COLLEGE TER BEOORDELING VAN GENEESMIDDELEN

Public Assessment Report

Scientific discussion

Famotidine Glenmark 10 mg, 20 mg and 40 mg film-coated tablets (famotidine)

NL/H/6281/001-003/DC

Date: 30 July 2026

This module reflects the scientific discussion for the approval of Famotidine Glenmark 10 mg, 20 mg and 40 mg film-coated tablets. The procedure was finalised on 16 April 2026. For information on changes after this date please refer to the 'steps taken after finalisation' at the end of this PAR.

List of abbreviations

ASMF	Active Substance Master File
BE	Bioequivalence
CEP	Certificate of Suitability to the monographs of the European Pharmacopoeia
CHMP	Committee for Medicinal Products for Human Use
CMD(h)	Coordination group for Mutual recognition and Decentralised procedure for human medicinal products
CMS	Concerned Member State
EDMF	European Drug Master File
EDQM	European Directorate for the Quality of Medicines
EEA	European Economic Area
EMA	European Medicines Agency
ERA	Environmental Risk Assessment
ICH	International Conference of Harmonisation
MAH	Marketing Authorisation Holder
Ph.Eur.	European Pharmacopoeia
PL	Package Leaflet
RH	Relative Humidity
RMP	Risk Management Plan
RMS	Reference Member State
SmPC	Summary of Product Characteristics
TSE	Transmissible Spongiform Encephalopathy

I. INTRODUCTION

Based on the review of the quality, safety and efficacy data, the Reference Member State (RMS) has granted a marketing authorisation for Famotidine Glenmark 10 mg, 20 mg and 40 mg film-coated tablets, from Glenmark Arzneimittel GmbH.

10 mg strength
The product is indicated for:

- relief and symptomatic treatment of heartburn and acidity in adults and children over 16 years of age.

The delivery status for the 10 mg strength is 'only pharmacy or drugstore (UAD)'.

20 mg and 40 mg strength
The product is indicated in adults for:

- duodenal ulcer
- benign gastric ulcer
- Zollinger-Ellison-Syndrome
- prevention of recurrent duodenal ulcers (only for 20 mg)
- symptomatic treatment of mild reflux oesophagitis (only for 20 mg)
- treatment of mild to moderate reflux oesophagitis (only for 40 mg).

The delivery status for the 20 mg and 40 mg strengths is 'prescription only'.

A comprehensive description of the up-to-date indications and posology is given in the SmPC.

NL/H/6281/001/DC, 10 mg strength
The marketing authorisation for the 10 mg strength has been granted pursuant to Article 10(1) of Directive 2001/83/EC, which concerns a generic application. For this application reference is made to the European reference medicinal product (ERP) Pepcid 10 mg comprimidos recubiertos, which has been authorised in Spain (MA EU-Number 62090) since 1 May 1998. The current MAH is JNTL Consumer Health Spain S.L (Spain), (formally a division of Johnson & Johnson). This product is indicated in patients aged 16 years and above for the relief and symptomatic treatment of heartburn.

NL/H/6281/002-003/DC, 20 mg and 40 mg strengths
The application for the 20 mg and 40 mg strengths have been granted pursuant 10(3) of Directive 2001/83/EC (hybrid application), also making reference to the ERP Pepcid 10 mg comprimidos recubiertos (MA EU-Number 62090). The 20 mg and 40 mg strengths products differ from the ERP in pharmaceutical strength and in the proposed indications.

A bioequivalence study was conducted between the current product and the ERP. No other new studies were performed to investigate the clinical and non-clinical aspects of the product. To support this application the MAH has been submitted an overview based on the literature with the justification for bridging between their product and the product used in the literature, as no reference products are available for the 20 mg and 40 mg strengths.

This application has been assessed with The Netherlands as Reference Member State. No concerned member states (CMS) were involved in this procedure.

II. QUALITY ASPECTS

II.1 Introduction

Famotidine Glenmark 10, mg 20 mg and 40 mg are film-coated tablets and contain as active substance 10 mg, 20 mg or 40 mg of famotidine. The three strengths of the tablets can be distinguished by their colour, size and debossing are as follows:

Famotidine 10 mg is presented as pink coloured, circular, biconvex film-coated tablets debossed with "1V" on one side and plain on the other side, with a diameter of approximately 4 mm.

Famotidine 20 mg is presented as yellow coloured, circular, biconvex film-coated tablets debossed with "2V" on one side and plain on the other side, with a diameter of approximately 6 mm.

Famotidine 40 mg is presented as brown coloured, circular, biconvex film-coated tablets debossed with "4V" on one side and plain on the other side, with a diameter of approximately 8 mm.

The different strengths are dose proportional.

The excipients are:
Tablet core - microcrystalline cellulose (E460 (i)), pregelatinised starch, talc (E553b), silica colloidal anhydrous (E551) and magnesium stearate (E470b).

