SCHEDULING STATUS: S6

PROPRIETARY NAME: **SABAX MORPHINE SULPHATE 10 mg**

SABAX MORPHINE SULPHATE 15 mg

SABAX MORPHINE SULPHATE 30 mg

(AND DOSAGE FORM) INJECTION

COMPOSITION:

Each 1 ml contains:

Morphine sulphate 10 mg, 15 mg or 30 mg

Contains no sugar.

Preservative free

PHARMACOLOGICAL CLASSIFICATION:

A 2.9 Other analgesics

PHARMACOLOGICAL ACTION:

Pharmacodynamics

Morphine acts as an agonist particularly at μ receptors, and also d and K-receptors. Its effects are diverse and include analgesia, drowsiness, changes in mood, respiratory depression, decreased gastrointestinal motility, nausea, vomiting and alterations of the endocrine and autonomic nervous systems. The development of tolerance and physical dependence is a characteristic feature.

Pharmacokinetics

Morphine salts are well absorbed from the gastro-intestinal tract but have poor oral bioavailability since they undergo extensive first-pass metabolism in the liver and gut.

After subcutaneous or intramuscular injection morphine is readily absorbed into the blood.

The majority of a dose of morphine is conjugated with glucuronic acid in the liver and gut to produce morphine-3-glucuronide and morphine-6-glucuronide. The latter is considered to contribute to the analgesic effect of morphine. Morphine-3-glucuronide on the other hand may antagonise the analgesic action and might be responsible for the paradoxical pain observed in some patients given morphine.

Other active metabolites include normorphine, codeine, and morphine ethereal sulphate. Enterohepatic circulation probably occurs.

Morphine is distributed throughout the body but mainly in the kidneys, liver, lungs and spleen, with lower concentrations in the brain and muscles. Morphine crosses the blood-brain barrier less readily than more lipid soluble opiods such as diamorphine, but it has been detected in the CSF as its highly polar metabolites morphine-3-glucuronide and morphine-6-glucuronide. Morphine diffuses across the placenta and traces also appear in breastmilk and sweat.

About 35% is protein bound. Mean plasma elimination half lives of about 2 hours for morphine and 2.4 to 6.7 hours for morphine-3-glucuronide have been reported. Up to 10% of a dose of morphine may eventually be excreted, as conjugates, through the bile into the faeces. The remainder is excreted in the urine, mainly as conjugates. About 90% of total morphine is excreted in 24 hours with traces in urine for 48 hours or more.

INDICATIONS:

Relief of intractable pain not controlled with non-narcotic analgesics.

CONTRAINDICATIONS:

Usually not given pre-operatively to children under one year of age. Respiratory depression, especially in the presence of cyanosis and excessive bronchial secretion, and after operations on the biliary tract. In the presence of acute alcoholism, head injuries and conditions in which intracranial pressure is raised, during an attack of bronchial asthma or in patients with compromised respiratory function. In patients taking monoamine oxidase inhibitors or within 10 days of stopping such treatment.

WARNINGS:

DRUG DEPENDENCE FROM REPEATED ADMINISTRATION.

INTERACTIONS:

Morphine is contraindicated in patients taking monoamine oxidase inhibitors or within 10 days of stopping such treatment.

The depressant effects of morphine are enhanced by depressants of the central nervous system such as anaesthetics, hypnotics, sedatives and phenothiazines.

DOSAGE AND DIRECTIONS FOR USE:

Doses should generally be reduced in the elderly or debilitated or in patients with renal impairment.

Subcutaneous or intramuscular injection

Adults: 5 to 20 mg every 4 hours

Children: 1 to 5 years: 2,5 to 5 mg

6 to 12 years: 5 to 10 mg

Slow intravenous injection or as loading dose for continuous or patient controlled infusions:

Adults: up to 15 mg

Maintenance dose for continuous intravenous administration and continuous subcutaneous infusion: From 0,8 to 80 mg per hour.

Intrathecal dose ranges from 0,2 to 1,0 mg and must only be given as a single dose.

SIDE-EFFECTS AND SPECIAL PRECAUTIONS:

Side-Effects:

Side effects have been ranked according to frequency within each System Organ Class.

