IRISH MEDICINES BOARD ACT 1995

MEDICINAL PRODUCTS(LICENSING AND SALE)REGULATIONS, 1998

(S.I. No.142 of 1998)

PA1315/001/001
Case No: 2020932

The Irish Medicines Board in exercise of the powers conferred on it by the above mentioned Regulations hereby grants to

Eurand S.p.A.

Via Martin Luther King 13, **20060 Pessano con Bornago (MI)**, **Italy**

an authorisation, subject to the provisions of the said Regulations, in respect of the product

Sloket Capsules Modified Release

The particulars of which are set out in Part I and Part II of the attached Schedule. The authorisation is also subject to the general conditions as may be specified in the said Regulations as listed on the reverse of this document.

This authorisation, unless previously revoked, shall continue in force from **26/06/2006** .

Signed on behalf of the Irish Medicines Board this

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A person authorised in that behalf by the said Board.

Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Sloket 200mg prolonged-release hard capsules

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Ketoprofen 200 mg

For full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Prolonged-release capsule, hard.

Hard gelatin capsules with opaque white cap and body, containing off-white almost-spherical pellets.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Rheumatoid arthritis, osteoarthritis, ankylosing spondylitis, gout, non-infectious arthropathy, acute articular and periarticular disorders, sciatica, painful musculo-skeletal conditions and the management of the pain of dysmenorrhoea.

4.2 Posology and method of administration

The usual dose is one capsule daily with food.

Elderly

NSAIDs should be used with particular caution in elderly patients who are more prone to adverse events. The lowest dose compatible with adequate safe clinical control should be employed.

Treatment should be reviewed at regular intervals and discontinued if no benefit is seen or intolerance occurs

4.3 Contraindications

Active peptic ulceration, gastrointestinal disease, a history of recurrent peptic ulceration or chronic dyspepsia. Severe renal dysfunction. Sloket should not be given to patients with a history of hypersensitivity reactions (e.g. bronchospasm, rhinitis, urticaria) in response to ketoprofen, aspirin or non-steroidal anti inflammatory drugs. Severe bronchospasm may be precipitated in patients suffering from, or with a history of bronchial asthma or allergic disease.

4.4 Special warnings and precautions for use

1. Sloket should be used with caution in patients with a history of peptic ulceration or inflammatory bowel disease. Patients with chronic dyspepsia should be carefully monitored.

2. In patients with renal cardiac or hepatic impairment, caution is required since the use of NSAIDs may result in deterioration of renal function. Assessment of renal function should occur prior to the initiation of therapy and regularly thereafter.

3. As with other propionic acid derivatives Ketoprofen exhibits moderate plasma protein binding. Patients receiving anticoagulants, hydantoins and protein-bound sulphonamides must therefore be closely monitored.

4. Undesirable effects may be reduced by using the minimum effective dose for the shortest possible duration. Patients treated with NSAIDs long term should undergo regular medical supervision to monitor for adverse events.

5. Elderly patients are particularly susceptible to the adverse effects of NSAIDs. Prolonged use of NSAIDs in the elderly is not recommended. Where prolonged therapy is required, patients should be reviewed regularly.

6. As NSAIDs can interfere with platelet function, they should be used with caution with patients with intra-cranial haemorrhage and bleeding diathesis.

4.5 Interaction with other medicinal products and other forms of interaction

1. **It is considered unsafe to take NSAIDS in combination with warfarin or heparin unless under direct medical supervision**

2. Plasma protein-binding drugs, e.g. anticoagulants, sulphonamides, sulphonylurea, hypoglycaemics hydantoins, might necessitate modification in dosage.

3. Similar acting drugs such as aspirin or other non-steroidal anti-inflammatory drugs should not be administered concomitantly with ketoprofen as the potential for adverse reactions is increased.

4. Serious interactions have been recorded after the use of high dose methotrexate with non-steroidal anti-inflammatory agents including ketoprofen.