Tablet coat - polyvinyl alcohol-partially hydrolysed (E1203), talc (E553b), titanium dioxide (E171), macrogol, lecithin (soya) (E322), iron oxide yellow (E172) (in the 10 mg, 20 mg and 40 mg strengths) and iron oxide red (E172) (in the 10 mg and 40 mg strengths).

The film-coated tablets are packed in Alu-Alu foil (aluminium/cold form foil) or polyvinyl chloride/ aluminium (PVC/Alu) blisters.

II.2 Drug Substance

The active substance is famotidine, an established substance described in the Pharmacopoeia (Ph.Eur.). Famotidine is a white or yellowish-white crystalline powder or crystals, very slightly soluble in water. Famotidine exhibits polymorphism. Polymorphism in the drug substance is controlled by the drug product manufacturer. Famotidine is achiral.

The CEP procedure is used for the active substance. Under the official Certification Procedures of the EDQM of the Council of Europe, manufacturers or suppliers of substances for

pharmaceutical use can apply for a certificate of suitability concerning the control of the chemical purity and microbiological quality of their substance according to the corresponding specific monograph, or the evaluation of reduction of Transmissible Spongiform Encephalopathy (TSE) risk, according to the general monograph, or both. This procedure is meant to ensure that the quality of substances is guaranteed and that these substances comply with the Ph.Eur.

Manufacturing process

A CEP has been submitted. Therefore no details on the manufacturing process have been included.

Quality control of drug substance

The active substance specification is considered adequate to control the quality and meets the requirements of the monograph in the Ph.Eur. and the CEP, with additional requirements for particle size distribution. Polymorphism is controlled using the same method applied by the drug substance manufacturer. Residual solvents are controlled in line with the CEP and the specification applied by the drug substance manufacturer. Potential mutagenic impurity is adequately controlled in line with the applicable ICH guidelines. The specification is acceptable in view of the route of synthesis and the various European guidelines.

Batch analytical data demonstrating compliance with this specification have been provided for two batches per manufacturing site.

Stability of drug substance

The active substance is stable for 60 months when stored under the stated conditions. Assessment thereof was part of granting the CEP (and has been granted by the EDQM).

II.3 Medicinal Product

Pharmaceutical development

The product is an established pharmaceutical form and its development is adequately described in accordance with the relevant European guidelines. The development of the product has been described, the choice of excipients is justified and their functions are explained. Formulation development and optimisation have been adequately described. The comparative dissolution experiments complementary to the bioequivalence study have been performed in line the conditions described with the EMA guideline on bioequivalence. The proposed biowaiver of strength is acceptable from a quality point of view. *In vitro* dissolution studies complementary to the bioequivalence (BE) studies have been conducted using the same test and reference batches used in the BE study. Similarity in dissolution properties was demonstrated without the need to calculate f_2 factors at the following conditions: 0.1N HCl and pH 4.5 acetate buffer. The MAH concluded that similarity of the dissolution profiles was also demonstrated at the pH of 6.8 based on f_2 calculations is also agreed. *In vitro* dissolution

tests in support of the biowaiver of strengths for the 20 mg and 40 mg have been submitted. The biowaiver of strength is acceptable from a quality point of view, see details in section IV.2.

The development of the *in vitro* dissolution method is adequately described. The proposed dissolution method has been justified and its discriminatory power has been sufficiently demonstrated.

Manufacturing process

The choice of excipients is justified and their functions explained. The manufacturing process consists of the following main steps: sifting of raw materials, granulation, drying, sift and milling, wet mixing, drying, pre-lubrifaction and lubrification blending, tablet compression, film coating and packaging. The product is manufactured using conventional manufacturing techniques.

The manufacturing process has been adequately validated according to relevant European guidelines. Process validation data on the product has been presented for three production batches of each strength manufactured at the proposed minimum commercial scale. This is considered sufficient in view of the manufacturing process and taking into account the percentage in size of the minimum commercial batch compared to the maximum batches size.

Control of excipients

The excipients comply with Ph. Eur. requirements where applicable, or with other relevant compendial requirements. In-house requirements are applied to the coating materials. These specifications are acceptable.

Quality control of drug product

The finished product specifications are adequate to control the relevant parameters for the dosage form. The specification includes tests for appearance, identity, identification of colour, average mass, loss on drying, dissolution, assay, uniformity of dosage units, related substances and microbiological quality. The release and shelf-life specifications are identical with the exception of the limits for related substances and loss on drying. Limits in the specification have been justified and are considered appropriate for adequate quality control of the product. An adequate nitrosamines risk evaluation report has been provided. No risk for presence of nitrosamines in the drug product was identified.

Satisfactory validation data for the analytical methods have been provided.

Batch analytical data have been submitted for three batches of each strength, manufactured at commercial scale at the proposed production site, demonstrating compliance with the specification.

