

## Summary of Product Characteristics

### 1. NAME OF THE MEDICINAL PRODUCT

Naloxone Hydrochloride Injection USP 20 micrograms/ml

### 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 2ml of solution contains 40 micrograms (0.04mg) Naloxone Hydrochloride present as Naloxone Hydrochloride Dihydrate.

### 3. PHARMACEUTICAL FORM

Solution for injection  
Clear, colourless, sterile solution.

### 4. CLINICAL PARTICULARS

#### 4.1 Therapeutic indications

For the reversal of opioid depression, including respiratory depression, caused by natural or synthetic opioids, the agonist-antagonists nalbuphine and pentazocine, or dextropropoxyphene. Naloxone may also be used for the diagnosis of suspected opioid overdose. Naloxone may be used to reverse respiratory and other CNS depression in the neonate, resulting from administration of narcotic analgesics to the mother during labour.

#### 4.2 Posology and method of administration

Naloxone is for intravenous, intramuscular or subcutaneous injection. It may also be administered by intravenous infusion.

Opioid overdose (known or suspected)

Adults: An initial dose of 400 to 2000 micrograms (0.4mg to 2mg) of naloxone may be given intravenously and may, if required, be repeated at 2 to 3 minute intervals. The diagnosis of opioid-related toxicity should be reconsidered if there is still failure to respond after a total of 10mg of naloxone has been administered. If intravenous administration is impracticable, naloxone may be administered by the intramuscular or subcutaneous route.

The duration of action of some opioids (including dextropropoxyphene, dihydrocodeine and methadone) may exceed that of naloxone. In these circumstances, an intravenous infusion of naloxone will provide sustained antagonism of the opioid and obviate the need for repeated injections. Naloxone may be diluted for intravenous infusion in 0.9% (normal) saline or 5% dextrose in water or saline. Addition of 2mg of naloxone to 500ml of one of these solutions provides a concentration of 4 micrograms/ml (0.004mg/ml). Mixtures should be used within 24 hours and any unused solution should be discarded after this time. The rate of infusion should be titrated according to the patients response.

Post-operative use: Dosage is individually titrated to maintain adequate analgesia while gaining optimum respiratory response. The usual intravenous dose is 100 to 200 micrograms (0.1 to 0.2mg), i.e. approximately 1.5 to 3 micrograms (0.0015 to 0.003mg) per kg bodyweight with a 2 minute interval between each 100 microgram (0.1mg) increment administered.

Depending on the type of opioid, the dose and the time interval from its last administration, repeat doses of naloxone may be required within one to two hours and may be administered by intramuscular injection or by intravenous infusion in order to produce a more sustained effect.

#### Children:

The usual initial dose is 10 micrograms (0.01mg) per kg body weight, intravenously. If adequate response does not occur a dose of 100 micrograms (0.1mg) per kg body weight may be administered. Alternatively, naloxone may be administered by intravenous infusion, if appropriate or if the I.V. route is not feasible, it may be given I.M. or S.C. in divided doses.

#### Neonatal Use:

For opioid-induced depression, the usual initial dose is 10 micrograms (0.01mg) per kg body weight, I.V., I.M. or S.C. This dose may be repeated, if required, at 2 to 3 minute intervals. Alternatively, a single dose of 200 micrograms (0.2mg) i.e. approximately 60 micrograms (0.06mg) per kg body weight, may be administered intramuscularly at birth although the onset of action is slower after I.M. injection.

An adequate airway should be established prior to administering naloxone to the apnoeic infant.

### **4.3 Contra indications**

Naloxone should not be administered to patients with a known hypersensitivity to it.

### **4.4 Special warnings and precautions for use**

Naloxone is not effective in depression due to non-narcotic substances such as barbiturates, tranquillizers, anaesthetics etc.

Repeated dosage may be necessary in view of the prolonged duration of action of some narcotics.

Patients should be kept under constant surveillance.

Abrupt reversal of narcotic depression may result in nausea, vomiting, sweating, tachycardia, increased blood pressure, tremulousness, seizures and cardiac arrest. In postoperative patients, larger than necessary dosage of naloxone may result in significant reversal of analgesia and excitement. Hypotension, hypertension, ventricular tachycardia and fibrillation, and pulmonary oedema have been associated with the use of naloxone postoperatively (see 4.8 Undesirable Effects).