The following adverse reactions have been reported and may occur with **SABAX MORPHINE SULPHATE:**

Cardiac disorders:

Less Frequent: Bradycardia, Tachycardia, Pounding heartbeat

Gastrointestinal disorders:

Frequent: Nausea and vomiting, Constipation

Less Frequent: Dry mouth, Gastrointestinal irritation (stomach cramps or pain), paralytic ileus or toxic megacolon

General disorders and administration site conditions:

Frequent: Unusual tiredness or weakness

Less Frequent: Redness, swelling, pain or burning at site of injection

Hepatobiliary disorders:

Less Frequent: Biliary spasm

The following side-effects have been reported but frequencies are unknown: Hepatotoxicity

Immune system disorders:

Frequent: Histamine release (decreased blood pressure, fast heartbeat, increased sweating, redness or flushing of the face, wheezing or troubled breathing)

Less Frequent: Allergic reaction (skin rash, hives, and/or itching; swelling of face)

Metabolism and nutrition disorders:

Less Frequent: Loss of appetite

Musculoskeletal and connective tissue disorders:

Less Frequent: Muscle rigidity (especially in muscles of respiration), trembling or uncontrolled muscle movements

Nervous system disorders:

Frequent: Drowsiness

Less Frequent: Headache, Paradoxical CNS stimulation (unusual excitement or restlessness, especially in children), Blurred or double vision

The following side-effects have been reported but frequencies are unknown: Convulsions, Tinnitus (ringing or buzzing in the ears)

Psychiatric disorders:

Less Frequent: False sense of wellbeing, General feeling of discomfort or illness, Nervousness or restlessness, Insomnia, Confusion, Hallucinations, Mental depression,

The following side-effects have been reported but frequencies are unknown: Nightmares or unusual dreams

Renal and urinary disorders:

Less Frequent: Ureteral spasm (difficult or painful urination, frequent urge to urinate, Antidiuretic effect

Respiratory, thoracic and mediastinal disorders:

Less Frequent: Atelectasis; bronchospastic allergic reaction; laryngeal edema; allergic laryngospasm; respiratory depression

Vascular disorders:

Less Frequent: Dizziness, feeling faint or light-headedness, Hypotension

The following side-effects have been reported but frequencies are unknown: Increased blood pressure

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:

Respiratory depression and hypotension with circulatory failure and deepening coma. Death may occur from respiratory failure. Naloxone hydrochloride 400 µg is given subcutaneously, intramuscularly or intravenously, repeated at intervals of two to three minutes if necessary. If naloxone is not available, nalorphine hydrobromide may be given intravenously in doses of 5 to 10 mg, repeated in 15 minutes if necessary up to a total of 40 mg. In severe poisoning, a single dose of 40 mg may be given. Alternatively, levallorphan tartrate 1 mg intravenously, followed if necessary by one or two doses each of 500 µg, may be given. The circulation should be maintained with infusions of dextrose injection and suitable electrolyte solutions. Assisted respiration may be necessary.

The use of naloxone, nalorphine and levallorphan in addicts tolerant to morphine may induce withdrawal symptoms.

IDENTIFICATION:

A clear, colourless to slightly yellowish brown solution.

PRESENTATION:

SABAX MORPHINE SULPHATE 10 mg: 1 ml amber, closed, easy break glass ampoules or 2 ml amber, closed, one point cut (OPC) glass ampoules, containing 1 ml of solution, packed in unit cartons or polystyrene cartons in sizes of 5's, 10's, 50's and 100's.

SABAX MORPHINE SULPHATE 15 mg: 1 ml amber, closed, easy break glass ampoules or 2 ml amber, closed, one point cut (OPC) glass ampoules, containing 1 ml of solution, packed in unit cartons or polystyrene cartons in sizes of 5's, 10's, 50's and 100's.

SABAX MORPHINE SULPHATE 30 mg: 1 ml amber, closed, easy break glass ampoules or 2 ml amber, closed, one point cut (OPC) glass ampoules, containing 1 ml of solution, packed in unit cartons or polystyrene cartons in sizes of 5's, 10's, 50's and 100's.

STORAGE INSTRUCTIONS:

Store below 25 °C and protect from light. KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBER:

SABAX MORPHINE SULPHATE 10 mg: B1242

SABAX MORPHINE SULPHATE 15 mg: B1243

SABAX MORPHINE SULPHATE 30 mg: B1244

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION:

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