Stability of drug product

Stability data on the product has been provided on three production scale batch of each strength packaged in both types (Alu-Alu foil) or (PVC/Alu) of blisters proposed for marketing. The batches were stored at 25°C/60% RH (24 months) and 40°C/75% RH (6 months). The conditions used in the stability studies are according to the ICH stability guidelines. The data presented confirm compliance with specification. The results under accelerated storage

conditions show no significant changes for the 20 mg and 40 mg strengths, for the 10 mg strength a significant decreased in the assay results was observed. Photostability studies were performed in accordance with ICH recommendations and showed that the product is stable when exposed to light. Based on the data submitted, the following shelf life and storage condition were granted:

Alu-Alu foil
30 Months. No specific storage conditions needed to be included in the SmPC or on the label.

PVC/Alu
27 months. Store below 30°C.

Specific measures concerning the prevention of the transmission of animal spongiform encephalopathies
There are no substances of ruminant animal origin present in the product nor have any been used in the manufacturing of this product, so a theoretical risk of transmitting TSE can be excluded.

II.4 Discussion on chemical, pharmaceutical and biological aspects

Based on the submitted dossier, the Reference Member State considers that Famotidine Glenmark 10 mg, 20 mg and 40 mg are film-coated tablets have a proven chemical-pharmaceutical quality. Sufficient controls have been laid down for the active substance and finished product.

No post-approval commitments were made.

III. NON-CLINICAL ASPECTS

III.1 Pharmacology, pharmacokinetics and toxicology

The sought-after indications were already approved for other Famotidine 20 mg and 40 mg tablets on the market. Because the indications of Famotidine Glenmark differ from the reference medicinal products Pepcid 10 mg, a more in-depth assessment on the primary pharmacology has been performed. The provided non-clinical pharmacodynamic literature supports partly the use of famotidine for the indications listed by the MAH. H_2-receptor inhibition has been shown in several *in vitro* studies. *In vivo* data from rats and dogs demonstrated the efficacy of famotidine in the prevention, reduction and healing of gastric and duodenal ulcers. In most studies famotidine was at least as good (or better) than other frequently used pharmaceuticals for the same indications, such as cimetidine and ranitidine. Since the symptoms of Zollinger-Ellison syndrome are caused by increased gastric acid secretion, the provided literature on gastric- and duodenal ulcers also supports this indication. *In vitro* and *in vivo* data from rats demonstrated the efficacy of famotidine in inhibiting reflux esophagitis (Bisson et al., 1993) (Gladziwa et al., 1993; Langtry et al., 1989; Laskin et al., 1993).

III.2 Ecotoxicity/environmental risk assessment (ERA)

At the time of submission of this application, after 1 September 2024, the revised ERA guideline (EMEA/CHMP/SWP/4447/00 Rev. 1- Corr.*) was applicable. Therefore, the MAH was requested to update the ERA for famotidine and provided a PBT screening as well as a Phase I risk assessment.

Famotidine is a histamine H_2 receptor antagonist. It is not an antibiotic, antiparasitic, or endocrine active substance. For the PBT screening, the MAH provided a publication in which the octanol and water partition coefficient has been experimentally determined using both the shake flask method (accepted method according to revised ERA guideline) and the pH titration technique. According to the shake flask method, the log Kow of famotidine is -1.127, which is below the trigger value of 4.5 requiring further PBT assessment.

For the Phase I risk assessment, the MAH has refined F_{pen} based on prevalence and treatment regimen. The refinement is not fully in accordance with the updated ERA guideline (EMEA/CHMP/SWP/4447/00 Rev. 1 - Corr.) and therefore not acceptable.

Summary of main study results Phase I

Substance (INN/Invented Name):	*famotidine*
CAS-number (if available):	*76824-35-6*

PBT/vPvB screening			
Study type	Test protocol	Result	Conclusion
Bioaccumulation potential- log Kow	OECD 107	*-1.127*	Potential PBT: *N*

Phase I			
Parameter	Value	Unit	Conclusion
PEC_{sw}, *default*	*tbd*	µg/L	≥ 0.01 threshold: *Y*
Other concerns (e.g. chemical class)			N

Conclusions on studies

A bioaccumulation potential is not indicated based on the log K_{OW} < 4.5. A definitive PBT/vPvB assessment is not required. However, the available data do not allow to conclude definitively on the potential risk of active substance to the environment. The ERA cannot be finalised as the dossier is incomplete. Using the default F_{pen} and a MDD of 800 mg, a PEC_{sw} of 4 µg/L can be calculated, requiring a Phase II assessment.

The MAH committed to update the Environmental Risk Assessment (Phase I and Phase II assessment) and provide a yearly report on the progress.

III.3 Discussion on the non-clinical aspects

Pharmacodynamic, pharmacokinetic and toxicological properties of famotidine are well-known. As famotidine is a widely used, well-known active substance, the MAH has not provided additional non-clinical studies, and further studies are not required. The non-clinical overview provided based on literature review is thus appropriate.

