VI.2 Elements for a Public Summary

VI.2.1 Overview of disease epidemiology

Meniere's disease is a long-lasting disease that affects a substantial number of patients every year worldwide. The disease is characterised by intermittent episodes of a spinning motion lasting from minutes to hours, with fluctuating hearing loss, ringing in the ear, and pressure inside the ear. Meniere's disease remains a difficult disease to diagnose, especially in the early stages when not all its symptoms might be present. Therefore, the proportion of the population found to suffer from this disease is difficult to ascertain. Most studies suggest it occurs more commonly in females than in males. This disease seems to be much more common in adults in their age between aged 30 years to 50 years than in younger people, although it has been noted in children. Meniere's disease runs in families; several studies have indicated that in one out of five cases family members have similar symptoms. This disease also seems to affect more white people of northern European descent than it does the African and black races **[Sajjadi H & Paparella MM, 2008].**

VI.2.2 Summary of treatment benefits

The mechanism of action of the drug may be a pressure reduction of the fluid contained in the membranous labyrinth of the inner ear through improved microvascular circulation. Furthermore, betahistine may also inhibit the activity of the cranial nuclei involved in transmitting balance information from the inner ear to the brain (vestibular nuclei). Unlike other vestibular sedatives, betahistine does not delay or inhibit the vestibular compensatory mechanism, a process in the brain that allows it to adapt to the disease, and does not impair mental alertness.. Betahistine is a safe and effective drug for the treatment of symptoms of Ménière’s syndrome, clinical studies support the claimed effects. If used appropriately (according to the SPC) it is highly safe. Practical experience of betahistine on the market in a large number of patients has also confirmed its safety. The available medical literature is considered sufficient to evaluate the safety of Betahistin 2care4 Film-coated Tablets in the proposed therapeutic indication.

VI.2.3 Unknowns relating to treatment benefits

There are insufficient data available on safety and efficacy of betahistine in children below 18 years. There are no adequate data from the use of betahistine in pregnant women. It is not known whether betahistine is excreted in human milk. There are limited data available from clinical studies in the geriatric population. There are no specific clinical trials available in patients with renal impairment and hepatic impairment.

VI.2.4 Summary of safety concerns

Important identified risks:

Risk	What is known	Preventability
Allergy to betahistine or to any of the other ingredients used for preparation of betahistine tablet (Hypersensitivity reactions; anaphylaxis and angioneurotic oedema)	There have been reports of allergic reactions (hypersensitivity) following use of betahistine tablets. These reactions may include swelling, itching, rash, and urticaria. In patients already suffering from urticaria, rashes or allergic rhinitis, betahistine may aggravate these symptoms.	Yes, the patient should not be given betahistine tablets if he or she is allergic to betahistine or to any of the other ingredients of this medicine. The patient should talk to the treating physician or pharmacist before taking betahistine tablet if he or she has nettle rash, skin rash or a cold in the nose caused by an allergy, since these complaints may be exacerbated.
Use in patients with rare tumour of the adrenal gland called phaeochromocytoma (Severe hypertension in patients with phaeochromocytoma)	In patients with phaeochromocytoma, betahistine may induce the release of chemical substances called catecholamines from the tumour of the adrenal gland resulting in abnormal rise in blood pressure which may be fatal.	Yes, the treating physician should not administer betahistine to patients already suffering from phaeochromocytoma.

Important potential risks:

Risk	What is known
Use in patients suffering from condition of airway obstruction called bronchial asthma (Use in patients with bronchial asthma)	Few patients may not tolerate betahistine which may result in asthma or bronchospasm. However, this clinical intolerance has been shown in a relatively few patients. Therefore, patients with bronchial asthma need to be carefully monitored during treatment with betahistine.

Missing information:

Risk	What is known
Use in children below 18 years	Betahistine is not recommended for use in children and adolescents below 18 years of age, as there is no information on efficacy and safety in these age groups.

Risk	What is known
Use in pregnancy and breast-feeding (lactation)	There are no adequate data from the use of betahistine in pregnant women. Therefore, it is recommended that betahistine should not be used during pregnancy unless clearly necessary. It is not known whether betahistine is excreted in human milk. The importance of the medicine to the mother should be weighed against the benefits of nursing and the potential risks for the child.

VI.2.5 Summary of additional risk minimization measures by safety concern

Summary of Product Characteristics (SmPC) of Betahistin 2care4 Film-coated Tablets (Generic Specialty Pharma Ltd) 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 (PIL). All these risk minimization measures are given in SmPC and PIL of Betahistin 2care4 24 mg Film-coated Tablets (Generic Specialty Pharma Ltd). No additional risk minimization measures have been proposed for this generic medicine.

VI.2.6 Planned post authorisation development plan

No post authorisation study is planned for this product.

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

Major changes to the Risk Management Plan over time

Version	Date	Safety Concerns	Comment
1.0	2015-01-12	New document.	
1.1	2015-08-05	Update based on Answers to LIST OF OUTSTANDING QUESTIONS: list of safety concern has been edited: • Hypersensitivity to betahistine or to any of the excipients" was changed to "Hypersensitivity reactions; anaphylaxis and angioneurotic oedema" • "Use in patients with phaeochromocytoma" was changed to "Severe hypertension in patients with phaeochromocytoma". • "Use in the geriatric population" and "Use in renal and hepatic impairment" were removed	Update based on Answers to LIST OF OUTSTANDING questions DK/H/2474/001-003/DC Day 100 AR.
1.2	2016-01-03	Update based on Answers to LIST OF OUTSTANDING QUESTIONS:	Update based on Answers to LIST OF OUTSTANDING

Version	Date	Safety Concerns	Comment
		SmPC and PiL have been edited as well as part VI.2 Elements for a Public Summary.	questions DK/H/2474/001-003/DC Day 120 AR.