Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Famotidine Clonmel Healthcare 20 mg film-coated tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Famotidine Clonmel Healthcare 20 mg
Each film-coated tablet contains 20 mg of famotidine.
Excipient with known effect
Each film-coated tablet contains 0.105 mg lecithin (derived from soya oil).

For the full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Film-coated tablet.
Yellow coloured, round, biconvex film-coated tablets debossed with "2V" on one side. Approximately 6 mm in diameter.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Famotidine Clonmel Healthcare is indicated in adults for:

- Prevention of recurrent duodenal ulcers
- Duodenal ulcer
- Benign gastric ulcer
- Zollinger-Ellison syndrome
- Symptomatic treatment of mild reflux oesophagitis

4.2 Posology and method of administration

Posology
Prevention of recurrent duodenal ulcers
20 mg of famotidine in the evening

Duodenal ulcers and benign gastric ulcers
40 mg of famotidine once before going to sleep.

Zollinger-Ellison syndrome
Providing there has not been previous therapy with antisecretory medications, Zollinger-Ellison syndrome therapy should start by administering 20 mg of famotidine every 6 hours. Depending on the acid secretion and the patient's clinical response, a dosage titration should be performed as treatment continues until the desired acid levels have been reached (e.g. < 10 mEq/h in the hour preceding the next dose of famotidine). If the desired inhibition of acid secretion cannot be attained with a daily dosage of 800 mg, alternative treatment should be considered to regulate acid secretion, since no long-term experience with dosages of more than 800 mg of famotidine/day have been recorded.
Treatment should be continued for as long as clinically necessary.
Patients who have previously undergone H_2 receptor antagonist treatment can begin famotidine treatment at a higher dosage than the initial dosage that is usually recommended. The dosage depends on the severity of the disease and the dosage of previous medications.

Symptomatic treatment of mild reflux oesophagitis (only for 20 mg)
A daily dosage of twice 20 mg of famotidine is recommended.

Duration of treatment

Prevention of recurrent duodenal ulcers
With regards to the maintenance therapy for preventing the recurrence of duodenal ulceration, the recommended maintenance dose of 20 mg has been continued effectively in clinical studies of 12 months duration.

Duodenal ulcers and benign gastric ulcers
In treating duodenal ulcers and benign gastric ulcers, therapy should be conducted for 4 to 8 weeks. This period, however, may be shortened if endoscopy reveals that the ulcer has healed. If an endoscopic examination does not yield such findings, the treatment should be continued for another 4 weeks.

Zollinger-Ellison syndrome
Treatment should be continued for as long as clinically necessary.

Symptomatic treatment of mild reflux oesophagitis (only for 20 mg)
Generally, treatment should be conducted for 6 weeks, if necessary for 12 weeks.

Special populations

Renal impairment
Famotidine is primarily eliminated via the kidneys. For patients with impaired renal function in whom creatinine clearance is less than 30 mL/min, the daily dosage of famotidine should be reduced to 50 %.

Dialysis patients should also take dosages that are reduced to 50 %. Famotidine should be administered at the end of dialysis or thereafter since some of the active ingredient is removed via dialysis.

Hepatic impairment
No famotidine dose adjustment is needed in patients with hepatic impairment.

Elderly
No famotidine dose adjustment based on age is needed in the elderly. However, age-related impairment of renal function should be considered when determining the dosage (see above and section 5.2).

Paediatric population
The efficacy and safety of famotidine in children have not been established. No recommendation on a posology can be made.

Method of administration
Famotidine Clonmel Healthcare should be swallowed whole with some liquid. It does not need to be taken at mealtimes.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
If symptoms of hypersensitivity develop, famotidine should be discontinued.

Famotidine Clonmel Healthcare contains soya lecithin and must not be used in patients who are hypersensitive to peanut or soya.

4.4 Special warnings and precautions for use

General
Famotidine should not be administered in case of minor gastrointestinal complaints.

In case of long-term treatment with high dosage, monitoring of blood count and liver function is recommended.

In case of long-standing ulcer disease, abrupt withdrawal after symptom relief should be avoided.

In patients with duodenal ulcers and benign gastric ulcers the *H. pylori* status should be determined. Whenever possible, patients with *H. pylori* should undergo eradication therapy to eliminate the bacteria.

Gastric malignancy

Malignancy cannot necessarily be ruled out when treatment with famotidine has a positive effect on the symptoms. Appropriate diagnostic measures should be used to determine the non-malignancy of an ulcer before famotidine treatment is undertaken.

Impaired renal function
Famotidine is primarily eliminated via the kidneys and partially broken down in the liver. Caution must therefore be exercised in patients with impaired renal function.

The daily dosage should be reduced for patients with impaired renal function (see section 4.2).