IV. CLINICAL ASPECTS

IV.1 Introduction

Famotidine is a well-known active substance with established efficacy and tolerability. A clinical overview has been provided, which is based on scientific literature. The member states agreed that no further clinical studies are required, besides one bioequivalence study, which is discussed below. Additionally, a biowaiver of strengths were requested.

IV.1 Pharmacokinetics

Pharmacokinetics overview

Famotidine kinetics are linear (SmPC Epci AC, Ireland). Oral bioavailability is approximately 40 %. Peak plasma concentrations, which are respectively 50 to 60 µg/L and approximately 78 µg/L after administration of 20 mg and 40 mg, are achieved 1-3.5 hours after administration (Campoli-Richards et al., 1986). Repeated administration does not lead to an accumulation of the active ingredient (Famotidine Tablets, USP product monograph).

The apparent volume of distribution of famotidine after intravenous administration was reported to be 1.14 to 1.42 L/kg, however, the volume of distribution following oral administration nor the distribution of famotidine into human tissues and fluids have been described. Following oral administration of famotidine 20 mg to 5 healthy volunteers the mean proportion of drug which was plasma bound was 21.8% at 2 hours after administration, 19.3% at 3 hours, and 15.1% at 4 hours (Campoli-Richards et al., 1986; Echizen et al., 1991).

Famotidine is excreted in the urine and faeces. Mean urinary recovery of unchanged famotidine was from 25 to 30% of orally administered doses. The elimination half-life in the plasma is approximately 2.5 to 4 hours (Echizen et al., 1991).

Famotidine S-oxide is the only known metabolite of the drug in humans. After intravenous administration of famotidine, about 2 to 8% of the dose was recovered in urine as famotidine S-oxide in humans. The biological activity of famotidine S-oxide, if any, is currently unknown (Campoli-Richards et al., 1986; Echizen et al., 1991).

The maintenance dosage of famotidine for patients with renal insufficiency should be reduced according to the individual CL_{cr} (Creatinine Clearance) (Therapeutic Goods Administration (TGA) Australia) because the elimination half-life and area under the plasma concentration-time curve were significantly increased.

No relevant drug interactions have been identified (Locniskar et al., 1986).

Bioequivalence

The MAH conducted a bioequivalence study in which the pharmacokinetic profile of the test product Famotidine Glenmark 40 mg, film-coated tablets (Glenmark Arzneimittel GmbH, Germany) was compared with the pharmacokinetic profile of the reference product Pepcid 10 mg comprimidos recubiertos (JNTL Consumer Health Spain S.L, Spain).

The choice of the reference product in the bioequivalence study has been justified by comparison of dissolution study results and composition. The formula and preparation of the bioequivalence batch was identical to the formula proposed for marketing.

Biowaiver of strengths

The following requirements for granting the biowaiver for the 10 mg and 20 mg famotidine film-coated tablets based on the bioequivalence study with the highest strength of 40 mg have been met:

- the strengths have been manufactured by the same process and manufacturer
- the pharmacokinetics can be considered dose linear
- the compositions are qualitatively similar and dose proportional.
- Comparative dissolution experiments in three dissolution media (pH 1.2, 4.5 and 6.8) with the lower strength were performed. The paddle method with an agitation speed of 50 rpm and a volume of 900 mL were used, which complies with the bioequivalence Guideline.

At pH 1.2 and 4.5, the dissolution profiles showed a dissolution percentage above 85% within 15 min for all strengths and were considered similar.
At pH 6.8, the calculated f2-values met the acceptance criteria of 50-100, and thus, the dissolution profiles of the two strengths were considered similar.

All RSD (residual standard deviation) values were found to be less than 20% for the first time point and less than 10% for all subsequent time points, complying with the Bioequivalence Guideline. According to the Guideline on the investigation of bioequivalence (CPMP/EWP/QWP/1401/98 Rev. 1/ Corr **) the additional strengths of famotidine film-coated tablets meet the general bio-waiver acceptance criteria. Therefore biowaivers for the strength 10 mg and 20 mg were granted.

Bioequivalence study 111-22

Design

An open label, balanced, randomised, two-treatment, two-sequence, two-period, single-dose, crossover, oral bioequivalence study was carried out under fasted conditions in 47 healthy, adult human participants (38 male and 9 female), aged 21-44 years. Each subject received a single dose (40 mg) of one of the two famotidine formulations (reference (4 tablets x 10 mg) or tests (1 tablet x 40 mg). The tablet was orally administered with 240 mL water after overnight fasting for at least 10 hours. There were two dosing periods, separated by a washout period of three days.

Blood samples were collected pre-dose and at 0.25, 0.5, 0.75, 1, 1.25, 1.5, 1.75, 2., 2.25, 2.5, 2.75, 3, 3.25, 3.5, 4, 6, 9, 12, 15, 18, 24 hours after administration of the products.

The design of the study is acceptable.

