Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Selexidin 400 mg Injection, Powder and Solvent for solution for injection.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each powder vial contains mecillinam 400 mg

3 PHARMACEUTICAL FORM

Powder and solvent for solution for injection.
Powder: White to off-white crystalline powder.
Solvent: Clear colourless liquid.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

In the treatment of systemic infections due to micro-organisms sensitive to this anti-infective.

4.2 Posology and method of adminstration

For intramuscular or intravenous (by slow injection or infusion) use.

Adults and Children

For Intramuscular Use
The contents of the vial are dissolved in 2ml of water for injection.

For Intravenous Use
The contents of the vial are dissolved in 4ml of water for injection (10%w/v solution) for slow injection, or by infusion over 15 - 30 minutes after adding to sodium chloride injection or 5% dextrose for injection.

Urinary Tract Infections:
The usual dose is 5mg/kg bodyweight every 6 to 8 hours.

Enteric Fever:
The usual dose is 12.5 to 15mg/kg bodyweight every 6 hours.

Severe Gram Negative Infections:
The usual dose is 10mg/kg every 6 hours.

Probenecid may be used concurrently.

Mecillinam may be combined where appropriate with a broad spectrum penicillin or cephalosporin. The usual dose of each compound in the combination is used.

4.3 Contraindications

Use in patients hypersensitive to selexidin, penicillins or cephalosporins, and also in patients with Reye's or Reye-like syndromes.

Patients with disorders known to be leading to severe carnitine deficiency such as methylmalonic aciduria and propionic acidaemia.

Mecillinam should not be used during the first half of pregnancy.

4.4 Special warnings and special precautions for use

Patients on long-term therapy should have regular assessments of liver and kidney function.

In the presence of renal insufficiency adjustment of dosage level or interval may be necessary to avoid unduly high levels of mecillinam.

Prolonged treatment with an anti-infective may result in the development of infections due to organisms resistant to the anti-infective.

Because of the possibility of carnitine depletion Selexidin is not recommended for prolonged use especially in children, or in those with existing metabolic disorders or in children on concurrent therapy with valproate.

4.5 Interaction with other medicinal products and other forms of interaction

Simultaneous administration of probenecid reduces the excretion of mecillinam and hence increases the blood levels of the antibiotic.

Clearance of methotrexate from the body can be reduced by concurrent use of penicillins.

Synergistic interaction may be seen when selexidin is given concurrently with other beta-lactam antibiotics.

4.6 Pregnancy and lactation

Tests in two animal species have shown no teratogenic effects. Data on a large number of exposed pregnancies indicate no adverse effects of pivmecillinam on pregnancy or on the health of the fetus/newborn child. To date, no other relevant epidemiological data are available.

In keeping with current practice, the drug should be only be used in pregnancy if considered essential by the physician.

It is excreted in breast milk presenting the risk of candidiasis and also of CNS toxicity due to prematurity of the blood brain barrier. There is also a theoretical risk of later sensitisation.

4.7 Effects on ability to drive and use machines

Presumed to be safe or unlikely to produce an effect.

4.8 Undesirable effects

Very common	>1/10
Common	>1/100 and <1/10
Uncommon	>1/1,000 and <1/100
Rare	>1/10,000 and <1/1,000
Very rare	<1/10,000

The most frequent reported undesirable effects are gastrointestinal disorders and various skin reactions. Allergic reactions, change in blood counts and hepatic function disorders have been reported in isolated cases.

Based on pooled data from clinical studies including more than 700 patients receiving parental treatment undesirable effects occurred in less than 10% of patients. Treatment was withdrawn in less than 1% of patients due to undesirable effects.

Based on post-marketing data, the total undesirable effect ‘ reporting rate’ is very rare being approximately 7:100,000 treatment courses.

- Gastrointestinal disorders

Antibiotic associated colitis
Diarrhoea
Vomiting
Nausea
Abdominal pain

- Skin and subcutaneous tissue disorder

Rash
Urticaria
Pruritus
Angioneurotic oedema

- Hepatobiliary disorders

Hepatic function abnormal
Slight reversible increase in ASAT, ALAT, alkaline phosphatase and bilirubin

- Immune system disorders

Anaphylactic

- Blood and lymphatic system disorders

Thrombocytopenia
Granulocytopenia
Leucopenia
Eosinophilia

4.9 Overdose

There has been no experience of overdosage with Mecillinam. Treatment should be restricted to symptomatic and supportive measures.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Selexidin is the amidino-penicillanic acid, mecillinam.

5.2 Pharmacokinetic properties

Peak serum levels averaging 6 microgram/ml and 12 microgram/ml are obtained following intramuscular doses of 200mg and 400mg respectively. Intravenous injection produces initially very high concentrations, which rapidly decline as the compound is excreted.

The serum half life is 1.2 hours and the protein binding amounts to 5 - 10%. Approximately 50 - 60% of the dose may be recovered in the urine within the first 6 hours. Mecillinam is partly excreted in the bile giving rise to biliary concentrations about three times the serum level. Concurrent administration of probenecid delays the renal excretion of mecillinam.

5.3 Preclinical safety data

No additional data.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Powder:
None

Solvent:
Water for Injections

6.2 Incompatibilities

Do not add mecillinam to infusion fluids containing other antibiotics.

6.3 Shelf Life

Unopened: 3 years
The product should be used immediately after opening/reconstitution.

6.4 Special precautions for storage

Store below 25°C.

6.5 Nature and contents of container

Powder container:
Colourless, 6ml, Type I Ph. Eur. glass vial, closed with butyl rubber stopper and aluminium cap, containing 400 mg of powder.
Solvent container:
Colourless 6 ml, Type I Ph.Eur. glass vial, closed with butyl rubber stopper and aluminium cap, containing 6 ml of water for injection.

6.6 Instructions for use and handling

For single use only. Prepare solution immediately before use. Discard any used contents. The reconstituted solution should be complete and clear.

7 MARKETING AUTHORISATION HOLDER

LEO Laboratories Limited,
Cashel Road,
Dublin 12.

8 MARKETING AUTHORISATION NUMBER

PA 46/29/1

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 17th January 1979

Date of last renewal: 17th January 2004

10 DATE OF REVISION OF THE TEXT

February 2005