Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Pepcid AC 10 mg Film-coated Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 10 mg famotidine

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Film-coated tablet.
Pale-rose, rounded-square tablet with FA10 engraved on one side.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

The short-term symptomatic relief of heartburn, indigestion (dyspepsia) and excess acid.
Prevention of these symptoms when associated with meals including nocturnal symptoms.

4.2 Posology and method of administration

Posology

Adults and children 16 years of age or older:

Dosage : 10mg

Dosage interval:

1 tablet (10mg) for symptomatic relief of heartburn, indigestion (dyspepsia) and excess acid.

or

1 tablet (10mg) taken 15 minutes prior to meals to prevent these symptoms.

or

1 tablet (10mg) taken within one hour before the evening meal for prevention of nocturnal symptoms.

Maximum intake in 24 hours: 2 tablets (20mg).

The maximum treatment period is 2 weeks.

Special populations

Elderly
No dosage adjustment is necessary for the elderly.

Paediatric populations
Pepcid AC is not recommended for use in children less than 16 years of age.
The safety and effectiveness of oral famotidine have not been established in paediatric patients.

Renal Impairment

A dosage adjustment may be necessary in patients with a creatinine clearance less than 10 mL/min. Patients with renal impairment should consult a physician before use (please refer to section 4.4 – Special Warnings and Special Precautions for Use).

Hepatic Impairment
No dosage adjustment is required in hepatic impairment.

Method of administration
For oral use. The tablets should be swallowed whole with a glass of water and not chewed.

4.3 Contraindications

Cross sensitivity in this class of compounds has been observed. Therefore, famotidine should not be administered to patients with a history of hypersensitivity to other H_2-receptor antagonists.

Hypersensitivity to famotidine or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

In clinical trials, patients with other underlying acid related gastro-intestinal diseases (e.g. duodenal ulcer, gastric ulcer) did not experience complications; in general, they did not exhibit a clinically significant deterioration in their condition.

Patients over 50 who are experiencing heartburn for the first time and patients of any age who have noticed unintentional weight loss should consult a physician before using the product. Malignancy should be excluded, as treatment with famotidine may alleviate symptoms and delay diagnosis.

Patients should stop use and consult a physician if symptoms persist or worsen, or if they experience dysphagia (difficulty swallowing) odynophagia (pain on swallowing), severe vomiting, melaena (black stools), choking or chest pain.

Since Pepcid is excreted primarily by the kidney, caution should be observed in patients with impaired renal function. Patients with renal impairment should consult a physician before using the product. A reduction in daily dosage should be considered if creatinine clearance falls below 10 mL/min.

Paediatric use
Safety and efficacy are not established for children.

Use in elderly
When Pepcid was administered to elderly patients in clinical trials, no increase in the incidence or change in the type of drug-related side effects was observed. No dosage adjustment is required based on age.

4.5 Interaction with other medicinal products and other forms of interaction

Pepcid AC does not interact with the cytochrome P450-linked drug metabolising enzyme system. Compounds metabolised by this system which have been tested in man have included warfarin, theophylline, phenytoin, diazepam, propranolol, aminopyrine and antipyrine. Famotidine does not appear to affect the disposition of these drugs when they are taken orally.

Indocyanine green as an index of hepatic blood flow and/or hepatic drug extraction has been tested and no significant effects have been found.

Studies in patients stabilized on phenprocoumon therapy have shown no pharmacokinetic interaction with famotidine and no effect on the pharmacokinetic or anticoagulant activity of phenprocoumon.

Alterations of gastric pH may affect the bioavailability of certain drugs resulting in a decrease in the absorption of atazanavir.

The absorption of ketoconazole and itraconazole could be reduced. Ketoconazole should be given 2 hours before famotidine administration. Patients should consult a physician before using this product together with itraconazole. Concomitant use of famotidine with the antifungal agent itraconazole results in significantly reduced peak and trough plasma concentrations of itraconazole, which may result in reduced antifungal efficacy. Co-administration of posaconazole oral-suspension with

famotidine should be avoided if possible, since famotidine may reduce the absorption of posaconazole oral-suspension during concomitant use.

Due to its H2-antagonist effect, famotidine may also decrease the absorption of the following compounds:
- Rilpivirine,
- Cyanocobalamine,
- Most of tyrosines kinase inhibitors (excluding vandetanib, imatinib). Co -administration of famotidine with the tyrosine kinase inhibitors (TKIs) dasatinib, erlotinib, gefitinib, pazopanib may decrease plasma concentrations of TKIs resulting in lower efficacy, therefore co-administration of famotidine with these TKIs is not recommended. For further specific recommendations please refer to the product information of individual TKI medicinal products.

