

Part VI: Summary of the risk management plan

Summary of risk management plan for FAMOTIDINA DOC (famotidine)

This is a summary of the risk management plan (RMP) FAMOTIDINA DOC. The RMP details important risks of FAMOTIDINA DOC, how these risks can be minimised, and how more information will be obtained about FAMOTIDINA DOC' risks and uncertainties (missing information).

FAMOTIDINA DOC' summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how FAMOTIDINA DOC should be used.

Important new concerns or changes to the current ones will be included in updates FAMOTIDINA DOC' RMP.

I. The medicine and what it is used for

FAMOTIDINA DOC 20&40 mg, film-coated tablets are authorised for:

- Duodenal ulcers and prevention of relapses of duodenal ulceration.
- Benign gastric ulcers.
- Zollinger-Ellison syndrome.
- Symptomatic treatment of mild to moderate reflux oesophagitis.

II. Risks associated with the medicine and activities to minimise or further characterise the risks

Important risks of FAMOTIDINA DOC, together with measures to minimise such risks and the proposed studies for learning more about FAMOTIDINA DOC' risks, are outlined below.

Measures to minimise the risks identified for medicinal products can be:

- Specific information, such as warnings, precautions, and advice on correct use, in the package leaflet and SmPC addressed to patients and healthcare professionals;
- Important advice on the medicine's packaging;
- The authorised pack size — the amount of medicine in a pack is chosen so to ensure that the medicine is used correctly;
- The medicine's legal status — the way a medicine is supplied to the patient (e.g. with or without prescription) can help to minimise its risks.

Together, these measures constitute *routine risk minimisation* measures.

In addition to these measures, information about adverse reactions is collected continuously and regularly analysed, including PSUR assessment so that immediate action can be taken as necessary. These measures constitute *routine pharmacovigilance activities*.

If important information that may affect the safe use of FAMOTIDINA DOC is not yet available, it is listed under 'missing information' below.

II.A List of important risks and missing information

Important risks of FAMOTIDINA DOC are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely taken. Important risks can be regarded as identified or potential. Identified risks are concerns for which there is sufficient proof of a link with the use of FAMOTIDINA DOC. Potential risks are concerns for which an association with the use of this medicine is possible based on available data, but this association has not been established yet and needs further evaluation. Missing information refers to information on the safety of the medicinal product that is currently missing and needs to be collected (e.g. on the long-term use of the medicine);

Summary of safety concerns	
Important identified risks	<ul style="list-style-type: none">• Hypersensitivity (allergic reactions, including symptoms of anaphylaxis and angiooedema)• Renal impairment• Use in patients with renal impairment• Drug interactions• Stevens Johnson syndrome / toxic epidermal necrolysis
Important potential risks	<ul style="list-style-type: none">• Exposure during pregnancy• Use in lactation
Missing information	<ul style="list-style-type: none">• Use in children <12 years of age/Use in pediatric population

II.B Summary of important risks

Important identified risks: <i>Hypersensitivity (allergic reactions, including symptoms of anaphylaxis and angiooedema)</i>	
Evidence for linking the risk to the medicine	As reported in SmPC and in scientific literature there is evidence of a link with the intake of famotidine and the development of the reported event.
Risk factors and risk groups	Patients allergic to the active substances or to any excipients.
Risk minimisation measure	Specific information, such as warnings, precautions, and advice on correct use, in the package leaflet and SmPC addressed to patients and healthcare professionals; Important advice on the medicine's packaging; The authorised pack size — the amount of medicine in a pack is chosen so to ensure that the medicine is used correctly; The medicine's legal status — the way a medicine is supplied to the patient (e.g. with or without prescription) can help to minimise its risks.

	Together, these measures constitute <i>routine risk minimisation measures</i> .
Additional pharmacovigilance activities	None

Important identified risks: Renal impairment	
Evidence for linking the risk to the medicine	Echizen H, Ishizaki T. Clin Pharmacokinet. Clinical pharmacokinetics of famotidine. 1991 Sep;21(3):178-94. doi: 10.2165/00003088-199121030-00003
Risk factors and risk groups	Especially elderly patient on therapy with famotidine.
Risk minimisation measure	Specific information, such as warnings, precautions, and advice on correct use, in the package leaflet and SmPC addressed to patients and healthcare professionals; Important advice on the medicine's packaging; The authorised pack size — the amount of medicine in a pack is chosen so to ensure that the medicine is used correctly; The medicine's legal status — the way a medicine is supplied to the patient (e.g. with or without prescription) can help to minimise its risks. Together, these measures constitute <i>routine risk minimisation measures</i> .
Additional pharmacovigilance activities	None

Important identified risks: Use in patients with renal impairment	
Evidence for linking the risk to the medicine	Maples HD , James LP, Stowe CD, Jones DP, Hak EB, Blumer JL, Vogt B, Wilson JT, Kearns GL, Wells TG; Network of Pediatric Pharmacology Research Units..J Famotidine disposition in children and adolescents with chronic renal insufficiency. Clin Pharmacol. 2003 Jan;43(1):7-14. doi: 10.1177/0091270002239700.)
Risk factors and risk groups	Patient with renal impairment on therapy with famotidine especially children and adolescent with chronic renal insufficiency.
Risk minimisation measure	Specific information, such as warnings, precautions, and advice on correct use, in the package leaflet and SmPC addressed to patients and healthcare professionals; Important advice on the medicine's packaging; The authorised pack size — the amount of medicine in a pack is chosen so to ensure that the medicine is used correctly; The medicine's legal status — the way a medicine is supplied to the patient (e.g. with or without prescription) can help to minimise its risks.