According to the SmPC of the product, food has no influence on the absorption of famotidine. The medicinal product may be taken without reference to food intake. Therefore, a food interaction study is not deemed necessary. The bioequivalence study under fasting conditions is in accordance with CPMP/EWP/QWP/1401/98 Note for Guidance on the investigation of bioavailability and bioequivalence.

Analytical/statistical methods
The analytical method has been adequately validated and is considered acceptable for analysis of the plasma samples. The methods used in this study for the pharmacokinetic calculations and statistical evaluation are considered acceptable.

Results
A total of 50 participants were dosed. Four participants were withdrawn from the study due to mild or moderate adverse events (period I: one participant due to vomiting. Period II, one participant due to vomiting and two due to vomiting and fever. One participant dropped out with consent). 47 participants completed the study and were included in the pharmacokinetic and statistical analysis.

Table 1. Pharmacokinetic parameters (non-transformed values; arithmetic mean ± SD, t_{max} (median, range)) of famotidine, 40 mg under fasted conditions.

Treatment N=47	**AUC_{0-t} (ng.h/mL)**	**$AUC_{0-\infty}$ (ng.h/mL)**	**C_{max} (ng/mL)**	**t_{max} (h)**
Test	1287 ± 443	1332 ± 462	198.7 ± 66.3	2.00 (0.75-4.00)
Reference	1270 ± 475	1314 ± 500	187.9 ± 61.7	2.25 (0.75-4.00)
***Ratio (90% CI)**	102.3 (95.8-109.2)	102.4 (96.0-109.2)	105.7 (98.7-113.1)	---

$AUC_{0-\infty}$	Area under the plasma concentration-time curve from time zero to infinity
AUC_{0-t}	Area under the plasma concentration-time curve from time zero to the last measurable plasma concentration / to t = 24 hours
C_{max}	Maximum plasma concentration
t_{max}	Time after administration when maximum plasma concentration occurs
CI	Confidence interval

**ln-transformed values*

Conclusion on bioequivalence study:
The 90% confidence intervals calculated for AUC_{0-t}, $AUC_{0-\infty}$ and C_{max} are within the bioequivalence acceptance range of 80 – 125%. Based on the submitted bioequivalence study Famotidine Glenmark 40 mg is considered bioequivalent with Pepcid coated tablets 10 mg.

Biowaivers of strengths for the 10 mg and 20 mg strengths were granted based on the submitted dissolution data of the 10 mg, 20 mg and 40 mg strengths. The results of study 111-22 with the 40 mg formulation can be extrapolated to the lower strengths product of 10 mg and 20 mg, according to conditions in Guideline on the Investigation of Bioequivalence CPMP/EWP/QWP/1401/98 Rev. 1/Corr*, section 4.1.6.

The MEB has been assured that the bioequivalence study has been conducted in accordance with acceptable standards of Good Clinical Practice (GCP, see Directive 2005/28/EC) and Good Laboratory Practice (GLP, see Directives 2004/9/EC and 2004/10/EC).

IV.2 Pharmacodynamics

No new pharmacodynamic studies were performed by the MAH. Pharmacodynamic data are derived from the published literature. This is acceptable. The submitted documentation describes the general pharmacodynamic effects of famotidine appropriately.

Famotidine is a competitive inhibitor of H_2 receptor. Famotidine inhibits basal and stimulated gastric acid secretion in a dose-dependent manner after oral administration of 5 to 40 mg. Maximal effect is achieved by the 40 mg dose (Chremos, 1986). Upon oral administration, the onset of the antisecretory effect of famotidine occurs within one hour (Bisson et al., 1993). Duration of inhibition of secretion by famotidine doses of 20 and 40 mg is 10 to 12 hours (Chremos, 1986). The pharmacodynamic effects of famotidine increase at increasing famotidine dosages. Hence, there is a positive dose-response relationship (Laskin et al., 1993).

The submitted documentation supports the inhibitory pharmacodynamic effect of 5-40 mg famotidine on the gastric acid secretion in healthy volunteers. In patients with gastroesophageal reflux disease, famotidine 20 and 40 mg twice daily reduce the intraoesophageal acid exposure into the normal range as measured by 24 hour intraoesophageal pH monitoring. These data support the primary pharmacodynamic effects of famotidine 20 and 40 mg twice daily for gastroesophageal reflux disease i.e. symptomatic reflux oesophagitis (Shaqran et al., 2023). The evaluated dosage is the proposed recommended dosage of famotidine for the proposed reflux oesophagitis indications of famotidine. This is acceptable.

Inhibitory pharmacodynamic effects of famotidine on the gastric secretion were also observed in patients with a duodenal ulcer (Langtry et al., 1989).

