Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Actal 500mg Oral Gum

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

One oral gum contains:

Hydrotalcite 500 mg.

For excipients, see 6.1.

3 PHARMACEUTICAL FORM

Oral gum
Cream to honey coloured triangular pastille on the surface.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

For the symptomatic treatment of heartburn and acid-induced gastric complaints.

4.2 Posology and method of administration

Adults & Adolescents aged 13 years and over:
1-2 pieces of oral gum to be taken several times a day up to a maximum daily dose of 8 pieces, between meals and before going to bed, or when acid- induced gastric complaints occur (refer to section 4.4).

The pieces of oral gum should be chewed well before swallowing.

Infants & Children aged 12 years and below:
Actal Oral Gum is not recommended for use in this age group as no data are available on efficacy and safety.

4.3 Contraindications

Do not use Actal Oral Gum in the presence of hypersensitivity to the active substance or to any of the other excipients, severe renal insufficiency (creatinine clearance < 30ml / min), hypophosphataemia.

Patients with rare heredity problems of fructose intolerance should not take this medicine.

4.4 Special warnings and precautions for use

The following special warnings and precautions for use are related to the two major components of hydrotalcite, magnesium and aluminium.

Patients with mild to moderate renal insufficiency (creatinine clearance ≥ 30 ml/min) should use this product with great caution. Chronic use of hydrotalcite by these patients may cause encephalopathy (aluminium) or hypermagnesaemia (magnesium) in rare cases.

In patients with impaired renal function long-term and high dose therapy should be avoided.

Chronic use in combination with a low phosphate diet (e.g. malnutrition) may cause hypophosphataemia, with a risk of osteomalacia. Therefore, chronic use should be avoided.

In long term use, the aluminium concentrations in the blood must be monitored regularly and should not exceed 40 microgram/l.

Severe and persisting symptoms can be a sign of peptic ulcer disease or malignancy. If symptoms do not improve during treatment with Actal Oral Gum within 14 days the doctor should be consulted and further examinations should be carried out. If tarry, black stool or haematemesis occur the doctor should be contacted immediately.

No clinical trial results are available on the efficacy and safety of Actal Oral Gum in children.

This product contains ethanol (alcohol), less than 100mg per dose.

As with the maximum daily dose of Actal Oral Gum the maximum amount for the excipient maltitol is above 5g, Actal Oral Gum may have mild laxative effect.

4.5 Interaction with other medicinal products and other forms of interaction

Actal Oral Gum can reduce the absorption of other drugs, such as cardiac glycosides, tetracyclines and quinolones (e.g. ciprofloxacin), from the gastrointestinal tract. Consequently an interval of 1-2 hours should be allowed between the administration of Actal Oral Gum and other medicines.

Increasing the pH of the urine, may change the elimination of some drugs. This may cause for example a possible decrease in salicylate levels or an increase in quinidine levels.

Simultaneous administration of Actal Oral Gum and acid-containing beverages (fruit juices, wines etc.) increases the uptake of aluminium from the intestine and should be avoided.

4.6 Pregnancy and lactation

The risk-benefit ratio should be carefully assessed before using Actal Oral Gum in pregnant women. No cases of undesirable effect during pregnancy and lactation have been reported to date.

During pregnancy, Actal Oral Gum should be administered in the lowest possible dose and the treatment period should be short in order to avoid aluminium loading in the foetus.

Animal studies have shown aluminium salts to have harmful effects on the offspring (see “Preclinical safety data”).

Aluminium compounds pass into the breast milk. However, a risk to the newborn is not to be expected as only very small quantities are taken up.

4.7 Effects on ability to drive and use machines

None.

4.8 Undesirable effects

Metabolism and nutrition disorders:
With chronic use in high doses aluminium containing products may in rare cases (≥ 0.01% - < 0.1% of all treated patients) cause ‘phosphate deficiency syndrome’.

Gastrointestinal disorders:
In rare cases (≥ 0.01% - < 0.1% of all treated patients) high doses can cause soft stools and gastrointestinal complaints (e.g. diarrhoea).

General disorders and administration site conditions:
In very rare case (< 0.01% of all treated patients) allergic reactions have been observed in association with the use of Actal Oral Gum.

4.9 Overdose

None known to date.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antacid.
ATC Code: A02AD04.

Hydrotalcite has acid binding as well as dose- and pH-dependent bile acid and lysolecithine adsorbing properties. Animal studies have indicated that hydrotalcite has a cytoprotective effect.

Hydrotalcite buffers in the optimal range of pH 3-5 and the intragastric pH is increased for about 2 hours.

Intracerebral aluminium deposits have been found in patients with dialysis encephalopathy and dialysis patients can develop aluminium-associated osteomalacia. Aluminium-associated microcytic, hypochromic anaemia has also been observed.

5.2 Pharmacokinetic properties

The lattice layer structure of hydrotalcite is dissolved pH-dependently and aluminium and magnesium ions are released intragastrically. These are then precipitated as carbonates and phosphates in the small intestine. In the presence of food, the precipitation process may also take place in the stomach.

Some of the aluminium ions which are contained in hydrotalcite are absorbed and lead to a temporary increase in the serum aluminium concentration as well as to a rise in renal aluminium excretion. The serum aluminium levels remain within the normal range.

Magnesium is also absorbed to a small extent. However, the serum magnesium concentration generally remains constant due to renal elimination.

Renal insufficiency and long-term administration of high doses can result in hypermagnesaemia and gradual aluminium infiltration especially in the nerve and bone tissue.

5.3 Preclinical safety data

Animal studies have shown that aluminium taken up by the nerve tissue has neurotoxic effects.

Symptoms of magnesium intoxication include central nervous disorders, muscle weakness, areflexia, fatigue, paresis, coma and cardiac arrhythmia.

Reproduction toxicology (aluminium salts):

Studies in various animal species (rabbit, mouse) have shown that aluminium permeates the placenta and accumulates in foetal tissue, predominantly in the bones. After exposure during pregnancy, elimination via the mother’s milk persists for some time.

After oral administration to mice (57.5mg aluminium/kg/day) embryo lethality, increased incidence of cleft palates and vertebral deformation were observed. Rat foetuses showed reduced ossification (133mg aluminium/kg/day). Postnatal

effects of exposure to aluminium include an increased rate of stillbirths, perinatal mortality, retarded growth, behavioural changes, biochemical changes in the brain (long-term effect, lowest effective dose: 10-20mg aluminium/kg/day).

In animal studies aluminium infiltration in the bone substance is clearly higher in foetuses than in adult animals. Studies in premature human neonates have shown that aluminium accumulates in the bones after intravenous administration. Similar conditions can be assumed to exist in foetuses *in utero*.

Mutagenic and carcinogenic potential:

Mutagenicity studies have not indicated any relevant mutagenic potential. No studies are available on the carcinogenic potential.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Maltitol liquid
Acacia
Xanthan gum
Maltodextrin
Saccharin sodium
Sodium cyclamate
Caramel flavour
Ethanol
Light liquid paraffin
Beeswax white

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

2 years.

6.4 Special precautions for storage

Do not store above 30°C.

6.5 Nature and contents of container

Aluminium foil blister of PVC/PVDC with 10 pieces of oral gum. Packs with 10, 20, 30, 50 or 100 pieces of oral gum.

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

Seven Seas Limited
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8 MARKETING AUTHORISATION NUMBER

PA 417/15/1

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