IRISH MEDICINES BOARD ACTS 1995 AND 2006

MEDICINAL PRODUCTS(CONTROL OF PLACING ON THE MARKET)REGULATIONS,2007

(S.I. No.540 of 2007)

PA1410/033/001
Case No: 2056854

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

Transferred from PA0021/047/001.

Bayer Limited

The Atrium, **Blackthorn Road**, **Dublin 18**, **Ireland**

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

Alka Antacid 500 mg Chewable Tablets

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 **24/10/2008** until **25/05/2010**.

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

Alka Antacid 500mg Chewable Tablets.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains hydrotalcite 500 mg.

For excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Chewable tablets.

White round tablets with peppermint-like odour.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Symptomatic relief in the following conditions: indigestion; hyperacidity; dyspepsia; gastric and duodenal ulceration; gastritis; heartburn, especially when associated with reflux oesophagitis or hiatus hernia and heartburn in pregnancy.

4.2 Posology and method of administration

Adults and the elderly

One or two tablets three to four times daily to be taken one to two hours before or after meals, before bedtime, or as symptoms occur.

The tablets should be chewed or crushed before swallowing.

The maximum daily dose is eight tablets (4g).

Renal Impairment

Caution should be exercised in patients with impaired kidney function (creatinine clearance <30ml/min). Serum levels of magnesium and aluminium should be monitored. The serum level of aluminium should not exceed 40µg/l and the level of magnesium should remain within the normally accepted limits. Long-term and high-dose therapy should be avoided.

Children 6-12 years

Half the adult dose.

Not recommended for children under six.

4.3 Contraindications

Known hypersensitivity to the active, hydrotalcite, or any of the ingredients.

Severe renal insufficiency (creatinine clearance <30ml/min).

Hypophosphataemia.

4.4 Special warnings and precautions for use

The following special warnings and precautions for use are related to the magnesium and aluminium components of hydrotalcite:

- Chronic use of hydrotalcite by patients with mild to moderate renal insufficiency (creatinine clearance <30ml/min) may cause encephalopathy (aluminium) or hypermagnesaemia (magnesium) in rare cases.
- Chronic use in combination with a low phosphate diet (e.g. malnutrition) may cause hypophosphatemia, with a risk of osteomalacia.
- In long-term use, the aluminium concentrations in the blood must be monitored regularly and should not exceed 40 µg/ml.
- In patients with impaired renal functions long-term and high dose therapy should be avoided.
- Severe and persisting symptoms can be a sign of peptic ulcer disease or malignancy. If symptoms do not improve during treatment with Alka Antacid 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.

4.5 Interaction with other medicinal products and other forms of interaction

Hydrotalcite may reduce absorption of other drugs, such as cardiac glycosides, antibiotics, corticosteroids and iron salts, from the gastrointestinal tract. Consequently an interval of 1-2 hours should be allowed between the administration of Alka Antacid and other medicines.

Simultaneous administration of hydrotalcite and acid-containing beverages (fruit juices, wines etc.) may increase the uptake of aluminium from the intestine and should be avoided.

4.6 Pregnancy and lactation

No embryotoxicity or teratogenic effects were observed in animal studies with hydrotalcite. However, it should be avoided during the first trimester of pregnancy.

Aluminium compounds pass into the breast milk. However, hydrotalcite is not significantly absorbed within the therapeutic dose range. Therefore, it may be administered to lactating women.

4.7 Effects on ability to drive and use machines

None.

4.8 Undesirable effects

In rare cases high doses can cause soft stools and gastrointestinal complaints (e.g. vomiting and diarrhoea).

With chronic use in high doses, aluminium containing products may in rare cases cause ‘phosphate deficiency syndrome’.

4.9 Overdose

No cases of overdose with hydrotalcite have been reported.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC-classification

Hydrotalcite has acid binding as well as dose- and pH-dependent bile-acid and lysolecithine absorbing 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, and biochemical changes in the brain (long-term effect, lowest effective dose: 10-20 mg 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

Mannitol (E421)
Maize starch
Magnesium stearate
Saccharin sodium
Banana flavour
Peppermint flavour

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

Five years.

6.4 Special precautions for storage

There are no special storage conditions.

6.5 Nature and contents of container

Blister packs consisting of two separate strips of five tablets each, composed of PP backed with aluminium foil. Available in packs of 10, 20, 30 and 50 tablets.

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

Bayer Ltd
The Atrium
Blackthorn Road
Dublin 18
Ireland

8 MARKETING AUTHORISATION NUMBER

PA 1410/33/1

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 26th May 2000

Date of last renewal: 26th May 2005

10 DATE OF REVISION OF THE TEXT

October 2008