IRISH MEDICINES BOARD ACTS 1995 AND 2006

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

(S.I. No.540 of 2007)

PA0577/005/002
Case No: 2032354

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

McDermott Laboratories Ltd t/a Gerard Laboratories

35/36 Baldoyle Industrial Estate, **Grange Road**, **Dublin 13**, **Ireland**

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

Geramet 400mg Film-coated 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 **28/03/2008**.

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

Geramet 400 mg Film-coated tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains Cimetidine 400 mg.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Film coated tablets
Pale green oval film coated biconvex tablet embossed “CN400” on one side and “G” on the reverse.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

In the treatment of benign ulceration of oesophagus, stomach, upper intestinal tract (including post-operative stomal area) and the Zollinger-Ellison syndrome.

In the management of conditions benefiting from reduced gastric acid secretion.

In the long term maintenance management of benign peptic ulcer disease under regular surveillance.

4.2 Posology and method of administration

Adults:
The usual dose is 400 mg twice a day with breakfast and at bedtime. Alternatively patients with duodenal or benign gastric ulceration may be treated with a single dose of 800 mg at bedtime. Regimens of 200 mg thrice daily with meals and 400 mg nocte, or, if inadequate, 400 mg q.d.s. with meals and at bedtime may also be used.

In oesophageal reflux 400 mg q.d.s. with meals and at bedtime for 4 to 8 weeks is recommended.

In patients with very high gastric acid secretion (e.g. Zollinger-Ellison syndrome) it may be necessary to increase the dose to 400 mg q.d.s. or occasionally higher.

Treatment should be given initially for at least 4 weeks (6 weeks in the case of benign ulcer). In patients who may benefit from a reduction of gastric secretion, dosage may be reduced to a maintenance regimen of 400 mg at bedtime, or in the morning and at bedtime.

A similar maintenance regimen may be used to prevent relapse in patients with benign peptic ulceration. Patients on prolonged treatment (particularly those treated for more than one year) should be kept under regular surveillance.

Antacids may be used concurrently if required.

In the prophylaxis of haemorrhage from ‘stress’ ulceration doses up to a maximum of 2.4 g daily may be given in divided doses. 200-400 mg doses can be given every 4 to 6 hours by oral, nasogastric or parenteral routes (N.B. by direct intravenous injection a dose of 200 mg should not be exceeded - see parenteral dosage recommendations).

In the prophylaxis of acid aspiration (Mendelson's syndrome) a single dose of 400 mg may be given 90-120 minutes before induction of general anaesthesia or, in obstetric practice, at the start of labour. While such a risk persists a dose of up to 400 mg may be repeated (parenterally if appropriate) at 4 hourly intervals as required, up to the usual maximum of 2.4 g/day.

In pancreatic insufficiency, for protection of pancreatic enzyme supplements, 800-1600 mg/day may be given according to response in four divided doses, one to one and a half hours before meals.

The total daily dose by any route should not usually exceed 2400 mg.

Elderly:
In the normal adult dosage may be used unless renal function is markedly impaired.

Children:
Experience in children is less than that in adults. In children more than 2 years old, cimetidine 25-30 mg/kg body weight/day in divided doses may be administered by either the oral or parenteral routes.

The use of cimetidine in children less than 2 years old is not fully evaluated.

Patients with impaired renal function:
Dosage should be reduced in patients with impaired renal function when creatinine clearance is below 50 ml/minute.

Creatinine Clearance	**Daily Dosage**
30 - 50 ml/minute	200 mg q.d.s.
15 - 30 ml/minute	200 mg t.d.s.
0 - 15 ml/minute	200 mg b.d.

Patients receiving dialysis therapy:
Cimetidine is removed by haemodialysis, but not to any significant extent by peritoneal dialysis.

4.3 Contraindications

Hypersensitivity to cimetidine or any of its excipients.

4.4 Special warnings and precautions for use

Before initiation of cimetidine therapy for any gastric ulceration malignancy should be excluded by endoscopy, and biopsy if possible. Treatment with cimetidine can mask symptoms and assist transient healing of gastric cancer. The consequences of a potential delay in diagnosis should be kept in mind particularly in patients of middle age or over or with new or recently changed dyspeptic symptoms.

The safety of prolonged use is not fully established and care should be taken to keep patients on prolonged treatment (particularly those treated for greater than one year) under regular surveillance.

