VI.2 Elements for a Public Summary

VI.2.1 Overview of disease epidemiology

Allergic rhinitis is an allergic inflammation of the nasal airways that occurs when allergens (e.g. pollen, dust) are inhaled by an individual with a sensitized immune system. The allergen triggers the production of the immunoglobulin IgE that finally causes the release of inflammatory mediators such as histamine. This usually causes sneezing, itchy and watery eyes, swelling and inflammation of the nasal passages, and an increase in mucus production. Rhinitis (and sinusitis) are among the most common medical conditions and are frequently associated. In Western societies, an estimated 10% to 25% of the population have allergic rhinitis, with 30 to 60 million persons being affected annually in the United States. Treatment options include avoiding the allergen, other antihistamines, glucocorticoids given as nasal spray or systemically in severe cases.

Nettle rash (urticatia) is a kind of skin rash characterized by pale red, raised, itchy wheals that can appear anywhere on the surface of the skin. It is frequently caused by allergic reactions; however, there are many nonallergic causes. The reaction is caused by a release of inflammatory mediators, including histamine from cutaneous mast cells that leads to fluid leakage from blood vessels. Acute urticaria lasts less than 6 weeks. Urticaria lasting more than 6 weeks is defined as chronic urticaria, and an etiology is seldom identified. Chronic urticaria may have an autoimmune basis. Urticaria may affect up to 20% of the population at some time in their lives. In half of the patients, psychosocial factors are likely to contribute to the development of chronic urticaria. Treatment options include awareness of individual triggers, other antihistamines or systemic corticoids in severe cases.

VI.2.2 Summary of treatment benefits

Levocetirizine 5 mg is an antiallergic medication for the treatment of signs of illness (symptoms) associated with:

- allergic rhinitis (including persistant allergic rhinitis);
- nettle rash (urticaria).

VI.2.3 Unknowns relating to treatment benefits

The safety of Levocetirizine 5 mg has not been established in children under 6 years of age, breastfed infants exposed to maternal medication and during pregnancy.

VI.2.4 Summary of safety concerns

Table 10: Important identified risks

Risk in Lay Language (Clinical Term)	What is known	Preventability
Allergic reactions (Hypersensitivity reactions)	There is a possibility of developing allergic reaction(s) (that might include swelling of the mouth, tongue, face and/or throat, breathing or swallowing difficulties, hives, sudden fall in blood pressure leading to collapse or shock) if a person is hypersensitive to levocetirizine or other ingredients of the formulation.	Levocetirizine 5 mg should be discontinued promptly and appropriate treatment should be initiated in case of an allergic reaction.
Sleepiness, tiredness (Sedation [fatigue, somnolence])	Tests have shown no effects on mental alertness, the ability to react or the ability to drive in healthy people after taking levocetirizine in the	Patients intending to drive, engage in potentially hazardous activities or operate machinery should take their individual response to the

Risk in Lay Language (Clinical Term)	What is known	Preventability
	recommended dosage; however, based on clinical experience, fatigue, somnolence, and sleep disorders occurred commonly (≥1/100 to <1/10). Caution should be exercised when driving or operating machinery.	medicinal product into account and take actions to prevent the side-effects if needed.

Table 11: Important Potential risks

Risk in Lay Language (Clinical Term)	What is known
Mental disorders (opposite excitatory effect, depression, suicidal thought) (Psychiatric disorders [paradoxical excitation, depression, suicidal ideation])	The frequency of incidence of suicidal ideation and depression could not be established from available data. Children may initially show excitation and restlessness after taking Levocetirizine.
Fits (Convulsion)	The frequency of incidence of convulsion could not be established from available data.
Liver damage (Liver injury)	The frequency of incidence of abnormal liver function test could not be established from available data.
Inability to urinate (Urinary retention)	Levocetirizine may increase the risk of urinary retention; however, the frequency of incidence of urinary retention could not be established from available data.

Table 12: Missing information

Risk in Lay Language (Clinical Term)	What is known
Safety in children below 6 years of age	The use of levocetirizine is not recommended in children aged less than 6 years as the clinical safety has not been established.
Safety in breastfed infants exposed to maternal medication	For this medicinal product no clinical data on usage during breast-feeding are available.
Safety during pregnancy	For this medicinal product no clinical data on usage during pregnancy are available.

VI.2.5 Summary of risk minimisation measures by safety concern

The SmPC of Levocetirizine 5 mg, film-coated tablets, provides physicians, pharmacists and other HCPs with details on how to use the medicine, the risks and recommendations for minimising them.

This medicinal product has no additional risk minimisation measures for any of mentioned safety concerns.

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

Changes to the Risk Management Plan over time is provided in the table below.

Version	Date of sign-off	Safety Concerns	Comments
1.0	15 Jun 2016	**Important identified risks** 1. Hypersensitivity to levocetirizine or to other piperazine derivatives 2. Use in patients with renal impairment 3. Suicidal ideation 4. Urinary retention in patients with predisposing factors e.g. prostatic hyperplasia 5. Lactose intolerance **Important potential risks** 1. CNS depression and sedation with concomitant use of other CNS depressants, including alcohol 2. Overdose **Missing information** 1. Use during pregnancy and lactation 2. Use in children with renal impairment	First version of the RMP.
1.1	dd Apr 2017	**Important identified risks** • Hypersensitivity reactions • Sedation (fatigue, somnolence) **Important potential risks** • Psychiatric disorders (paradoxical excitation, depression, suicidal ideation) • Convulsion • Liver injury • Urinary retention **Missing information** • Safety in children below 6 years of age • Safety in breastfed infants exposed to maternal medication • Safety during pregnancy	List of safety concerns updated based on the comments in Type II variation Preliminary Variation Assessment Report (PT/H/0250/001/II/014) received from the Agency (PT, DE, IE). All relevant sections of the RMP updated. RMP aligned as per generic application and sections updated per latest Glenmark template. Addition of data in Part II: Module SV – Post-authorisation exposure. Minor formatting, style, and grammatical changes done in the RMP.