The MAH did not specifically discuss the pharmacodynamic effects of famotidine with respect to the prevention of recurrent duodenal ulcers, benign gastric ulcer, and Zollinger-Ellison-Syndrome. However, the general pharmacodynamic effects of famotidine are the same as for reflux oesophagitis. Therefore, the general inhibitory effects of famotidine on the gastric secretion also apply to the conditions for which no data on the pharmacodynamic effects of

famotidine have been submitted. Indications similar to those of Famotidine Glenmark have been accepted for other nationally or decentralised authorised famotidine medicinal products (e.g. Famotidine CF 20 mg and 40 mg (respectively NL/H/5592/001 and NL/H/5592/002)). For aforementioned reasons, no further substantiation is requested on the pharmacodynamic effects of famotidine for all applied indications.

No secondary pharmacological effects of famotidine have been reported for famotidine doses up to 40 mg twice daily.

No clinically important pharmacodynamic interactions between famotidine and other drugs or substances have been recorded.

In conclusion, the submitted documentation describes the general pharmacodynamic effects of famotidine appropriately. This is acceptable.

IV.3 Clinical efficacy

Famotidine Glenmark film-coated tablets in dose strengths of 10 mg, 20 mg and 40 mg are proposed for different indications with different posologies as described in Tabel 2. No clinical studies were conducted to evaluate the clinical efficacy of famotidine 10 mg, 20 mg and 40 mg tablets with respect to the proposed indications. Instead, an overview based on literature was submitted.

The physico-chemical and pharmacokinetic properties of Famotidine Glenmark 10 mg film-coated tablets are similar to those of the famotidine ERP Pepcid coated tablets 10 mg. Famotidine Glenmark 10 mg has also similar indications as the ERP (relief and symptomatic treatment of heartburn in adults and children over 16 years of age). Therefore, the clinical effects of the current product and the ERP in the authorised indications are considered similar and well-known.

Table 3. Famotidine Glenmark 10 mg, 20 mg and 40 mg film-coated tablets indications and posologies per strength

Indications	Posology		
	10 mg	20 mg	40 mg
Relief and symptomatic treatment of heartburn and acidity. It is indicated for adults and children over 16 years of age.	Take 1 tablet (10 mg) when symptoms appear, or take 1 tablet 1 hour before eating to avoid symptoms associated with food and drink. Maximum dose in 24 hours: 2 tablets (20 mg). Do not take the medicine for more than 1 week.	N/A	N/A

Duodenal ulcers and ventricle ulcers	N/A	40 mg once daily before going to sleep for 4-8 weeks. Depending on the presence or absence of ulcer healing upon endoscopy this period can respectively be shortened (exact duration not specified) or extended (maximum treatment period 12 weeks).	40 mg once daily before going to sleep for 4-8 weeks. Depending on the presence or absence of ulcer healing upon endoscopy this period can respectively be shortened (exact duration not specified) or extended (maximum treatment period 12 weeks).
Benign gastric ulcers	N/A	40 mg once daily at night for 4-8 weeks, unless earlier healing is revealed by endoscopy	40 mg once daily at night for 4-8 weeks, unless earlier healing is revealed by endoscopy
Prophylactic treatment of relapses duodenal ulcers	N/A	20 mg once daily in the evening up to 12 months duration	N/A
Zollinger-Ellison-Syndrome	N/A	start: 20 mg every 6 hours, up to 800 mg per day as long as clinically necessary	start: 20 mg every 6 hours, up to 800 mg per day as long as clinically necessary
Symptomatic treatment of mild to moderate reflux oesophagitis	N/A	20-40 mg twice daily for 6-12 weeks	40 mg twice daily for 6-12 weeks

Dose-response studies

The evaluated famotidine dosages in the submitted studies on famotidine 10 mg tablets for relief and symptomatic treatment of heartburn and acidity range between 10 and 40 mg daily. As far as data are available, the clinical effects of 10 mg famotidine tablets that were made by Merck, Johnsson & Johnson and allied companies have been evaluated in most of these studies (including Mann et al., 1995, Mann et al., 1997, Simon et al., 1995). The evaluated posology for these tablets (10 mg daily) in respective studies is in line with the recommended famotidine dosage for relief and symptomatic treatment of heartburn and acidity in patients aged 16 years and above (10-20 mg/day).

For the treatment of duodenal ulcers, the clinical effects of famotidine 20 mg once daily up to 40 mg twice daily have been evaluated in the submitted clinical studies. As far as data are available, the clinical effects of 20 and 40 mg famotidine tablets that were made by Merck, Johnsson & Johnson and allied companies have been evaluated in many of these studies (including Texter et al., 1986, Barbara et al., 1985, Reynolds, 1988, Alcalá-Santaella et al., 1989, Bianchi Porro et al., 1987). The evaluated famotidine posology for these tablets (20 mg once

or twice daily, 40 mg once to twice daily) in respective studies is in line with the recommended famotidine dosage in patients with duodenal ulcers (40 mg once daily before going to sleep).

