders: tingling/numbness of the extremities, trembling and generalised convulsions.

Psychiatric disorders: behavioural changes, including violent behaviour, nervousness, restlessness, excitement, irritability.

Respiratory, thoracic and mediastinal disorders: Pulmonary oedema and dyspnoea.

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 the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard.

4.9 Overdose

No documented reports of acute overdosage, either accidental or non-accidental, are available.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Naloxone is a specific narcotic antagonist and finds particular use in the off-set of respiratory depression caused by opioids.

5.2 Pharmacokinetic properties

Naloxone acts within two minutes of intravenous injection and usually within three to five minutes of subcutaneous or intramuscular injection. The plasma half life is approximately one to two hours.

5.3 Preclinical safety data

Animal toxicity and reproductive studies have not revealed any mutagenic, carcinogenic, teratogenic or embryotoxic effects, nor impaired fertility.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium chloride

Water for injections

Sodium hydroxide

Hydrochloric acid

6.2 Incompatibilities

Naloxone is stable in the range pH 2.5-5.0, but should not be added to infusion solutions with an alkaline pH. It is not compatible with solutions containing bisulphate, sulphites, or long chain/high molecular weight anions.

6.3 Shelf life

24 months

6.4 Special precautions for storage

Store in a cool place. Protect from light.

6.5 Nature and contents of container

1ml clear glass ampoules Type 1 (Ph.Eur).

Packs of 3, 10 or 50 ampoules

6.6 Special precautions for disposal

None.

7 MARKETING AUTHORISATION HOLDER

Wockhardt UK Limited

Ash Road North,

Wrexham, LL13 9UF

United Kingdom.

8 MARKETING AUTHORISATION NUMBER(S)

PL 29831/0148

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

30/07/1990 / 30/01/1997

10 DATE OF REVISION OF THE TEXT

21/02/2017