VI.2 Elements for a public summary

VI.2.1 Overview of disease epidemiology

Telmisartan/hydrochlorothiazide is a combination of an angiotensin II receptor antagonist and a thiazide diuretic used in the treatment of essential hypertension.

Hypertension is prevalent worldwide; accordingly, its epidemiology has been well studied. In many countries, 50% of the population older than 60 years has hypertension. Overall, approximately 20% of the world's adults are estimated to have hypertension. The 20% prevalence is for hypertension defined as blood pressure in excess of 140/90 mm Hg. The prevalence dramatically increases in patients older than 60 years. Hypertension is a major risk factor for stroke, myocardial infarction, vascular disease, and chronic kidney disease.

VI.2.2 Summary of treatment benefits

Based on the available data from clinical studies and clinical experience of several years, telmisartan/hydrochlorothiazide (telmisartan HCT) represents an effective drug in the treatment of patients with essential hypertension. Significant improvements of patients with telmisartan/hydrochlorothiazide treatment were reported from randomized controlled intervention trials.

Several studies have shown that telmisartan combination with HCT is more effective than telmisartan treatment alone.

Telmisartan given as monotherapy and in combination with HCT was compared with lisinopril as monotherapy and in combination with HCT in 578 patients with mild-to-moderate essential hypertension. During the maintenance period 56% of the telmisartan group and 55% of the lisinopril group were additionally treated with HCT. At the end of the maintenance period, diastolic blood pressure was controlled in 83% and 87% of the telmisartan and lisinopril patients, respectively, with blood pressure reductions of 23.8/16.6 mm Hg for telmisartan and 19.9/15.6 mm Hg for lisinopril. Telmisartan was concluded to be extremely effective in the treatment of mild-to- moderate hypertension both as monotherapy and in combination with HCT and is at least comparable in efficacy to lisinopril.

If administered as indicated in the Summary of Product Characteristics and taking into account the contra-indications, the warnings and precautions, telmisartan/hydrochlorothiazide can be considered effective in the approved indications and generally well tolerated.

VI.2.3 Unknowns relating to treatment benefits

Not applicable.

VI.2.4 Summary of safety concerns

Important identified risks

Risk	**What is known**	**Preventability**
Blood poisoning (Sepsis)	Blood poisoning is a severe infection with whole-body inflammatory response which can lead to death. This can happen by chance or could be	Monitoring of early symptoms of blood poisoning characterised by whole-body inflammatory response, rapid swelling of the

Risk	What is known	Preventability
	related to a mechanism currently not known. This side effect is rare (may affect up to 1 in 1,000 people) but is extremely serious.	skin and mucosa (angioedema) is advised. The patient should discontinue medication immediately and seek medical advice.
Impaired kidney function due to blockade of the hormone system that regulates blood pressure and water balance (Renal dysfunction as consequence of dual RAAS blockade)	The renin-angiotensin- aldosterone system (RAAS) is a hormone system that regulates blood pressure and water balance. As a consequence of inhibiting this hormone system, changes in kidney function have been reported in susceptible individuals, especially if combined with other medication that may affect this system. Up to 1 in 100 people may experience kidney impairment including acute kidney failure.	Telmisartan/hydrochlorothiazide tablets must not be given if patient has diabetes or impaired kidney function and is treated with a blood pressure lowering medicine containing aliskiren. Before taking telmisartan/hydrochlorothiazide tablets, patients should inform the doctor if they are taking any of the medicines used to treat high blood pressure such as aliskiren or an ACE-inhibitor (for example enalapril, lisinopril, ramipril), in particular if they have diabetes-related kidney problems Doctor may decide to check the kidney function, blood pressure, and the amount of electrolytes (e.g. potassium) in the blood at regular intervals.
Injury to the foetus (Foetotoxicity)	Telmisartan may cross the placenta and cause serious harm such as impaired kidney function, low blood pressure and increased blood potassium levels or even death in the developing foetus.	Telmisartan/hydrochlorothiazide is not recommended in early pregnancy, and must not be taken if a woman is more than 3 months pregnant. Patient must tell the doctor if she thinks she is (or might become) pregnant.
Low blood sugar in patients with diabetes (Hypoglycaemia (in diabetic patients))	Low blood sugars may occur in diabetic patients under insulin or antidiabetic therapy and telmisartan treatment. This side effect is rare (may affect up to 1 in 1,000 people).	Patients should tell the doctor if they are suffering from diabetes. Doctor may decide to check the sugar levels in the blood at regular intervals or adjust the dose of telmisartan/hydrochlorothiazide.

Important potential risks

Risk	What is known (Including reason why it is considered a potential risk)
Breakdown of damaged skeletal muscle (Rhabdomyolysis)	Patients treated with angiotensin II receptor antagonists may be at an increased risk of developing rhabdomyolysis. It is not known if telmisartan/hydrochlorothiazide may increase the risk of rhabdomyolysis.
Abnormal liver function in Japanese patients (Increase in hepatic-related adverse reactions in the Japanese population)	Abnormal liver function occurs rarely and may affect up to 1 in 1,000 people. Japanese patients are more likely to experience abnormal liver function. Most cases of abnormal liver function occurred in Japanese patients.
Malignancies	A review was carried out (by the EMA) to investigate a possible link between the use of this class of medicines and the occurrence of new cancers. The outcome was that there is no increased risk of cancer and that the benefits continue to outweigh the risks.

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 package leaflet (PL). 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

Not applicable. There are no studies in the post authorisation development plan.

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

Table 1. Major changes to the Risk Management Plan over time

Version	Date	Safety Concerns	Comment
1.0	Under Review	**Important identified risks:** • Sepsis • Renal dysfunction as consequence of dual RAAS blockade • Foetotoxicity • Hypoglycaemia • Drug interactions with medicinal products that may induce hyperkalaemia or hypokalaemia	Not applicable.

Version	Date	Safety Concerns	Comment
		Important potential risks: • Increase in hepatic-related adverse reactions in the Japanese population • Rhabdomyolysis • Interstitial lung disease • Severe cutaneous reactions • Suicide/self-injury • Malignancies **Missing information:** None.	
1.1	17 Dec 2013	**Important identified risks** • Sepsis • Renal dysfunction as consequence of dual RAAS blockade • Foetotoxicity **Important potential risks** • Increase in hepatic-related adverse reactions in the Japanese population • Rhabdomyolysis • Interstitial lung disease • Severe cutaneous reactions • Suicide/self-injury • Malignancies • Hypoglycaemia • Drug interactions with medicinal products that may induce hyperkalaemia or hypokalaemia **Missing information** None.	Safety concerns are sorted based on the RMS Day 180 Updated Assessment Report (FR/H/532-534/001-003).
1.2	29 Aug 2014	No changes	RMP was extended to also cover Telmisartan/Hydrochlorothiazide 40 mg/12.5 mg tablets.
2.0	04 Dec 2014	**Important identified risks** • Sepsis • Renal dysfunction as consequence of dual RAAS blockade • Foetotoxicity • Hypoglycaemia (in diabetic patients) **Important potential risks** • Rhabdomyolysis • Increase in hepatic-related adverse reactions in the Japanese population • Malignancies **Missing information**	Preliminary Variation Assessment Report (DK/H/2306/001-003/II/004 and DK/H/2307/001-003/II/007). Safety concerns are aligned with innovator, MicardisPlus.

Version	Date	Safety Concerns	Comment
		None.	