For the prevention of recurrent duodenal ulcers, the clinical effects of famotidine 20 mg once daily up to 40 mg twice daily have been evaluated in the submitted clinical studies. As far as data are available, the clinical effects of 20 and 40 mg famotidine tablets that were made by Merck, Johnsson & Johnson and allied companies have been evaluated in most of these studies (including Taha et al., 2009, Taha et al., 1996, Reynolds 1988, Hudson et al., 1997, Bank et al., 1991). The evaluated famotidine posology for these tablets (20 mg once to twice daily, 40 mg once to twice daily) in respective studies is in line with the recommended famotidine dosage for the prevention of recurrent duodenal ulcers (20 mg once daily in the evening).

For the treatment of benign gastric ulcers, the clinical effects of famotidine 20 mg once daily up to 40 mg twice daily have been evaluated in the submitted clinical studies. As far as data are available, the clinical effects of 20 and 40 mg famotidine tablets that were made by Merck, Johnsson & Johnson and allied companies have been evaluated in many of these studies (including Paoluzi et al., 1985, Bank et al., 1993, Brazer et al., 1989, Cochran et al., 1989, Perez Mota et al., 1990). The evaluated famotidine posology for these tablets (20 mg twice daily, 40 mg once to twice daily) in respective studies is in line with the recommended famotidine dosage in patients with benign gastric ulcers (40 mg once daily before going to sleep).

For the treatment of Zollinger-Ellison syndrome, the clinical effects of famotidine ≥ 50 up to 800 mg daily from 1 to 72 months, have been evaluated in the submitted clinical studies. As far as data are available, the clinical effects of 20 and 40 mg famotidine tablets that were made by Merck, Johnsson & Johnson and allied companies have been evaluated in most of these studies (including Vinayek et al., 1986, Langtry et al., 1989, Howard et al., 1985, Howard et al., 1987, Campoli-Richards & Clissold 1986, USFDA Clinical biopharmaceutical review of Pepcid 2025). The evaluated famotidine posology for these tablets (≥ 50 up to 800 mg daily) in respective studies is in line with the recommended famotidine dosage in patients with Zollinger-Ellison syndrome. The submitted literature supports the clinical efficacy of famotidine dosages up to 800 mg/day for Zollinger-Ellison syndrome.

For symptomatic treatment of mild reflux oesophagitis and treatment of mild to moderate reflux oesophagitis, the clinical effects of famotidine 20 mg twice daily up to 40 mg twice daily have been evaluated in the submitted clinical studies. As far as data are available, the clinical effects of 20 and 40 mg famotidine tablets that were made by Merck, Johnsson & Johnson and allied companies have been evaluated in most of these studies (including Sabesin et al., 1991, Wesdorp et al., 1993, Simon et al., 1994, Robinson et al., 1991, Wesdorp et al., 1997, Simon et al., 1995, Simon et al., 1996). The evaluated famotidine posology for these tablets (20 mg twice daily, 40 mg once to twice daily) in respective studies is in line with the recommended famotidine dosage for symptomatic treatment of mild reflux oesophagitis (20 mg twice daily) and treatment of mild to moderate reflux oesophagitis (40 mg twice daily).

The famotidine reference medicinal product in the current procedure is indicated in paediatric patients aged 16 years and above. According to the proposed SmPC of the 20 and 40 mg famotidine tablets, famotidine should not be used in paediatric patients due to insufficient information on the efficacy and safety of famotidine in these patients. In line with this, the

initially proposed indications of these tablets have therefore been limited to adult patients (SmPC guideline 2009, EMA guidance the wording of a therapeutic indication (EMA/CHMP/483022/2019)

Conclusion on clinical efficacy
Based on the submitted bioequivalence study, Famotidine Glenmark 40 mg film-coated tablets are considered bioequivalent with 4 tablets Pepcid 10 mg from JNTL Consumer Health (Spain) (see section IV.2). In addition, based on an acceptable biowaiver, this can be extrapolated to the 10 mg and 20 mg strength. The submitted literature for each applied indication includes publications on studies in which medicinal products of 20 mg and/or 40 mg famotidine were evaluated. The clinical effects with respect to the applied indications of Famotidine Glenmark 10 mg, 20 mg and 40 mg are similar to those of the famotidine medicinal products used in the literature. Based on this, it is considered that the results of the clinical effects obtained with the medicinal products used in the literature, can be applied to Famotidine Glenmark 10 mg, 20 mg and 40 mg film-coated tablets in their respective indications. Overall, the publications support the clinical efficacy of the recommended famotidine dosages for each indication. Further, the recommended famotidine posologies and treatment durations for the applied indications for each strength are in line with those of other famotidine medicinal products that have been authorised by means of another decentralised procedure (e.g. Famotidine CF 20 and 40 mg film-coated tablets (NL/H/5592/001-002).