Special populations

Elderly
Famotidine was administered to elderly patients in clinical studies, no increase in the incidence or change in the type of drug-related side effects was observed.

Paediatric population
The safety and efficacy of famotidine in children have not been established.

4.5 Interaction with other medicinal products and other forms of interaction

No clinically important metabolic interactions with other drugs or substances have been recorded.

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

Pharmacokinetic interactions
During concomitant use of substances whose absorption is affected by gastric acid levels, a possible change in the absorption of these substances should be considered. The absorption of ketoconazole or itraconazole can be reduced; ketoconazole should be administered two hours before administering famotidine.

Concomitant use of famotidine and antacids can reduce the famotidine absorption and lead to lower plasma levels of famotidine. Therefore, famotidine should be administered 1-2 hours before taking an antacid.

Concomitant use of sucralfate inhibits the absorption of famotidine. Therefore, sucralfate should as a rule not be administered within two hours of the famotidine dose.

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

Famotidine has been shown to reduce the bioavailability of atazanavir in dose dependant manner. This can be compensated for by an increased dose of atazanavir. However, when atazanavir/ritonavir combination is taken together with tenofovir, no dose dependency of this reduction is shown. Therefore, it is recommended that patients not taking tenofovir should be treated with maximally 20 mg famotidine, or, of a higher dose is needed, a dose increase of atazanavir should be considered. Patients taking atazanavir/ritonavir combination together with tenofovir should not be treated with famotidine.

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.

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.

4.6 Fertility, pregnancy and lactation

Pregnancy

In clinical practice, a large number of data on pregnant women exposed to famotidine (more than 1 000 pregnancy outcomes) indicates neither malformative nor foetotoxic effects.
Famotidine can be used during pregnancy if necessary.

Breast-feeding
Famotidine is excreted in human breast milk in small amounts and the amount received by the child corresponds to about 2 % of the maternal dose adjusted to the weight. No deleterious effects in breast-fed children have been reported. Therefore, famotidine can be used during breast-feeding.

Fertility
There are no clinical data on fertility. Animal studies do not show effects on fertility.

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

Summary of the safety profile
The most common adverse drug reactions were headache, dizziness, constipation and/or diarrhoea.

In this section frequencies of undesirable effects are defined as follows: Very common (≥ 1/10); common (≥ 1/100 to < 1/10); uncommon (≥ 1/1 000 to < 1/100); rare (≥ 1/10 000 to < 1/1 000); very rare (< 1/10 000), not known (cannot be estimated from the available data).

System Organ Class	Common	Uncommon	Rare	Very rare	Not known
Blood and lymphatic system disorders				Thrombocytopenia, leukopenia, agranulocytosis, pancytopenia.	
Immune system disorders			Hypersensitivity reactions (anaphylaxis, angioneurotic oedema, bronchospasm).		
Psychiatric disorders				Reversible psychological disturbances (e.g. hallucinations, disorientation, confusion, anxiety, agitation, depression).	
Nervous system disorders	Headache, Dizziness.			Paraesthesia, drowsiness, sleeplessness, epileptic seizures (grand mal).	
Gastrointestinal disorders	Constipation, Diarrhoea.	Dry mouth, nausea, vomiting, gastrointestinal complaints, flatulence, loss of appetite.			

Hepatobiliary disorders			Intrahepatic cholestasis (visible sign: jaundice).		Hepatitis.
Skin and subcutaneous tissue disorders		Rash, Pruritus.	Urticaria.	Alopecia.	Severe skin reactions (Stevens-Johnson syndrome/toxic epidermal necrolysis sometimes fatal).
Musculoskeletal and connective tissue disorders			Arthralgia.	Muscle cramps.	
Reproductive system and breast disorders				Impotence, reduced libido.	
General disorders and administration site conditions		Fatigue.		Feelings of tightness in the chest.	
Investigations			Increase in laboratory values (transaminases, gamma GT, alkaline phosphatase, bilirubin).		

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

There are no reports of overdosing with famotidine.

If this should occur, efforts should be made to inhibit absorption and relieve symptoms.

The usual measures to remove unabsorbed material from gastro-intestinal tract should be employed together with clinical monitoring and supportive therapy.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Drugs for acid related disorders, H_2-receptor antagonists, ATC code: A02BA03

Famotidine is a competitive histamine H_2 receptor antagonist which leads to the inhibition of gastric acid secretion mediated by the H_2 receptors. In addition to the gastric acid levels, the pepsin level is also reduced. To a lesser extent there is also a decrease in the volume of the basal gastric juice and the gastric juice secreted on stimulation. Pharmacological effects on the CNS, immunological, cardiovascular or respiratory parameters have not been observed.

The drug takes effect within an hour of oral administration and reaches its peak efficacy within 1-3 hours.

