Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Slo-Morph 30 mg Prolonged-release Capsules, hard.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Morphine Sulfate 30 mg

For excipients, see 6.1.

3 PHARMACEUTICAL FORM

Prolonged-release capsules, hard.

Size 4 capsules with natural, transparent bodies and opaque pink heads, with ‘Slo-Morph 30’ printed in black ink and containing off-white, spherical microgranules.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

For the prolonged relief of severe chronic pain, in particular pain associated with cancer.

4.2 Posology and method of administration

As directed by a medical practitioner.

Recommended dosage:

Adults
The recommended starting dose is 10-20 mg twice daily. Dosage can be increased under medical supervision according to the severity of the pain and the patient’s previous history of analgesic requirements.

Elderly
As with all narcotics, a reduction in dosage may be advisable in the elderly, as appropriate.

Children
Not recommended.

The capsules should not be chewed and should normally be swallowed whole. If the pain persists, or if the patient develops tolerance to morphine, the dosage may be increased by prescribing 10, 30, 60, 100 and 200 mg capsules in various combinations or alone to obtain the desired relief.

Patients previously treated with immediate-release oral morphine should receive the same daily dose of prolonged release capsules, but in two divided doses at 12-hour intervals.

Patients previously treated with parenteral morphine should be given a sufficiently increased dosage to compensate for any reduction of the analgesic effect associated with oral administration. The dosage should be adjusted, under careful medical supervision, to meet the individual requirements of each patient.

For patients who can not swallow the capsules, their contents can be administered directly in semi-solid food (puree, jam, yoghurt) or via gastric or gastrostomy tubes of a diameter of more than 16 F.G. with an open distal end or lateral pores. It is sufficient to rinse the tube with 30 to 50 ml of water.

4.3 Contraindications

Use in patients with the following conditions:

- Respiratory impairment.
- Acute abdominal syndrome of unknown origin.
- Severely impaired liver function.
- Cranial trauma and raised intracranial pressure.
- Convulsive state.
- Acute alcoholic intoxication and delirium tremens.
- Concurrent treatment with MAO (MAO = monoamine oxidase) inhibitors, or within two weeks of their use.
- Hypersensitivity to morphine.
- Use in children.

4.4 Special warnings and precautions for use

This product should only be given with great caution to elderly subjects, to patients with impaired hepatic and/or renal function or hypoadrenalism, in those in a state of shock or with asthma or decreased respiratory reserve.

Urinary retention may occur in patients with urethral or prostatic disease. Drug dependence may occur after treatment for one or two weeks with therapeutic doses. Therefore, this product should only be used when absolutely necessary. Sudden discontinuation of prolonged treatment results in the occurrence of a withdrawal syndrome.

4.5 Interaction with other medicinal products and other forms of interaction

Serious or fatal accidents have been observed after administration of pethidine in combination with monoamine oxidase inhibitors. It is not known whether this type of reaction may occur with other central analgesics. As a precautionary measure, opioid analgesics should not be administered until 15 days after withdrawal of MAO inhibitor treatment.

When used in conjunction with central nervous system depressants and tricyclic anti-depressants, the effects of morphine may be potentiated and there is a risk of overdosage.

4.6 Pregnancy and lactation

Since this product rapidly crosses the placental barrier, it should not be used during the second stage of labour or in premature delivery because of the risk of secondary respiratory depression in the newborn infant. If the mother is addicted, a withdrawal syndrome is observed in the newborn infant characterised by: convulsions, irritability, vomiting and increased mortality. As with all drugs, it is not advisable to administer it during pregnancy.

Morphine is excreted in breast milk.

4.7 Effects on ability to drive and use machines

Because of the decrease in vigilance induced by this drug, patients should be warned not to drive or operate machinery after taking this product.

4.8 Undesirable effects

The most common side effects at usual doses are nausea, constipation, confusion and occasionally vomiting.

Other possible effects include: sedation, confusion or excitation (particularly in elderly subjects in whom delirium and hallucinations may occur), increased intracranial pressure which may aggravate existing cerebral disorders, increased pressure in the main bile duct and urinary retention in cases of prostatic adenoma or urethral stenosis. Dry mouth, sweating, facial flushing, vertigo, bradycardia, palpitations, orthostatic hypotension, hypothermia, restlessness, changes of mood and miosis may also occur.

Mild respiratory depression occurs even at therapeutic doses. In the event of overdosage it may be severe, serious or even fatal.

Physical and psychological dependence may appear after administration of therapeutic doses for periods of 1 to 2 weeks. Some cases of dependence have been observed after only 2 to 3 days.

Withdrawal syndrome: this may occur a few hours after withdrawal of a prolonged treatment, and is maximal between the 36th and 72nd hours.

4.9 Overdose

Symptoms include respiratory depression, extreme miosis, hypotension, hypothermia, and coma. Treatment is by intravenous injection of naloxone 0.4 mg, repeated every 2 to 3 minutes if necessary, or by an infusion of 2 mg in 500 ml of normal saline or 5 % dextrose (0.004 mg/ml).

In subjects dependent on morphine-like drugs, withdrawal symptoms may occur following injection of a high dose of naloxone. It should therefore be injected in gradually increasing doses to such subjects.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Morphine is an opioid analgesic. It acts mainly on the central nervous system and smooth muscle.

Morphine exerts an analgesic action, and affects psychomotor behaviour: depending on the dose administered, it induces sedation (> 1 cg) or, in some cases, excitation (<1 cg). At high doses, greater than those required to produce analgesia, it induces somnolence and sleep.

5.2 Pharmacokinetic properties

Absorption
This is a prolonged release form, which makes possible twice-daily oral administration. Morphine is immediately absorbed from the digestive tract following oral administration. The maximum serum concentrations of morphine are obtained in 2 to 4 hours.

Distribution
The percentage of binding to plasma proteins after absorption is low (about 34 %). There is no clearly defined correlation between the plasma concentration of morphine and the analgesic effect.

Metabolism
A considerable quantity of morphine is metabolised by the liver to glucuronides, which undergo enterohepatic recirculation.

Excretion
The product is eliminated essentially in the urine, by glomerular filtration, mainly as glucuronides. A small amount (less than 10 %) is eliminated in the faeces.

5.3 Preclinical safety data

None stated.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Capsule Contents
Sugar Spheres (sucrose and maize starch microgranules)
Macrogol 4000
Ethylcellulose aqueous dispersion
Dibutyl sebacate
Talc

Capsule shell
Gelatin
Quinoline yellow (E 104)
Titanium dioxide (E 171)
Black iron oxide ink (E 172)

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

3 years.

6.4 Special precautions for storage

Store below 25°C. Store in the original package.

6.5 Nature and contents of container

Blister packs (aluminium/PVC).

Boxes of 14, 30 and 60 capsules.

Not all pack sizes may be marketed.

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

Ethypharm SA
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78550 Houdan
France

8 MARKETING AUTHORISATION NUMBER

PA 0549/013/002

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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Date of last renewal: 23rd June 2003

10 DATE OF REVISION OF THE TEXT

31st May 2006