SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Pepcid Chewable Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Famotidine 10 mg
Magnesium hydroxide 165 mg
Calcium carbonate 800 mg

Excipients with known effect: lactose monohydrate, sucrose and glucose.

For the full list of excipients, see 6.1.

3 PHARMACEUTICAL FORM

Chewable tablet
Rose coloured, round, flat, chewable tablet embossed 'P'.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

The short-term symptomatic relief of heartburn, indigestion, acid indigestion, and hyperacidity.

4.2 Posology and method of administration

Posology
Adults and children 16 years of age or older:
One tablet to be chewed for the relief of symptoms. No more than two tablets to be taken in 24 hours.

Patients must seek medical advice if symptoms fail to respond, or if symptoms recur following self treatment with Pepcid.

The maximum continuous treatment period is 6 days. The patient should not purchase a second pack of tablets without the advice of a pharmacist or doctor.

Elderly
No dosage adjustment is necessary.

Paediatric population:
Children less than 16 years of age
Not recommended. The safety and efficacy of oral famotidine/antacid combination in the paediatric population have not yet been established.

Method of administration
For oral use. Chew tablet well before swallowing.

4.3 Contraindications

Contraindicated in patients with the following conditions:

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- Cross sensitivity in H2-receptor antagonists has been observed. Therefore, famotidine/antacid combination should not be administered to patients with a history of hypersensitivity to other H2-receptor antagonists.
- Moderate or severe renal failure.
- Severe hepatic impairment.

4.4 Special warnings and precautions for use

The following patient groups should consult a physician before taking this product:

- Patients suffering from any other illness or taking any medications either physician-prescribed or self-prescribed.
- Patients with pre-existing hypercalcaemia or hypermagnesaemia

Gastric cancer and simple indigestion can have some symptoms in common. Therefore, it is important that patients with symptoms such as unintentional weight loss, dysphagia, or anaemia, in addition to indigestion, or patients over 50 who are experiencing heartburn for the first time or with recently changed dyspeptic symptoms, should seek medical advice before starting any treatment, to avoid delay in investigation and 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, melena (black stools), choking or chest pain.

Patients who are taking non-steroidal anti-inflammatory drugs, especially the elderly, should consult their doctor before taking these tablets.

As Pepcid contains sucrose and lactose, it should not be taken by patients with fructose intolerance, glucose-galactose malabsorption syndrome, sucrase-isomaltase deficiency, lactase insufficiency or galactosaemia.

4.5 Interaction with other medicinal products and other forms of interaction

Famotidine

Famotidine does not interact with the cytochrome P450-linked drug metabolising enzyme system. Famotidine does not affect blood alcohol levels following oral ingestion of ethanol.

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

Antacids

Antacids can decrease the absorption of some medicines. Concomitant administration of Pepcid is therefore not indicated unless advised by a physician.

Patients should consult a physician before using this product together with any of the following drugs:

Itraconazole

Concomitant use of famotidine and magnesium hydroxide-containing antacids with the antifungal agent itraconazole results in significantly reduced peak and trough plasma concentrations of itraconazole, which may result in reduced antifungal efficacy.

Tetracycline hydrochloride; doxycycline

Magnesium hydroxide products may impair the absorption of certain orally administered antibiotics within the tetracycline group. The mechanism of action may be chelation with magnesium ions, resulting in the formation of a less soluble compound which is not readily able to penetrate the intestinal mucosa.

Ciprofloxacin

Calcium- or magnesium-containing antacids may reduce the bioavailability of ciprofloxacin through chelate formation.

Penicillamine

Magnesium-containing antacids may reduce the bioavailability of penicillamine through chelate formation.

Zinc sulfate

Calcium-containing antacids may reduce the bioavailability of zinc when administered as zinc sulfate, although the mechanism of this interaction is poorly understood.

Antiretroviral medications
Bio-availability of antiretroviral medications (e.g. integrase inhibitors such as raltegravir, dolutegravir, elvitegravir) is significantly reduced by metal-cation containing antacids and dietary supplements.

