RISK MANAGEMENT PLAN (RMP)

PART VI

SUMMARY OF ACTIVITIES IN THE RISK MANAGEMENT PLAN BY MEDICINAL PRODUCT

Active substance(s): Loratadine

Product(s) concerned: Claritine, Clarityn, Claritine Reditabs, Alertrin Anti-Allergie, Loratadine SP, and Lisino S.

MAH / MAA name: Bayer HealthCare.

Data lock point for this module: 10-Aug-2015

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Confidential

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The purpose of the information provided in this document is to make readers aware of the safety issues related to the use of loratadine. This document also gives information on the ways in which these issues can be prevented or minimized, if they occur.

VI.2 Elements for a Public Summary

VI.2.1 Overview of Disease Epidemiology

Epidemiology of a disease provides information on:

- The extent of the disease or condition
  - in different sets of people
  - in different regions of the world
- The causes and effects associated with the disease, and
- Control of the disease.

AllergicRhinitis:

An 'allergy' is a sensitivity of your immune system to something that is ordinarily harmless. When your body tries to get rid of the 'allergen' (foreign substance), you experience symptoms like sneezing, itchy, watery eyes, and a runny, stuffy nose. Rhinitis is an inflammation of the nasal passageways, particularly with discharge.

Typical allergens include pet dander (dead skin cells), pollen, dust mites, and mold. Common symptoms of allergic rhinitis include nasal congestion, sneezing, post-nasal drip, runny nose, watering eyes, nasal itching, headache, sleep disturbance, facial pain/pressure, and ear pain/pressure.

Allergic rhinitis occurs in persons of all races. The occurrence of allergic rhinitis seems to vary among different populations and cultures, which may be due to genetic differences, geographic factors or environmental differences, or other population-based factors. Allergic rhinitis may occur in persons of any age. In 80% of cases, allergic rhinitis develops by age 20 years. Among children in the Netherlands, the incidence rate of allergic rhinitis was lowest among those 0-4 year olds and highest among those 15-17 year olds. Allergic rhinitis appeared to occur slightly more frequently among men than women.

Urticaria: (Hives)

Hives or urticaria (ur-tih-KAR-e-uh) is a skin reaction that causes itchy, swollen, red bumps or welts on the skin that appear suddenly. They may be a result of the body's adverse reaction to certain allergens (foreign substance). Hives can appear anywhere on the body including the face, lips, tongue, or throat.

People who have other allergies are more likely to get hives. Chronic urticaria (hives) is diagnosed when the symptoms last for more than 6 weeks. Hives are extremely itchy and may be severe enough to disrupt work, school, or sleep. In most cases the cause of the chronic hives are unclear.

Studies have shown that chronic urticaria is present in between 0.5 and 1% of the population and tends to occur more frequently among women. The prevalence (proportion of the population) of chronic urticaria in children in the United Kingdom is approximately 0.1-0.3%. All age groups can experience chronic urticaria, but it is more common between the ages of 20 and 40 years.

VI.2.2 Summary of Treatment Benefits

Efficacy is the capacity of a medicine to produce a desired effect.

Loratadine is an antihistamine that reduces the effects of the natural chemical histamine in the body. Histamine can produce symptoms of sneezing, itching, watery eyes, and runny nose. Loratadine blocks the effects of histamine which can, in part, prevent an allergic reaction.

The main studies of loratadine included over 10,000 adults (greater than 12 years of age) with allergic rhinitis. Patients were randomly assigned to loratadine or placebo or clemastine (another antihistamine). In these studies, loratadine was better than placebo and similar to clemastine in improving the symptoms of allergic rhinitis.

Among these adults (greater than 12 years of age) 1,000 adults with chronic hives (urticaria) were randomly assigned to loratadine or placebo. In these studies loratadine was better than placebo in the management of chronic hives as demonstrated by a decrease in itching, redness and hives.

VI.2.3 Unknowns Relating to Treatment Benefits

Loratadine has not been studied in pregnant or breastfeeding woman and children less than two years of age. However, loratadine has been sold for more than 20 years (since 1988) and the safety profile has been well established. Therefore any limitations of the clinical program (studies) have been overcome by the extensive post approval experience.

VI.2.4 Summary of Safety Concerns

Important Identified Risks

Important identified risks are safety issues or undesirable effects for which there is sufficient proof of an association or link with the use of this medicine

Table 1 provides information on the important identified risks and their preventability.

