Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Lomotil 2.5mg / 0.025mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 2.5mg of diphenoxylate hydrochloride and 0.025mg of atropine sulphate.

Excipients - contains sucrose 53.5mg and sorbitol solution 3.10mg

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Tablet
White biconvex tablet with the name 'GS10' engraved on one side.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Adults only:

Adjunctive therapy to appropriate rehydration in acute diarrhoea.

4.2 Posology and method of administration

Route of administration

Oral.

Caution: The recommended dosage should not be exceeded. Once satisfactory control is achieved, dosage should be reduced to suit the requirements of the individual patient.

Adults only:

The recommended starting is four tablets followed by two tablets every six hours until the diarrhoea is controlled.

Elderly:

Consideration should be given to the presence of other diseases and concomitant drug therapy (see precautions).

Children:

Not recommended.

4.3 Contraindications

Lomotil is contraindicated in-patients with a known hypersensitivity to diphenoxylate hydrochloride or atropine, in-patients with jaundice, intestinal obstruction, acute ulcerative colitis, myasthenia gravis, pyloric stenosis, paralytic ileus, prostatic enlargement, in the treatment of diarrhoea associated with pseudomembranous enterocolitis and in patients with a raised intracranial pressure, and patients with head injury.

4.4 Special warnings and precautions for use

Appropriate fluid and electrolyte therapy should be given to protect against dehydration. If severe dehydration or electrolyte is present, Lomotil should be withheld until appropriate corrective therapy has been initiated. In some patients with ulcerative colitis, agents which inhibit intestinal mobility or delay intestinal transit time have been reported to induce toxic megacolon. Patients with ulcerative colitis should be observed carefully and Lomotil therapy should be discontinued promptly if abdominal distension or other untoward symptoms develop. Diphenoxylate should be avoided in patients with antibiotic-associated colitis or diarrhoea associated with entero-toxin-producing bacteria.

Lomotil should be used in extreme caution in patients with advance hepatorenal disease and in patients with abnormal liver function since hepatic comma may be precipitated.

Because a subtherapeutic dose of atropine is added to Lomotil, atropine effects may occur in susceptible individuals or in overdosage. Individual with Down's Syndrome appear to have increased susceptibility to the actions of atropine.

Although single doses in therapeutic range produce little or no morphine like subjective effects, at high doses (40-60 mg) typical opioid effects are produced (see section 4.9)

Patients with rare hereditary problems of fructose intolerance, glucose, galactose, malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction

Diphenoxylate hydrochloride may potentiate the action of narcotic or sedative drugs such as barbiturates, tranquillisers and alcohol.

The following potential interactions have to be considered in the use of Lomotil Tablets:-
Opiod analgesics antagonises the effects of Domperidone, Metoclopramide, Cisapride.

Antimuscarinics such as atropine antagonise the muscarinic effects of Bethanecol/Carbachol, Galantamine, Donepezil, Neostigmine/pyridostigmine, and Pilcarpine.

Memantine possibly enhances the effects of antimuscarinics.

Absorption of Levodopa possibly reduced by antimuscarinics.

Antimuscarinics reduces the absorption of Ketoconazole.

The anticholinergic effects of this product may be enhanced by the concomitant administration of Amantadine, Anthihistamines (sedative and non-sedative), Clozapine, Disopyramide, Fluspiriline, Loxapine, MAOI's, Nefopam, Olanzapine, Phenothiazines, Quantiapine, Remoxipride, Terfenadine, Tricyclic antidepressasnts, and Zotepine.

Dry mouth prevents the dissolution of sublingual nitrate tablets, such as glyceryl trinitrate.

4.6 Fertility, pregnancy and lactation

Pregnancy
Safety of Lomotil in human pregnancy has not been established, although animal teratology and reproduction studies have demonstrated no adverse effects. Lomotil should not be used in pregnancy unless considered essential by the physician.

Lactation
Diphenoxylate hydrochloride and atropine sulphate may be excreted in human milk. Lomotil should not be used in nursing mothers.