Famotidine may decrease the absorption of Ulipristal.

Antacids may decrease the absorption of famotidine and lead to lower plasma concentrations of famotidine. Famotidine should therefore be taken 1 - 2 hours before the administration of an antacid.

Risk of loss of efficacy of calcium carbonate when co-administered as phosphate binder with famotidine in haemodialysis patients.

Famotidine does not affect blood alcohol levels following oral ingestion of ethanol.

The administration of probenecid can delay the elimination of famotidine. Concomitant use of probenecid and famotidine should be avoided.

The concomitant use of sucralfate should be avoided within two hours of the famotidine dose.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are no adequate and well-controlled studies in pregnant women. This product should not be used during pregnancy unless the potential benefit of treatment to the mother outweighs the possible risks to the developing foetus.

Lactation

Famotidine is distributed in breast milk. A risk to newborns / infants cannot be excluded. A decision must be made whether to discontinue breast-feeding or to discontinue / abstain from therapy with famotidine taking into account the benefit of breast-feeding for the infant and the benefit of therapy for the mother.

4.7 Effects on ability to drive and use machines

Some patients have experienced adverse reactions such as dizziness and headache while taking famotidine. Patients should be informed that they should avoid driving vehicles or operating machinery or doing activities which require prompt vigilance if they experience these symptoms (see section 4.8).

4.8 Undesirable effects

Adverse drug reactions (ADRs) identified during clinical trials and post-marketing experience with famotidine are listed below by System Organ Class (SOC). The frequencies are defined in accordance with current guidance, as:
Very Common (≥1/10),
Common (≥1/100, <1/10),
Uncommon (≥1/1,000, <1/100),
Rare (≥1/10,000, <1/1,000),
Very rare (<1/10,000),
Not known (cannot be estimated from the available data).
ADRs are presented by frequency category based on incidence in adequately designed clinical trials or epidemiology studies.

System Organ Class (SOC)	Frequency	Adverse Drug Reaction (Preferred Term)
Blood and lymphatic system disorders	Very rare	Agranulocytosis

		Leucopenia** Neutropenia Pancytopenia** Thrombocytopenia
Immune system disorders	Very rare	Hypersensitivity (Anaphylactic reaction, Angioedema, Bronchospasm)
Metabolism and nutrition disorders	Uncommon	Decreased appetite
Psychiatric disorders	Very rare	Agitation Anxiety disorder Confusional state Depression Disorientation Hallucination Insomnia Libido decreased Mental disorder
Nervous system disorders	Common*	Headache Dizziness
	Uncommon	Dysgeusia
	Rare*	Somnolence
	Very rare	Generalised tonic-clonic seizure (particularly in patients with impaired renal function) Paraesthesia Seizure
Cardiac disorders	Very rare	Atrioventricular block (with H_2-receptor antagonists administered intravenously)
Respiratory, thoracic and mediastinal disorders	Very rare	Interstitial lung disease (sometimes fatal)
Gastrointestinal disorders	Common	Constipation Diarrhoea
	Uncommon	Abdominal discomfort and pain Abdominal distension Dry mouth Flatulence Nausea and /or Vomiting
Hepatobiliary disorders	Rare	Liver disorder**
	Very rare	Cholestatic jaundice Hepatitis
Skin and subcutaneous tissue disorders	Uncommon	Rash Pruritus Urticaria
	Very rarely	Alopecia Stevens-Johnson syndrome / Toxic epidermal necrolysis (sometimes fatal)
Musculoskeletal and connective tissue disorders	Very rare	Arthralgia Muscle spasms
Reproductive system and breast disorders	Rarely	Gynaecomastia***
	Very rare	Erectile dysfunction
General disorders and administration site conditions	Uncommon	Asthenia Fatigue
	Very rare	Chest discomfort
	Rare	Malaise
Investigations	Very rare	Hepatic enzyme abnormal

* not significantly greater than placebo ($p<0.05$)
** A causal relationship to therapy with famotidine has not been established
*** Reversible on discontinuing treatment

No clinically significant increase in endocrine or gonadal function has been reported.

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, website: www.hpra.ie.

4.9 Overdose

The adverse reactions in overdose cases are similar to the adverse reactions encountered in normal clinical experience (see section 4.8).

The usual measures to remove unabsorbed material from the gastro-intestinal tract, clinical monitoring and supportive therapy should be employed.
Patients with Zollinger-Ellison syndrome have tolerated doses up to 800 mg/day for more than a year without development of significant side effects.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: H_2 Receptor Antagonist, ATC code: A02BA03.

Pepcid AC is a potent competitive H_2-receptor antagonist. Pepcid AC has a rapid onset of action and, at the recommended doses, has a long duration of action and is highly effective at relatively low blood concentrations.