4.6 Fertility, pregnancy and lactation

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.

Famotidine is excreted in human milk and magnesium salts may enter breast milk and cause diarrhoea in infants; 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 / antacid combination 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 from clinical trials and during post-marketing experience with Famotidine/Magnesium hydroxide/Calcium carbonate are included in the table below. The frequencies are provided according to the following convention:

Very common	≥1/10
Common	≥1/100 and < 1/10
Uncommon	≥1/1,000 and <1/100
Rare	≥1/10,000 and <1/1,000
Very rare	<1/10,000
Not known	(cannot be estimated from the available data)

ADRs identified are presented by frequency category based on 1) incidence in adequately designed clinical trials or epidemiology studies, if available or 2) when incidence is unavailable, frequency category is listed as ‘Not known’.

SOC Frequency Category	**Adverse Event Preferred Term**

Blood and lymphatic system disorders	
Rare	Leukopenia
Rare	Pancytopenia
Immune System Disorders	
Rare	Anaphylactic reaction
Rare	Hypersensitivity
Metabolism and nutrition disorders	
Rare	Decreased appetite
Psychiatric Disorders	
Not known	Nervousness
Nervous System Disorders	
Common	Headache
Uncommon*	Dizziness
Uncommon*	Dysgeusia
Rare*	Somnolence
Not known	Paraesthesia
Gastrointestinal Disorders	
Uncommon*	Abdominal discomfort
Uncommon*	Abdominal pain
Uncommon*	Diarrhoea
Uncommon*	Dry mouth
Uncommon*	Flatulence
Uncommon*	Nausea
Uncommon*	Oropharyngeal discomfort
Uncommon*	Oropharyngeal pain
Uncommon*	Vomiting
Rare	Abdominal pain upper
Rare	Constipation
Not known	Abdominal distension
Not known	Abnormal faeces
Not known	Dyspepsia
Not known	Eructation
Not known	Thirst
Hepatobiliary disorders	
Rare	Jaundice cholestatic
Rare	Liver disorder
Skin and Subcutaneous Tissue Disorders	
Uncommon*	Rash
Rare	Angioedema
Rare*	Pruritus
Rare	Urticaria
Very rare	Alopecia

Musculoskeletal and connective tissue disorders	
Rare	Arthralgia
Reproductive system and breast disorders	
Rare	Gynaecomastia
General Disorders and Administrative site Conditions	
Uncommon*	Asthenia
Uncommon*	Fatigue
Rare	Malaise
Investigations	
Rare	Hepatic enzyme abnormal

*not significantly greater than Placebo (<0.05)

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 the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

No specific symptoms of overdose have been identified with this particular combination of substances.

Famotidine
No specific symptoms of overdose have been identified.

Calcium Carbonate
Overdosage may result in hypercalcemia which may be associated with nausea, vomiting, constipation, mental status changes, lethargy, and weakness. Chronic overdose of calcium carbonate alone or with other calcium salts combined with alkali may result in milk-alkali syndrome, which presents typically with hypercalcaemia, alkalosis, and renal dysfunction. Patients with renal insufficiency and renal failure may be predisposed to this condition.

Magnesium Hydroxide
The oral ingestion of magnesium rarely results in toxicity in patients with normal renal function. Signs of hypermagnesaemia typically begin to develop with plasma levels around 4 mEq/L (4.8 mg/dL). Symptoms generally correlate to magnesium blood levels; however there is variability among literature reports in patients with similar blood levels.

Symptoms associated with blood levels between 4 and 10 mEq/L (4.8-12 mg/dL) include nausea, vomiting, flushing, somnolence, and hypotension. Symptoms that appear at or above plasma levels of 10 mEq/L (12 mg/dL) include ECG changes, loss of deep tendon reflex, paralysis of voluntary muscle, and respiratory depression.
Around 15 mEq/L (18 mg/dL) heart block and cardiac arrest may occur.

