VI.2 Elements for a Public Summary

VI.2.1 Overview of disease epidemiology

Ulcerative colitis (UC)
Ulcerative colitis is a chronic bowel disease with unknown cause, giving inflammation with ulcerations in the mucosa in parts of or in the whole large bowel and in the rectum. The disease may occur at all ages but is most commonly diagnosed between the ages of 15 and 40. There is at present no medical cure for the disease. Medical treatment is aimed at diminishing and shortening the periods of active disease.

The highest incidence rates for ulcerative colitis are reported form northern Europe, the United Kingdom, and North America, with figures ranging between 2 and 24 newly diagnosed patients per 100,000 persons per year. During the last decade rising figures have also been reported from other parts of the world.

Crohn's Disease (CD)
Crohn's disease is a chronic bowel disease with unknown cause, giving inflammation with ulcerations, abscesses and fibrosis in delimited, but often multiple sections of the bowel. The disease can develop anywhere in the gastrointestinal canal from the mouth to the anus, but is mostly seen in the lower parts of the small bowel and in the large bowel. There is at present no medical cure for the disease. Medical treatment is aimed at diminishing and shortening the periods of active disease and to counteract complications.

The highest incidence rates for Crohn's disease are reported form northern Europe, the United Kingdom, and North America, with figures ranging between 1 and 15 newly diagnosed patients per 100,000 persons per year. During the last decade rising figures have also been reported from other parts of the world.

VI.2.2 Summary of treatment benefits

No curative medical treatment exists today for Ulcerative colitis or Crohn's disease, hence the medical treatment for Ulcerative colitis and Crohn's disease at present is aimed at successful induction of remission and maintenance of remission, to diminish and shorten flares, prolong periods of quiescent disease, reduce the risk of future surgery, counteract development of complications and co-morbidities and improve quality of life.

Mesalazine is a well characterized class of compound developed through numerous clinical trials, and with many years of marketing exposure in the clinical setting.

For Ulcerative colitis, the efficacy of PENTASA in the treatment of active disease for induction of remission as well as of quiescent UC for maintenance of remission is well established, through data from many clinical trials and more than 25 years of treatment experience, including a favourable safety profile in daily doses up to 4 g. With the presented MOTUS trial the efficacy and safety of once daily dosing for induction of remission in mild to moderate UC has been established.

PENTASA has been evaluated in a number of clinical trials and used for more than 25 years in the treatment of active and quiescent mild to moderate CD with a favourable safety profile in daily doses up to 4 g. Recent data indicate the treatment benefit to be greater in certain groups of CD patients than in the overall patient population.

VI.2.3 Unknowns relating to treatment benefits

There is limited experience as far as efficacy is concerned in paediatric population. According to the Ferring's CCDS/SmPC, the use in children below the age of 6 years old is not recommended due to lacking documentation.

VI.2.4 Summary of safety concerns

Important identified risks		
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**
Kidney disorders (symptoms include blood in the urine, and/or oedema (swelling due to build up of fluid), change in the urine color) (**Impairment of renal function**)	Kidney disorders which symptoms include blood in the urine, and/or oedema (swelling due to build up of fluid), change in the urine color affecting less than 1 of 10,000 patients treated with mesalazine	Yes, by continuous monitoring for early symptoms. The concurrent use of other known nephrotoxic agents should increase monitoring frequency of renal function
Liver disorders (symptoms include jaundice (yellowing of the skin and/or eyes) and/or pale bowel motions) (**Impairment of hepatic function**)	Liver disorders which symptoms include jaundice (yellowing of the skin and/or eyes) and/or pale bowel motions affecting less than 1 of 10,000 patients treated with mesalazine	Yes, by continuous monitoring for early symptoms
Inflammation of some areas of the heart (myocarditis and pericarditis) which can cause shortness of breath and chest pain or palpitations (rapid or irregular heartbeats) (**Reversible myocarditis / pericarditis**)	Mesalazine-induced inflammations of some areas of the heart have been reported rarely. Most cases of mesalazine-induced cardiovascular toxicity occur 2–4 weeks after the initial exposure to the drug, although presentation may be delayed in the setting of concomitant steroid administration	Yes, although rare, may represent a life-threatening disorder that requires immediate discontinuation of the mesalazine-containing product and adequate supportive treatment. It is suggested that every patient, on mesalazine, presenting with acute chest pain, shortness of breath, or any additional cardiovascular concern undergoes an

		electrocardiogram, cardiac enzymes, and an echocardiogram to rule out this rare drug-induced disorder.
Inflammation of the pancreas (symptoms include back and/or stomach pain, increase in enzymes) (**Acute pancreatitis**)	Inflammation of the pancreas (symptoms include back and/or stomach pain, increase in enzymes) affecting between 1 and 10 of every 10,000 patients treated	Yes, by continuous monitoring during the clinical course of U. When the possibility of drug-induced pancreatitis is considered, discontinuation of its administration must be weighed.
Symptoms include coughing, bronchospasm, chest discomfort or pain on breathing, breathing difficulties, bloody and/or excessive phlegm (**Respiratory disorders**)	Pulmonary complications are extremely rare, and only sporadic cases have been reported. Respiratory symptoms, most often a non-productive cough, chest discomfort or pain on breathing, breathing difficulties, bloody and/or excessive phlegm may appear immediately, a few days after drug initiation or several months to 2 years after initial administration.	Yes, by continuous and careful monitoring for early symptoms during a course of treatment.
Decrease in the numbers of certain blood cells, which can cause unexplained bleeding, bruising, fever or sore throat (**Blood dyscrasias**)	There have been a few case reports of patients taking mesalazine who developed decrease in platelets, and certain other blood cells.	Yes, by continuous monitoring for early symptoms.

VI.2.5 Summary of risk minimisation measures by safety concern

For the PENTASA CCDS, SmPC and the PIL, see Annex 2.

All medicines have a 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 PIL. The measures in these documents are known as routine risk minimisation measures.

This medicine has no additional risk minimisation measures.

VI.2.6 Planned post authorisation development plan

A safety and efficacy trial on QUINTASA mesalazine for induction of remission and maintenance of remission in adult patients with active UC in the US is planned.

There is also an early plan for a safety and efficacy trial on PENTASA rectal suspension in ulcerative colitis in China.

No other clinical trials are planned at present.

List of studies in post-authorisation development plan
There are no studies listed.

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

Table 1: Changes to the Risk Management Plan over time

Version	Date	Safety Concerns	Comment
2.0	28 April 2014	Editorial. For all the safety concerns the routine risk minimisation measures are CCDS and PIL, and there are no additional routine risk minimisation measures. In addition, statement added regarding the use of CCDS and SmPC in Part V and Part VII. Furthermore, pooled clinical trial data has been added.	Following request by the DKMA, RMP part II, V, VI and VII have been updated accordingly.
	31 July 2014	Editorial. For all the safety concerns the routine risk minimisation measures are CCDS/SmPC and PIL, and there are no additional routine risk minimisation measures. In addition, statement added regarding the use of CCDS/SmPC in Part II, V and Part VI. Furthermore, added a sentence below table V.1 that wording may vary in SmPC's.	Following request by the DKMA, RMP part I, II SII, V, VI and VII have been updated accordingly.