

VI.2 Elements for a public summary

VI.2.1 Overview of disease epidemiology

Ulcerative colitis (UC) is a form of inflammatory bowel disease (IBD). It is characterised by the ulcers or open sores of the colon (large intestine).^{1,2} The cause of this disorder is multifactorial and not fully understood but it is treated as an autoimmune disease.³

In Europe, incidence rates of ulcerative colitis range from 1.5 to 20.3 cases per 100,000 individuals per year. The disease is more frequent in northern countries of the world, as well as in northern areas of individual countries or other regions. Rates tend to be higher in more affluent countries.⁴

The peak age of onset for IBD is 15 to 30 years old. About 10% of cases occur in individuals under 18 years of age. Previously noted racial and ethnic differences seem to be narrowing.⁴

VI.2.2 Summary of treatment benefits

Long-term use of mesalazine was proven in numerous clinical trials to be very effective and safe for the prevention of inflammatory relapses in patients with UC.⁷ Mesalazine is therefore the treatment of first choice, not only for induction of remission but - at least as relevant - also in maintaining the remission.⁴¹ Moreover, mesalazine was shown to reduce the incidence of colorectal cancer (CRC), a malignancy which is among the most frequent cancers in the population but which is even further increased in patients with UC.⁷⁷ In conclusion, aminosalicylates like mesalazine are considered the foundational and first-line agents for the treatment of patients with UC.^{1,78-81}

VI.2.3 Unknowns relating to treatment benefits

There are limited data on the use of Salofalk 1g tablets in pregnant and breast-feeding women. Therefore Salofalk 1 g tablets should only be used during pregnancy and breast-feeding, if the potential benefit outweighs the possible risk. Furthermore, there is also limited information for children between the age of 6 years and 18 years.

VI.2.4 Summary of safety concerns

Table 33 Important identified risks

Important Identified Risk	What is known	Preventability
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Inflammation of the kidney(s) affecting the interstitium (part of the kidneys) (Interstitial nephritis)	Renal impairment is a very rare, but potentially serious, adverse event in mesalazine recipients. Fortunately the symptoms of this adverse drug reaction are mostly reversible with cessation of therapy. ³⁷	Salofalk 1 g tablets are contraindicated in cases of severe impairment of renal function. Blood tests and urinary status should be determined prior to and during treatment, at the discretion of the treating physician.
Disease affecting lungs (Pulmonary disease)	Diseases affecting lungs (pulmonary diseases) caused by mesalazine are very rare. Fortunately the symptoms of these adverse drug reactions are mostly reversible with cessation of therapy. ³⁷	Patients with diseases affecting lungs, in particular asthma, should be very carefully monitored during a course of treatment with Salofalk 1 g tablets.
Hypersensitivity reactions	Hypersensitivity reactions represent adverse drug reactions known to occur with a broad	Patients with a known hypersensitivity to salicylates or any of the excipients should not

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Important Identified Risk	What is known	Preventability
	variety of approved drugs and may be mild to severe. ⁴⁸ However, frequency of hypersensitivity reactions during treatment with mesalazine is very low.	take the product.
Liver related disease (Hepatic disease)	Liver disorders are very rare undesirable effects of mesalazine treatment.	Blood tests should be performed prior to and during treatment with mesalazine. Patients with impaired liver function should be treated with caution.
Blood disorders	Blood disorders are very rare and mostly reversible with cessation of therapy.	Blood tests should be performed prior to and during treatment with mesalazine.
Interaction with azathioprine, 6mercaptopurine and thioguanine	Mesalazine could cause a drug interaction which can result in an increased risk of bone marrow depression (blood disturbances). ^{51,52}	This interaction should be taken into account in patients who are concomitantly treated with these drugs.

Table 34 Important potential risks

Important Potential Risk	What is known (including reason why it is considered a potential risk)
Interaction with warfarin	There is weak evidence that mesalazine might decrease the anti-clotting (anticoagulant) effect of warfarin. This interaction may potentially lead to a higher risk of blood clotting within blood vessels (thrombosis) in patients treated with warfarin.

Table 35 Missing information

Safety in pregnancy and lactation	<p>Pregnancy is no longer considered a contraindication to the use of mesalazine. In fact, physicians are specifically advised not to interrupt therapy or reduce the mesalazine dose in response to pregnancy.</p> <p>Further there have been publications that mesalazine increased the risk for preterm delivery and consequently decreased birth weight. These differences, however, are most likely associated with the mothers' underlying disease (IBD).</p> <p>Salofalk 1 g tablets should only be used during pregnancy and breast-feeding, if the potential benefit outweighs the possible risk.</p>
Safety and efficacy in children below the age of 6 years	<p>There is limited information regarding safety and efficacy in children below the age of 6 years for Salofalk 1 g tablets.</p>

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VI.2.5 Summary of additional minimisation measures by safety concern

Not applicable.

VI.2.6 Planned post-authorisation development plan (if applicable)

Not applicable.

VI.2.7 Summary of changes to the risk management plan over time

This is the first version of the RMP