	Together, these measures constitute <i>routine risk minimisation measures</i> .
Additional pharmacovigilance activities	None

Important identified risks: *Drug interaction*

Evidence for linking the risk to the medicine	As reported in SmPC and in scientific literature there is evidence of a link with the intake of famotidine and interactions with some Drugs as ketoconazole, itraconazole, sucralfate, probenecid, atazanavir/ritonavir and tenofovir that interfere with the therapy's outcome .
Risk factors and risk groups	Patients on concomitant therapy with the above Drugs described.
Risk minimisation measure	Specific information, such as warnings, precautions, and advice on correct use, in the package leaflet and SmPC addressed to patients and healthcare professionals; Important advice on the medicine's packaging; The authorised pack size — the amount of medicine in a pack is chosen so to ensure that the medicine is used correctly; The medicine's legal status — the way a medicine is supplied to the patient (e.g. with or without prescription) can help to minimise its risks. Together, these measures constitute <i>routine risk minimisation measures</i> .
Additional pharmacovigilance activities	None

Important identified risks: *Stevens Johnson syndrome/toxic epidermal necrolysis*

Evidence for linking the risk to the medicine	<p>- Brunner M, Vardarman E, Goldermann R, Goerz G, Niederau D, Merk HF, Scharffetter-Kochanek K. Toxic epidermal necrolysis (Lyell syndrome) following famotidine administration. Br J Dermatol. 1995 Nov;133(5):814-5. doi: 10.1111/j.1365-2133.1995.tb02765.x.</p> <p>- Scheinfeld N, Wesson K, Perry P, Weinberg J. Acute generalized exanthematous pustulosis resembling toxic epidermal necrolysis caused by famotidine. Acta Derm Venereol. 2003;83(1):76-7. doi: 10.1080/00015550310002873.</p>
Risk factors and risk groups	Patients with dermatological pathologies and with allergy to famotidine in medical history
Risk minimisation measure	Specific information, such as warnings, precautions, and advice on correct use, in the package leaflet and SmPC addressed to patients and healthcare professionals; Important

	<p>advice on the medicine's packaging; The authorised pack size — the amount of medicine in a pack is chosen so to ensure that the medicine is used correctly; The medicine's legal status — the way a medicine is supplied to the patient (e.g. with or without prescription) can help to minimise its risks.</p> <p>Together, these measures constitute <i>routine risk minimisation measures</i>.</p>
Additional pharmacovigilance activities	None

Important potential risks: *Exposure during pregnancy*

Evidence for linking the risk to the medicine	<p>-Garbis H, Elefant E, Diav-Citrin O, Mastroiacovo P, Schaefer C, Vial T, Clementi M, Valti E, McElhatton P, Smorlesi C, Rodriguez EP, Robert-Gnansia E, Merlob P, Peiker G, Pexieder T, Schueler L, Ritvanen A, Mathieu-Nolf M. Pregnancy outcome after exposure to ranitidine and other H2-blockers. A collaborative study of the European Network of Teratology Information Service. <i>Reprod Toxicol</i>. 2005 Mar-Apr;19(4):453-8. doi: 10.1016/j.reprotox.2004.09.002.</p> <p>-Matok I, Gorodischer R, Koren G, Sheiner E, Wiznitzer A, Uziel E, Levy A. The safety of H(2)-blockers use during pregnancy. <i>J Clin Pharmacol</i>. 2010 Jan;50(1):81-7. doi: 10.1177/0091270009350483. Epub 2009 Sep 29.</p>
Risk factors and risk groups	Pregnant woman
Risk minimisation measure	<p>Specific information, such as warnings, precautions, and advice on correct use, in the package leaflet and SmPC addressed to patients and healthcare professionals; Important advice on the medicine's packaging; The authorised pack size — the amount of medicine in a pack is chosen so to ensure that the medicine is used correctly; The medicine's legal status — the way a medicine is supplied to the patient (e.g. with or without prescription) can help to minimise its risks.</p> <p>Together, these measures constitute <i>routine risk minimisation measures</i>.</p>
Additional pharmacovigilance activities	None

Important potential risks: *Use in lactation*

Evidence for linking the risk to the medicine	<p>Hagemann TM. Gastrointestinal medications and breastfeeding. <i>J Hum Lact</i>. 1998 Sep;14(3):259-62. doi: 10.1177/089033449801400321.</p>
---	--

Risk factors and risk groups	Breastfeed children
Risk minimisation measure	<p>Specific information, such as warnings, precautions, and advice on correct use, in the package leaflet and SmPC addressed to patients and healthcare professionals; Important advice on the medicine's packaging; The authorised pack size — the amount of medicine in a pack is chosen so to ensure that the medicine is used correctly; The medicine's legal status — the way a medicine is supplied to the patient (e.g. with or without prescription) can help to minimise its risks.</p> <p>Together, these measures constitute <i>routine risk minimisation measures</i>.</p>
Additional pharmacovigilance activities	None

II.C Post-authorisation development plan

II.C.1 Studies which are conditions of the marketing authorisation

There are no studies which are conditions of the marketing authorisation or specific obligation of FAMOTIDINA DOC.

II.C.2 Other studies in post-authorisation development plan

There are no studies required for FAMOTIDINA DOC.