Table 1 Summary of Important Identified Risks

Risk	What is Known	Preventability
Allergic reactions such as rash, swelling of face, shortness of breath, hives and itching. As well as, severe allergic reactions with swelling of the face, lips, tongue, and/or throat (which may cause difficulty in breathing or swallowing)	Allergic reactions can occur with any medicine and are known to occur with loratadine.	Patients should not take loratadine if they are allergic to loratadine or any of the ingredients in loratadine. Patients should stop use of loratadine and ask a doctor if an allergic reaction to loratadine occurs. If a severe allergic reaction occurs seek medical help right away.
Abnormal liver function including inflammation of liver and abnormal liver function tests	Abnormal liver function (including inflammation of the liver and abnormal liver function tests) are known to occur with loratadine.	Patients should ask a doctor before taking loratadine if they have liver disease. Your doctor should determine if you need a different dose.
Seizures (convulsions or fits)	Seizures have been reported in patients taking loratadine. Seizures can have many causes, including medicines, high fevers, head injuries and certain diseases. Most seizures last from 30 seconds to 2 minutes and do not cause lasting harm. Patients who experience seizures should speak to a doctor.	Patients should ask a doctor before taking loratadine if they have epilepsy, history of seizures,or recent head injury. If you have a seizure for the first time, stop the use of loratadine and seek medical help right away.
Abnormal or irregular heartbeat: Heartbeats faster than normal (tachycardia) and/or feeling a rapid heartbeat (palpitations).	A heartbeat that is faster than normal (tachycardia) and palpitations have been reported in patients taking loratadine. Palpitations are often described as a feeling a rapid heartbeat, a pounding in the chest, or feeling missed or skipped beats of the heart. Many factors can affect your heart beat, such as having fever, heart attacks, smoking, stress and some medications. Patients who experience an irregular or a faster than normal heartbeat should speak to a doctor.	Before you take loratadine, tell your doctor or pharmacist if you are a smoker, have high blood pressure, heart disease or have any other medical conditions. If you experience an abnormal or irregular heartrate, seek medical help right away.

Important Potential Risks

Important potential risks are safety concerns for which there is a possible link with the use of a medicine, but this link has not been confirmed.

Table 2 Summary of Important Potential Risks

Risk	What is Known
Restlessness, increased involuntary body movements (psychomotor hyperactivity)	Restlessness, with increased involuntary body movements has been reported in patients taking loratadine. These increased movements may also make the individual feel restless (feeling of unrest or discomposure). Movement disorders can be caused by nerve diseases, injuries, autoimmune diseases, infections and certain medications. Patients who experience movement disorders or restlessness should speak to a doctor.
Mental (psychiatric) disorders: seeing or hearing things that are not really there (hallucinations)	Hallucinations can be caused by high fever, brain disorders, drug and alcohol intoxication and some medications. Patients who experience hallucinations should speak to a doctor or medical professional.
Behavior/mood related changes in children (including anger, agitation and aggressive behavior)	Abnormal behavior can be caused by high fever, brain disorders, and some medications. Patients who experience abnormal behavior should speak to a doctor or medical professional.
Eye disorders including eye swelling, dry eye and visual impairment	Eye symptoms may involve changes in vision, changes in the appearance of the eye, or an abnormal sensation in the eye. A person who has eye symptoms should be checked by a doctor.
Severe skin disorders (including Stevens-Johnson syndrome/Toxic Epidermal Necrolysis)	Stevens-Johnson syndrome and toxic epidermal necrolysis are two forms of the same life-threatening skin disease that cause rash, skin peeling, and sores on the mucous membranes. People with or suspected of having Stevens-Johnson syndrome or toxic epidermal necrolysis are hospitalized immediately. Any drugs suspected of causing the disorder are immediately discontinued.
Drug-drug interactions	Drug-drug interactions occur when two or more drugs react with each other. This drug-drug interaction may cause unexpected side effects. It's always important to share with your doctor and pharmacist all of the medications you're taking. This includes your prescriptions medications, over-the-counter (OTC) drugs, vitamins, nutritional supplements (nutritional shakes, protein powders, etc.), herbal remedies, and any illegal or recreational drugs.

Missing information

Missing information is information about the safety of a medicine which is not available at the time of submission of a particular risk management plan.

Table 3 provides missing information with the medicinal product.

Table 3 Summary of Missing Information

Missing Information	What is Known
Use in breast-feeding	The use of loratadine is not recommended while breast feeding. Loratadine can pass into your breast milk when loratadine is taken by the mother. Tell a doctor if you are breastfeeding before using loratadine.
Use in children less than 2 years of age	The safety and efficacy of loratadine in children under 2 years of age have not been established.

VI.2.5 Summary of Risk Minimization 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 minimizing 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 minimization measures.

This medicine has no additional risk minimization measures.

VI.2.6 Planned Post-authorization Development Plan

VI.2.6.1 List of Studies in Post-authorization Development Plan

There are no studies in the post-authorization development plan for this medicine.

VI.2.6.2 Studies which are a Condition of the Marketing Authorization

There are no studies in the post authorization development plan for this medicine.

VI.2.7 Summary of Changes to the Risk Management Plan over Time

None