4.7 Effects on ability to drive and use machines

Some of the undesirable effects such as sedation, drowsiness or dizziness may affect the ability to drive or operate machines. If affected, patients should be advised not to drive or operate machinery.

4.8 Undesirable effects

Adverse reactions reported included:

Central nervous:
Malaise/lethargy/sedation/somnolence, confusion, dizziness, restlessness, depression, euphoria, hallucinations, headache and giddiness.

General disorders:
Fever
Atropine effects such as flushing and hypothermia may occur.

Cardiac disorders:
The atropine side effects of Lomotil Tablets include cardiac irregularities such as arrhythmias, bradycardia, tachycardia, and palpitations.

Allergic:
Anaphylaxis, angioedema, urticaria and pruritus.

Gastrointestinal system:
Paralytic ileus, toxic megacolon, gastrointestinal intolerance such as nausea and vomiting, anorexia, constipation, abdominal discomfort and dry mouth.

Skin and Subcutaneous tissue
Atropine effects such as dryness of skin and mucous membranes may occur.

Respiratory, thoracic and mediastinal disorders
Respiratory depression in children(atropine effect).

Renal and Urinary Disorders
Atropine effects such as urinary retention and difficulty in micturition may occur.

Eye disorder:
Dilation of pupils with loss of accommodation, photophobia, increased intra-ocular pressure, very rarely angle closure glaucoma can occur.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via
HPRA Pharmacovigilance,
Earlsfort Terrace,
IRL - Dublin 2;
Tel: +353 1 6764971;
Fax: +353 1 6762517;
Website: www.hpra.ie; E-mail: medsafety@hpra.ie.

4.9 Overdose

Accidental overdose may produce narcosis with respiratory depression or atropine poisoning or both, particularly in children. Symptoms of overdose include dryness of the skin and mucous membranes, flushing, hypothermia and

tachycardia, nystagmus, pinpoint pupils, hypotonic reflexes, lethargy, coma and severe respiratory depression. The onset of symptoms of overdose may be considerably delayed and respiratory depression may not become evident until as late as 12-30 hours after ingestion and may occur in spite of initial response to narcotic antagonists. Continuous observation should be maintained for at least 48 hours.

If respiratory depression develops, naloxone, a specific antidote, should be administered. The duration of action of naloxone hydrochloride is considerably shorter than that of diphenoxylate hydrochloride and repeated injections of the antidote may be required. Establishment of a patient airway and artificial ventilation may be needed. If the patient is not comatose, gastric lavage and administration of slurry of an activated charcoal may be indicated.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

The active ingredients diphenoxylate hydrochloride is a synthetic opioid derivative with selective effects on gastrointestinal smooth muscle. It is essentially devoid of “morphine type subjective effects” at therapeutic doses. Atropine sulphate is included in the formulation as an anti-abusing agent contributing to the safe use of the product. The dose of atropine sulphate contained in each tablet is subtherapeutic therefore a pharmaceutical effect due to atropine should not be detected taken at normal therapeutic doses.

5.2 Pharmacokinetic properties

Diphenoxylate hydrochloride is well absorbed from the gastrointestinal tract and extensively metabolised in the liver to diphenoxylate acid (difenoxin) and hydroxydiphenoxylic acid. It is excreted mainly as metabolites in the Urine and bile.

5.3 Preclinical safety data

Not applicable.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Magnesium stearate
Talc
Light liquid paraffin
Sucrose
Acacia
Sorbitol Solution

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

5 years.

6.4 Special precautions for storage

Do not store above 30°C.
Store in the original package in order to protect from light

6.5 Nature and contents of container

Lomotil tablets may be supplied in pvc/foil blister packs of 8, 100, 500, and 1000.

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

Mercury Pharmaceuticals Ltd
Capital House
85 King William Street
London EC4N 7BL
United Kingdom

8 MARKETING AUTHORISATION NUMBER

PA 899/7/1

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 24 May 1980

Date of last renewal: 24 June 2010

10 DATE OF REVISION OF THE TEXT

May 2015