Duration of action, plasma concentration and urinary recovery are dose related.

Pepcid AC reduces the acid and pepsin content, as well as the volume of basal, nocturnal and stimulated gastric secretion.

In clinical trials, Pepcid AC provided effective and rapid symptom relief. When administered 15 minutes before a test meal, famotidine reduced symptoms that would otherwise have been expected. Administration of famotidine before an evening meal prevented nocturnal acid-related symptoms and therefore prevented symptom-related interference with sleep.

After oral administration, a dose-response relationship was clearly demonstrated for doses from 0.5 to 10 mg famotidine in terms of raising gastric pH between and after meals. Famotidine doses of 2.5 to 10 mg were demonstrated to produce a statistically significant effect on gastric pH as compared to placebo. The onset of effect for the 5 and 10 mg doses was seen at approximately 1.5 hours post-dose, while that of the 2.5 mg dose was not seen until 2.5 hours post-dose.
The maximum effect, as measured by peak mean pH value, occurred at 3.5 hours. The activity of the 5 and 10 mg doses continued until approximately 9 hours post-dose in daytime studies. Additionally, two night-time studies demonstrated that famotidine 10mg statistically significantly increased gastric pH for 12 hours post-dose as compared to placebo. Famotidine is well tolerated at these dose levels.

Systemic effects of famotidine in the CNS, cardiovascular, respiratory or endocrine systems were not noted in clinical pharmacology studies. Serum hormone levels, including prolactin, cortisol, thyroxine (T_4) and testosterone were not altered after treatment with famotidine.

5.2 Pharmacokinetic properties

Pepcid AC obeys linear kinetics.

In pharmacokinetic studies in the elderly, no clinically significant age-related changes were detected.

Compared to historical data from younger subjects, age does not appear to affect the bioavailability of single doses of famotidine: however, the elimination appears to be reduced in elderly subjects compared with younger subjects.

Famotidine is rapidly absorbed with dose-related peak plasma concentrations occurring at 1-3 hours. The mean bioavailability of an oral dose is 40-45%. Bioavailability is not clinically affected by the presence of food in the stomach. Pepcid AC undergoes minimal first-pass metabolism. Repeated doses do not lead to accumulation of the drug.

Protein binding in the plasma is relatively low (15-20%). The plasma half-life after a single oral dose or multiple repeated doses (for five days) was approximately three hours.

Metabolism of the drug occurs in the liver, with formation of the inactive sulphoxide metabolite.

Following oral administration, the mean urinary excretion of the absorbed dose of famotidine is 65-70%. Of the total oral dose administered, 25-30% is recovered as unchanged compound in the urine. Renal clearance is 250-450 ml/min, indicating some tubular excretion. A small amount may be excreted as the sulphoxide.

A 10mg chewable tablet of Pepcid AC was found to be bioequivalent to a 10mg film-coated tablet of Pepcid AC.

5.3 Preclinical safety data

The LD_{50} of famotidine in CD-1 mice and Sprague-Dawley rats was in excess of 5g/kg (orally) and in excess of 400mg/kg intravenously.

Extensive preclinical safety studies have been performed in dogs, rats, mice and rabbits using oral and intravenous routes of administration of famotidine.

Minimal toxicological effects (after acute, subacute or chronic administration) have been observed, even at extremely high dosage levels (4000mg/kg/day) and for extended periods of administration. (2000mg/kg/day for 105 weeks).

No evidence of teratogenic, mutagenic or carcinogenic effects or alteration of reproductive function have been seen. In a 106-week study in rats and a 92-week study in mice given oral doses of up to 2000mg/kg/day (approximately 5000 times the maximum recommended human dose), there was no evidence of carcinogenic potential for famotidine.

Famotidine was negative in the microbial mutagen test (Ames test) using *Salmonella typhimurium* and *Escherichia coli* with or without rat liver enzyme activation at concentrations of up to 10000 microgram/plate. In *in vivo* studies in mice, a micronucleus test and a chromosomal aberration test, no evidence of mutagenic effect was observed.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Pregelatinised maize starch
Microcrystalline cellulose
Talc
Magnesium stearate
Hypromellose
Hyprolose
Titanium dioxide (E171)
Carnauba wax
Red iron oxide (E172)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Store in the original package.

6.5 Nature and contents of container

PVC/PE/PVDC/Al blisters of 6, 12 and 18 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

Johnson & Johnson (Ireland) Limited
Airton Road
Tallaght
Dublin 24
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8 MARKETING AUTHORISATION NUMBER

PA0330/053/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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10 DATE OF REVISION OF THE TEXT

April 2024