Administration should be carried out only with great caution in patients who have received large doses of narcotics or are narcotic addicts, in order to avoid precipitation of an acute abstinence syndrome. Similar caution is required with neonates whose mothers have received large doses of opioids or are dependent on them.

Resuscitative measures for maintenance of a free airway, artificial ventilation, cardiac activity and blood pressure should be available.

Naloxone should be used with caution in patients with cardiac irritability.

### **4.5 Interaction with other medicinal products and other forms of interactions**

See Section 4.4

### **4.6 Pregnancy and lactation**

Although reproduction studies in animals have not demonstrated any teratogenic or embryotoxic effects, naloxone should be administered during pregnancy only if considered essential by physician. Naloxone crosses the placenta. It is not known whether naloxone is excreted in breast milk, therefore caution is required when naloxone is administered to a nursing mother.

### **4.7 Effects on ability to drive and use machines**

Not applicable

#### **4.8 Undesirable effects**

Nausea and vomiting have been reported in some post-operative patients who received naloxone in doses higher than those recommended; a direct relationship has not been established.

There have been reports of hypotension, hypertension, ventricular tachycardia and fibrillation, and pulmonary oedema. These have occurred in postoperative patients, most of whom had pre-existing cardiovascular disorders or received other drugs which may have similar adverse cardiovascular effects. 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 potentially cardiotoxic drugs.

#### **4.9 Overdose**

There have been no reports of acute overdosage with naloxone.

### **5. PHARMACOLOGICAL PROPERTIES**

#### **5.1 Pharmacodynamic Properties**

Naloxone is a specific opioid antagonist. It is an essentially pure antagonist in the sense that it does not possess agonist or morphin-like properties. Although the mechanism of the drug's action has not been fully elucidated, naloxone appears to antagonise the effects of opioids by competing for the same receptor sites. When naloxone is given intravenously, the onset of action is generally apparent within two minutes, onset of action is only slightly less rapid when the drug is administered subcutaneously or intramuscularly. The duration of action is dependent on the dose and route of administration and may be one to four hours or shorter.

#### **5.2 Pharmacokinetic properties**

Although absorbed readily from the gastrointestinal tract, naloxone undergoes extensive first-pass metabolism in the liver before reaching the systemic circulation and thus must be administered parenterally. It is rapidly absorbed from parenteral sites of injection and is metabolised in the liver, mainly by glucuronide conjugation, and excreted in urine. Naloxone has a short plasma half-life of approximately one hour after parenteral administration.

#### **5.3 Preclinical safety data**

No further relevant information other than that which is included in other sections of the Summary of Product Characteristics.

### **6. PHARMACEUTICAL PARTICULARS**

#### **6.1 List of excipients**

Sodium Chloride  
Dilute Hydrochloric Acid  
Water for Injections

#### **6.2 Incompatibilities**

No drugs should be added to naloxone solution unless compatibility is known.  
Naloxone should not be mixed with preparations containing bisulphite, metabisulphite, long-chain or high molecular weight anions or any solution having an alkaline pH.

### **6.3 Shelf life**

4 years (48 months)

### **6.4 Special precautions for storage**

Do not store above 25°C. Protect from light.

### **6.5 Nature and contents of container**

Clear glass with green one point-cut (OPC) ampoules, glass type I Ph Eur. with yellow and green rings.

Pack sizes: 3 x 2 ml; 5 x 2 ml and 10 x 2 ml ampoules.

### **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**

If only part used, discard the remaining solution.

## **7. MARKETING AUTHORISATION HOLDER**

Antigen Pharmaceuticals Limited  
Roscrea  
Co. Tipperary

## **8. MARKETING AUTHORISATION NUMBER**

PA 73/111/1

## **9. DATE OF FIRST AUTHORIZATION/RENEWAL OF AUTHORISATION**

3 October 1989/3 October 1999

## **10. DATE OF REVISION OF THE TEXT**

September 2009