Care should be taken in patients treated with any of the following drugs as interactions have been reported with NSAIDs:

- Anti-hypertensives – Reduced anti-hypertensive effect
- Diuretics – reduced diuretic effect. Diuretics can increase the risk of nephrotoxicity of NSAIDs
- Cardiac Glycosides – NSAIDs may exacerbate cardiac failure, reduce GFR and increase plasma cardiac glycoside levels
- Lithium – decreased excretion of lithium
- Cyclosporin – increased risk of nephrotoxicity with NSAIDs
- Corticosteroids –Increased risk of gastrointestinal bleeding
- Aminoglycosides – reduction in renal function in susceptible individuals, decreased elimination of aminoglycoside and increased plasma concentrations
- Probenecid – reduction in metabolism and elimination of NSAIDs and metabolites
- Oral hypoglycaemic agents – Inhibition of metabolism of sulfonylurea drugs, prolonged half life and increased risk of hypoglycaemia.

4.6 Pregnancy and lactation

No embryotoxic or teratogenic effects have been demonstrated with ketoprofen. Nevertheless it is recommended to avoid ketoprofen unless considered essential.

4.7 Effects on ability to drive and use machines

Sloket does not normally produce any effects on ability to drive or use machines.

4.8 Undesirable effects

Gastrointestinal disturbances can occur, other minor effects such as headache, dizziness, mild confusion may occur less commonly.

Major gastrointestinal adverse effects such as peptic ulceration, haemorrhage or perforation may rarely occur. Skin rashes and bronchospasm have also been reported. Reversible increases in BUN or serum creatinine can occur, particularly in patients with existing renal damage or on concurrent diuretic therapy. Ketoprofen is also known to precipitate photosensitivity.

4.9 Overdose

Symptoms of acute ketoprofen intoxication are drowsiness, abdominal pain and vomiting, but adverse effects seen after overdosage with propionic acid derivatives such as hypotension, bronchospasm and gastrointestinal haemorrhage should be anticipated.

Owing to the slow release characteristics of the product it should be expected that ketoprofen will continue to be absorbed for up to 16 hours after ingestion.

Gastric lavage aimed at recovering pellets that may still be in the stomach should be performed if the patient is seen soon enough after ingestion. Treatment is otherwise supportive and symptomatic.

Administration of activated charcoal in an attempt to reduce absorption of ketoprofen should be considered.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group
Ketoprofen is a Non-steroidal Anti-inflammatory Drug (NSAID) with analgesic, anti-inflammatory and anti-pyretic activity.

Mechanism of Action
Ketoprofen is an inhibitor of cyclooxygenase, hence it prevents the generation of inflammatory prostanoids from Arachadonic acid during the inflammatory cascade.

5.2 Pharmacokinetic properties

(a) General Characteristics of the Active Substance(s)

After oral dosing with conventional formulations ketoprofen is almost completely absorbed from the gastro-intestinal tract. The drug kinetics fit a two compartment model, with a terminal half-life of 1.52 hours. The sustained release properties of Sloket mean that the half life is extended to 8 hours thus enabling once daily dosing. 90% of the oral dose is excreted in the urine, mostly as conjugates (glucuronate or hydroxyl derivatives) whereas only 8% appears in the faeces. The metabolites are not active and there seems to be no induction of drug metabolising enzymes in the liver. A significant effect of meal size and composition on the bioavailability of oral ketoprofen has been reported resulting in delayed absorption and an increase of the T_{max} values.

(b) Characteristics in patients

As expected from its excretion features, in subjects with chronic renal failure the elimination half-life is significantly prolonged.

5.3 Preclinical safety data

Not relevant.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sugar spheres
Povidone K30
Poly(methyl)methacrylates
Talc

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

3 years.

6.4 Special precautions for storage

Do not store above 25°C. Store in the original package.

6.5 Nature and contents of container

Blister packs containing 3 and 28 capsules.
(Pack size of 3 capsules is for sampling purposes only and not for marketing).

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

EURAND SpA
Via Martin Luther King 13
20060 Pessano con Bornago (MI)
Italy

8 MARKETING AUTHORISATION NUMBER

PA 1315/1/1

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 29th June 2001

10 DATE OF REVISION OF THE TEXT

July 2006