In patients on drug treatment or with illnesses which could cause a fall in blood cell counts, the possibility that H_2 receptor antagonism could potentiate this effect should be borne in mind.

Care should be exercised in renal and hepatic impairment.

4.5 Interaction with other medicinal products and other forms of interaction

Cimetidine can prolong the elimination of drugs metabolised by oxidation in the liver. Pharmacological interactions with a number of drugs e.g. diazepam, propranolol, have been demonstrated; only those with oral anti-coagulants, phenytoin and theophylline appear to date to be of clinical significance. Close monitoring of patients on cimetidine

receiving oral anticoagulants, phenytoin, and theophylline is recommended. A reduction in their dosage may be necessary.

4.6 Pregnancy and lactation

Animal studies and clinical data have not revealed any hazards from the use of cimetidine during pregnancy and lactation. Studies however, established that cimetidine crosses the placental barrier and is excreted in breast milk. Its administration during pregnancy and lactation should be avoided unless considered essential by the physician.

4.7 Effects on ability to drive and use machines

If patients experience dizziness, they should not drive.

4.8 Undesirable effects

The following frequencies are used to evaluate adverse events. Common (≥1/100 and < 1/10), Uncommon (≥1/1,000 and <1/100) and Rare (≥1/10,000 and <1/1,000). The following adverse events have been reported in conjuntion with Cimetidine 400mg:

The most common adverse events reported were Headache, dizziness and mild gastrointestinal problems. a full list of adverse events is available in the table below.

Table 1 Frequency of Adverse Events

System Organ Class	**Common (≥1/100 and <1/10)**	**Uncommon (≥1/1,000 and <1/100)**	**Rare (≥1/10,000 and <1/1,000)**
Reproductive System and breast disorders			Reversible Gynaecomastia, Reversible impotence
Gastrointestinal disorders	Diarrhoea		Acute pancreatitis
Nervous system disorders	Dizziness, fatigue, Headache		
Hepatobiliary disorders			Reversible liver damage
Renal and urinary disorders			Interstitial nephritis
Musculoskeletal and connective tissue disorder			Myaligia, Antrhralgia
Psychiatric disorders		Confusion (especially in the elderly or in very ill patients), Mood and behavioural changes, Insomnia.	
Skin and subcutaneous tissue disorders	Rash		
Blood and lymphatic system disorders			Thrombocytopenia

4.9 Overdose

Acute overdose involving doses over 20 g have been reported several times with no significant ill effects. Induction of vomiting and/or gastric lavage may be employed, in addition to supportive and symptomatic therapy.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: H2 - receptor antagonists, ATC code A02BA01.

Cimetidine is a histamine H_2 receptor antagonist which rapidly inhibits both basal and stimulated gastric secretion of acid and reduces pepsin output. It may also have a mucosal protective effect independent of its anti-secretory effect.

5.2 Pharmacokinetic properties

Cimetidine is well absorbed after oral dosing. It is metabolised in the liver and is excreted mainly through the kidney with a $T_{1/2}$ of about 3-4 hours. The effects on acid secretion are of longer duration.

5.3 Preclinical safety data

Relevant data are discussed in the pregnancy and lactation section.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet Core
Sodium starch glycolate
Povidone K29-32
Magnesium stearate
Maize starch
Microcrystalline cellulose

Tablet Coating
Opadry OY-S-8826 containing:
Hypromellose (E464)
Hyprolose
Titanium dioxide (E171)
Povidone
Macrogol 400
Iron oxide yellow (E172)
Indigo carmine aluminium lake (E132)
Iron oxide black (E172)

Tablet Polishing
Carnauba wax

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

3 years.

6.4 Special precautions for storage

Do not store above 25°C.

6.5 Nature and contents of container

a) Polyethylene container with urea white caps and Jayfilla ullage filler.

50 & 2500 tablets

b) Blister packaging (PVdC/Aluminium foil blisters)

60 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

McDermott Laboratories Limited
Trading as:
Gerard Laboratories
35/36 Baldoyle Industrial Estate
Grange Road
Dublin 13

8 MARKETING AUTHORISATION NUMBER

PA 577/5/2

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 27th November 1991
Date of last renewal: 27th November 2006

10 DATE OF REVISION OF THE TEXT

March 2008