Off-label use	• SmPC • PIL • Prescription only medicine	None
Use in the elderly	• SmPC • PIL • Prescription only medicine	None

VI.2 Elements for a Public Summary

VI.2.1 Overview of disease epidemiology

Ulcerative colitis (UC)
Ulcerative colitis (UC) is a chronic bowel disease with unknown cause, with inflammation and ulcerations in the lining of the large bowel and in the rectum. The disease can occur at any age but is most commonly diagnosed between the ages of 15 and 40. The main symptoms of UC are bloody diarrhoea and rectal urgency. The activity of the disease comes and goes in cycles, with fairly healthy periods between periods of active disease. There is currently no medical cure for the disease. Medical treatment aims to reduce and shorten the periods of active disease. In cases of severe illness and failure of medical treatment the large bowel can be removed surgically. The mortality rate for patients with UC is not different from the general population. UC often runs in parallel with other immunological diseases.

VI.2.2 Summary of treatment benefits
CORTIMENT has been shown to be effective in the treatment of active, mild to moderate UC in large, placebo-controlled clinical trials. The main alternative in treatment of these patients is aminosalicylates, or 5-ASA. However, 5-ASA is not effective in all patients, and CORTIMENT may offer a treatment alternative without increasing the risk for severe side effects which is seen with systemic corticosteroids.

VI.2.3 Unknowns relating to treatment benefits
There is little known regarding the effectiveness or safety of use of CORTIMENT in children under 18 years of age, and as a precaution, CORTIMENT is not recommended for treatment of UC in children.

VI.2.4 Summary of safety concerns

Summary of safety concerns		
Risk	**What is known**	**Preventability**
Safety concern in lay language (medical term)	**Brief summary in lay language**	**Whether risk can be minimised or mitigated, and how**
Potential relapse of Ulcerative Colitis	Relapse (worsening of symptoms) can occur due to the nature of the disease.	Yes, by continuous monitoring for early symptoms.
Paediatric studies/off-label use in children	The effect, including side effects, of CORTIMENT has not been studied in children.	Yes, CORTIMENT is not recommended in children. The benefit *versus* risk must be considered by the treating physician
Use in pregnancy/breastfeeding	The effect, including side effects, of CORTIMENT has not been studied in pregnant or breastfeeding women.	Yes, CORTIMENT might be taken with caution by pregnant or breastfeeding patients. The benefit *versus* risk must be considered by the treating physician
Use in co-morbid conditions e.g., liver or kidney disease (hepatic and renal insufficiency)	With liver and kidney disease or impaired function (e.g. in the elderly), there is an increased risk for side effects when using CORTIMENT together with certain other drugs.	Yes, CORTIMENT might be taken with caution by patients with liver or kidney disease. The benefit *versus* risk must be considered by the treating physician
Use for other conditions than active UC (Off-label use)	There is no apparent use for CORTIMENT in patients who do not have active UC.	Yes, CORTIMENT is indicated for the treatment for the induction of remission in mild to moderate active ulcerative colitis. The prescription of this medicine should exactly follow the indication of this treatment.
Use in the elderly	There is an increased risk for side effects when using CORTIMENT together with certain other drugs, especially in elderly who may have an impaired liver or kidney function.	Yes, CORTIMENT might be taken with caution by elderly patients The benefit *versus* risk must be considered by the treating physician

VI.2.5 Summary of risk minimisation measures by safety concern

All medicines have a Summary of Product Characteristics (SmPC) which provides physicians, pharmacists and other health care professionals with details on how to use the medicine, the risks and recommendations for minimising them. An abbreviated version of this in lay language is provided in the form of the Patient Information Leaflet (PIL). The measures in these documents are known as routine risk minimisation measures.

General risk minimisation measures can be exemplified as follows but does not specifically apply for CORTIMENT:

1 Provision of information (educational material) to healthcare professionals/patients
2 Pharmacovigilance activities (surveillance and reporting of side effects)
3 Control at pharmacy level
4 Control of prescription size
5 Restricted access
6 Registries
7 Patient monitoring/screening
8 Controlled distribution
9 Pregnancy/prevention activities
10 Special packaging/extra label

Safety concern in lay terms (medical term)	Routine risk minimisation measure(s)	Additional risk minimisation measure(s)
Potential relapse of Ulcerative Colitis	• Relapse (worsening of symptoms) can occur due to the nature of the disease • Prescription only medicine	None
Paediatric studies/off-label use in children	• The treating physician will be informed according to the SmPC and the patient according to the PIL • Not recommended in children • Prescription only medicine	None
Use in pregnancy/lactation	• The treating physician will be informed according to the SmPC and the patient according to the PIL • Prescription only medicine	None
Use in co-morbid conditions e.g., liver or kidney disease (hepatic and renal insufficiency)	• The treating physician will be informed according to the SmPC and the patient according to the PIL • Prescription only medicine	None

Safety concern in lay terms (medical term)	Routine risk minimisation measure(s)	Additional risk minimisation measure(s)
Use for other conditions than active UC (off-label use)	• The treating physician will be informed according to the SmPC and the patient according to the PIL • Not recommended in other conditions • Prescription only medicine	None
Use in the elderly	• The treating physician will be informed according to the SmPC and the patient according to the PIL • Prescription only medicine	None

VI.2.6 Planned post authorisation development plan

There is no plan at present to conduct further clinical studies with CORTIMENT after it has been approved for use in ulcerative colitis.

List of studies in post-authorisation development plan

There are no studies planned.

VI.2.7 Summary of changes to the Risk Management Plan over time

Version	Date	Safety Concerns	Comment
0.1 (04 November 2010)	03 May 2011	**Identified risk:** Potential relapse of UC. **Potential risks:** peptic ulcer, hyperglycaemia, osteoporosis, adrenal dysfunction including endocrine disorders, immunosuppression including reactivation of quiescent viral illness, ocular events, psychiatric disorders. **Missing information:** Paediatric use, safety in patients with common comorbidities, off label use, use in pregnancy/lactation and use in the elderly.	NA

Version	Date	Safety Concerns	Comment
0.2	24 November 2011	As version 0.1	Minor corrections according to the submission procedure
1.0	27 November 2013	Potential risks were removed	Peptic ulcer was originally included due to one single event occurring in the ENTOCORT reference arm, giving an incidence comparable to the incidence in the general population. Moreover, the Budesonide-MMX formulation is a gastro-resistant extended release drug delivery technology for targeted delivery to the colon, preventing direct contact of budesonide with the gastro-duodenal mucosa. Budesonide also has a low systemic availability of 10-15%. The original RMP listed known side effects of systemic corticosteroids as potential risks: hyperglycaemia, osteoporosis, adrenal dysfunction including endocrine disorders, immunosuppression including reactivation of quiescent viral illness, ocular events and psychiatric disorders. These events are known side effects of conventional oral corticosteroids, with a systemic availability of 80-95% for prednisolone and 70-95% for

Version	Date	Safety Concerns	Comment
			methylprednisolone, therefore no any longer contemplated such as "potential risks" in this version of the RMP. Budesonide-MMX formulation was in phase II and III trials generally well tolerated and demonstrated a safety profile comparable to placebo, which is expected with an enteral glucocorticoid with low systemic availability of 10-15%. Glucocorticoid side effects reported were of similar frequencies in the placebo and the CORTIMENT 9 mg groups over 8 weeks treatment (10.5% and 10.2% of patients, respectively).