Individual oral doses of 20 mg and 40 mg effectively inhibited the basal night-time secretion of gastric acid; mean gastric acid secretion was inhibited over a period of 10 hours by 86 % and 94 %, respectively. The same doses, administered in the morning, inhibited the gastric acid secretion stimulated by eating for 3-5 hours p.a. by a mean of 76 % and 84 %, respectively.
8-10 hours after administration, the levels were at 25 % and 30 %, respectively, although the effect of one 20 mg dose

persisted for only 6-8 hours in some of the volunteers. Repeated administration did not lead to an accumulation of the active ingredient.

The basal night-time intragastric pH value was increased to a mean of 5 and 6.4 by evening doses of 20 mg and 40 mg of famotidine, respectively. When famotidine was administered after breakfast, the pH value in both the 20 mg and the 40 mg groups was increased to approximately 5 after 3 and 8 hours.

Famotidine had little or no effect on the fasting and postprandial serum gastrin levels. Gastric emptying and exocrine pancreas function were not affected by famotidine, nor were hepatic and portal blood flow. There was also no effect on endocrine function. Hormone levels of prolactin, cortisone, thyroxin (T_4) and testosterone remained unchanged under famotidine treatment.

5.2 Pharmacokinetic properties

Absorption
Famotidine is quickly resorbed after oral administration.

Oral bioavailability is about 40 %.

Peak plasma concentrations are achieved 1-3.5 hours after administration. Peak plasma concentrations are approximately 0.04 to 0.06 µg/mL after administration of 20 mg of famotidine and 0.075 to 0.1 µg/mL after administration of 40 mg of famotidine. Repeated administration does not lead to an accumulation of the active ingredient. Famotidine absorption is not influenced by concomitant food intake.

Distribution
Famotidine is found in the cerebrospinal fluid only to a limited extent. The fluid/plasma ratio 4 hours after administering 40 mg of famotidine intravenously was a mean of 0.1.

Famotidine is excreted in maternal milk. 6 hours after oral administration a milk/plasma concentration ratio of 1.78 was reached. The elimination half-life in the plasma is 2.6 to 4 hours.

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

Elimination
24 hours after oral administration, 25-30 % of the active ingredient is excreted via the urine unchanged; after intravenous administration, 65-70 % is excreted unchanged in urine. Renal clearance is 250-450 mL/min, which indicates tubular secretion. A slight amount can be eliminated as sulfoxide.

Linearity/non-linearity
Famotidine displays linear kinetics.

Renal insufficiency:
As renal function declines, renal and total clearance of famotidine decrease without there being an increase in non-renal elimination. The elimination half-life after intravenous injection of a single dose of 20 or 10 mg of famotidine is increased to 4.5-9 hours in moderate renal insufficiency (creatinine clearance 60-30 mL/min), to 10-12 hours in severe renal insufficiency (creatinine clearance < 30 mL/min) and to 18-27 hours in patients with terminal renal insufficiency or anuria. The amount of unchanged famotidine excreted with the urine is reduced to 60 % in patients with moderate renal insufficiency. In cases of severe renal insufficiency it is only 25 %.

Depending on the dialysis procedure (haemofiltration, 5-hour haemodialysis or continuous haemofiltration), dialysis patients have an elimination half-life of 7-14 hours after intravenous administration of 20 mg of famotidine; after oral administration of 20 mg of famotidine, it is 22.5 hours.

Liver function impairment
The pharmacokinetics of famotidine are unchanged in patients with liver function impairment.

Kinetics among older patients

Pharmacokinetic studies on older patients showed no signs of any clinically significant age-related changes; however, age-related impairment of renal function should be considered when determining the dosage.

5.3 Preclinical safety data

Preclinical data regarding famotidine reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential, and toxicity to reproduction.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core:
cellulose, microcrystalline (E 460 (i))
starch, pregelatinised
talc (E 553 b)
silica, colloidal anhydrous (E 551)
magnesium stearate (E 470b)

Tablet coat:
polyvinyl alcohol-partially hydrolysed (E 1203)
talc (E 553 b)
titanium dioxide (E 171).
macrogol
lecithin (soya) (E 322)
iron oxide yellow (E 172)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

30 months

6.4 Special precautions for storage

This medicine does not require any special storage conditions

6.5 Nature and contents of container

oPA/Alu/PVC//Alu or PVC/Alu blisters

Pack sizes: 10, 20, 28, 30, 50, 60 (20 mg only) or 100 film-coated 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

Clonmel Healthcare Ltd
Waterford Road
Clonmel, Co. Tipperary
E91 D768
Ireland

8 MARKETING AUTHORISATION NUMBER

PA0126/392/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 31st October 2025

10 DATE OF REVISION OF THE TEXT