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 of famotidine for more than a year without development of significant adverse effects.

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: H_2 ANTAGONIST/ANTACID, ATC code: A02BA53: famotidine, combinations.

Famotidine reduces the acid and pepsin production, as well as the volume of basal, nocturnal and stimulated gastric secretion. Magnesium hydroxide and calcium carbonate are antacids and neutralise intraluminal acid on contact. Pepcid combines the prolonged duration of effect of famotidine with the rapid onset of action of antacids and has an acid neutralisation capacity of 21 mEq per tablet.

A study measuring gastric and oesophageal pH conducted on 23 patients demonstrated that the administration of Pepcid with 60ml of water one hour after a high-fat evening meal produced an increase of oesophageal pH within 2 minutes. The increase of the gastric pH, above the increase observed with placebo and antacid alone, remained for 12 hours.

5.2 Pharmacokinetic properties

The pharmacokinetic properties of famotidine are not significantly modified when administered with magnesium hydroxide and calcium carbonate as Pepcid.

<u>Famotidine:</u>
Famotidine obeys linear kinetics. Famotidine is rapidly absorbed with dose-related peak plasma concentration occurring at 1-3 hours after administration. The mean bioavailability of an oral dose is 40-45 %. It is not modified when taken during meals. First-pass metabolism is minimal. 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 5 days) is approximately 3 hours. Metabolism occurs in the liver, with formation of an inactive metabolite, the sulfoxide. Following oral administration, the mean urinary excretion of famotidine is 65-70 % of the absorbed dose, 25 to 30 % as unchanged compound. Renal clearance is 250 to

450ml/min, indicating some tubular excretion. A small amount may be excreted as the sulfoxide. The half-life is prolonged in patients with renal impairment.

Antacids

Calcium carbonate and magnesium hydroxide are converted to soluble chloride salts by gastric acid. Approximately 10% of the calcium and 15-20% of the magnesium are absorbed, and the remaining soluble chlorides are reconverted to insoluble salts, and are eliminated in the faeces. In individuals with normal kidney function the small amounts of calcium and magnesium that are absorbed are rapidly excreted by the kidneys.

5.3 Preclinical safety data

Extensive preclinical safety studies have been performed with famotidine in dogs, rats, mice and rabbits using oral and intravenous routes of administration. Minimal toxicological effects (after acute, subacute or chronic administration) have been observed, even at extremely high dosage levels and for extended periods of administration. No evidence of teratogenic, mutagenic or carcinogenic effects or alteration of reproductive function has been seen.

Only limited toxicology data are available for magnesium hydroxide and calcium carbonate. These data indicate no special hazard for humans under normal conditions of use. Ossification abnormalities have been described in animals treated with calcium carbonate at high doses or long periods.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Dextrates
Confectioner's sugar (sucrose and maize starch)
Lactose monohydrate
Peppermint flavour (peppermint oil, modified food starch, maltodextrine, citric acid (E330), sodium ascorbate (E301), water)
Cellulose acetate
Magnesium stearate
Hypromellose (E464)
Hydroxypropyl cellulose (E463)
Sodium lauryl sulphate
Pregelatinised maize starch
Cream flavour (sweet orange oils, ethanol, esters of acetic and butanoic acids, aliphatic alcohols and ketones, phenols, aliphatic and aromatic aldehydes, benzaldehyde, dextrin, maltodextrine, glucose, corn starch, calcium silicate, powdered vanilla extract, heliotropine, vanillin, silicone dioxide, water)
Red ferric oxide (E172).

6.2 Incompatibilities

Not applicable

6.3 Shelf life

3 years for blister packs (PVC/ACLAR)

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

Blister packs (PVC/ACLAR) containing:

2, 4, 6, 8, 10 and 12 tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

McNeil Products Limited

Foundation Park

Roxborough Way

Maidenhead

Berkshire

SL6 3UG

United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL 15513/0348

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

15/12/2008

10 DATE OF REVISION OF THE TEXT

25/06/2019