IV.4 Clinical safety

According to the proposed SmPC, common (≥ 1/100 to < 1/10) adverse drug reactions of famotidine concern headache, dizziness, constipation, diarrrhoea. Uncommon (≥ 1/1 000 to < 1/100) adverse drug reactions of famotidine concern dry mouth, nausea, vomiting, gastrointestinal complaints, flatulence, loss of appetite, rash, pruritis, and fatigue.

The MAH submitted clinical safety data on famotidine from literature on duodenal ulcers, prophylactic treatment of relapses duodenal ulcers, benign gastric ulcers, reflux oesophagitis, Zollinger-Ellison syndrome (Barbara et al., 1985, Paoluzi et al., 1985, Howard et al., 1985, Miwa & Miyoshi, 1987, Saigenji et al., 1987, Robinsen et al., 1991, Howden & Tytgat, 1996). These data are presented and assessed in the clinical assessment report.

Overall, famotidine treatment was well tolerated in the submitted publications.

For duodenal ulcers (Barbara et al., 1985), benign gastric ulcer (Paoluzi et al., 1985), and reflux oesophagitis (e.g. Robinsen et al., 1991) the evaluated famotidine dosages in the submitted publications were similar to those that are proposed for respective indications in current marketing authorisation application. For other indications this is not known. Famotidine treatment was well tolerated at the evaluated dosages for aforementioned indications.

The clinical safety of famotidine at dosages of 800 mg per day or higher as long as clinically necessary for Zollinger-Ellison-Syndrome was initially unclear. Later, the MAH indicated that the available data from the submitted literature on famotidine in patients with Zollinger-Ellison syndrome, other famotidine medicinal products, the USFDA Adverse Event Reporting

System (FAERS) Public Dashboard (period 1986-2025), and the European EudraVigilance database (period 2003-2025) support an acceptable safety profile of famotidine within the recommended famotidine dosing range (80 – 800 mg/day) in patients with Zollinger-Ellison syndrome.

IV.5 Risk Management Plan

The MAH has submitted a risk management plan, in accordance with the requirements of Directive 2001/83/EC as amended, describing the pharmacovigilance activities and interventions designed to identify, characterise, prevent or minimise risks relating to Famotidine Glenmark 20 mg and 40 mg. At the time of approval, the most recent version of the RMP was version 0.2 (data lock point: 25 September 2024, date of final sign off: 29 August 2025).

Table 2. Summary table of safety concerns as approved in RMP

Important identified risks	None
Important potential risks	None
Missing information	None

The member states agreed that routine pharmacovigilance activities and routine risk minimisation measures are sufficient for the risks and areas of missing information.

IV.6 Discussion on the clinical aspects

For this authorisation, reference is made to the clinical studies and experience with the innovator product Pepcid 10 mg. No new clinical studies were conducted. The MAH demonstrated through a bioequivalence study that the pharmacokinetic profile of the product is similar to the pharmacokinetic profile of this reference product. Furthermore, Famotidine 20 mg and 40 mg are used in the proposed indications for decades within the European Union. The indications for Famotidine Glenmark 20 mg and 40 mg film-coated tablets are supported by publications from literature. The MAH demonstrated that the medicinal product applied for is similar to the product(s) described in the literature. Therefore, it is concluded that the clinical efficacy and safety results for famotidine reported in the literature can be applied to the proposed Famotidine Glenmark 10 mg, 20 mg and 40 mg film-coated tablets.

Risk management is adequately addressed. This hybrid medicinal product can be used instead of the reference product. The clinical aspects of this product are approvable.

V. USER CONSULTATION

The package leaflet (PL) has been evaluated via a user consultation study in accordance with the requirements of Articles 59(3) and 61(1) of Directive 2001/83/EC. The language used for the purpose of user testing the PL was English.
The test consisted of: a pilot test with 3 participants, followed by two rounds with 10 participants each. The questions covered the following areas sufficiently: traceability,

comprehensibility and applicability. The results show that the PL meets the criteria for readability as set out in the Guideline on the readability of the label and package leaflet of medicinal products for human use.

VI. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

Famotidine Glenmark 10 mg, 20 mg and 40 mg film-coated tablets have a proven chemical-pharmaceutical quality and are hybrid forms of Pepcid 10 mg, film coated tablets. Pepcid 10 mg is a well-known medicinal product with an established favourable efficacy and safety profile.

Bioequivalence has been shown to be in compliance with the requirements of European guidance documents.

The Board followed the advice of the assessors.

There was no discussion in the CMD(h). The MEB, on the basis of the data submitted, considered that bioequivalence has been demonstrated for Famotidine Glenmark 10 mg, 20 mg and 40 mg with the reference products, and have therefore granted a marketing authorisation. The decentralised procedure was finalised with a positive outcome on 16 April 2026.

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STEPS TAKEN AFTER THE FINALISATION OF THE INITIAL PROCEDURE - SUMMARY

Procedure number	Scope	Product Information affected	Date of end of procedure	Approval/ non approval	Summary/ Justification for refuse
N.A.	N.A.	N.A.	N.A.	N.A.	N.A.