VI.2 Elements for a Public Summary

VI.2.1 Overview of disease epidemiology

This medicinal product contains hydroxyzine as active ingredient. It is used for the symptomatic treatment of anxiety, nettle rash/hives (urticaria) and itching (pruritus).

Anxiety

Experiencing occasional anxiety is a normal part of life. However, people with anxiety disorders frequently have intense, excessive and persistent worry and fear about everyday situations. As with many mental health conditions, the exact cause of anxiety disorders isn't fully understood. Life experiences such as traumatic events appear to trigger anxiety disorders in people who are already prone to becoming anxious. Inherited traits also can be a factor. For some people, anxiety is linked to an underlying health issue. In some cases, anxiety signs and symptoms are the first indicators of a medical illness.

Examples of anxiety disorders include social anxiety disorder (social phobia), specific phobias and separation anxiety disorder.

In general, anxiety disorders develop relatively early in life. In 80–90% of cases, the disorder manifests before the age of 35, and the time between 10 and 25 years seems to be a high-risk period for the development of anxiety disorders.

Urticaria

Urticaria 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 as well. 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.

Itching

Itching is skin tingling or irritation that makes person want to scratch the itchy area. It's a symptom of many health conditions. Common causes are allergic reactions, eczema, dry skin, insect bites and stings, irritating chemicals, parasites such as pinworms, scabies, head and body lice, pregnancy, rashes and reactions to medicines.

Most itching is not serious. However, itching all over, hives that keep coming back or itching without an apparent cause, requires medical attention. Unexplained itching may be a symptom of a disease that could be serious.

VI.2.2 Summary of treatment benefits

Efficacy of hydroxyzine has been established in the many years of clinical use and is supported by the clinical data. Hydroxyzine is so called sedative antihistamine. It helps to relieve symptoms of urticaria and itching, but sedative and tranquilizing effect are also useful in symptomatic treatment of anxiety. Medical treatment of anxiety should always be only a supportive measure.

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**
Changes in electrical activity of the heart and disturbances in heart rhythm (Cardiac dysrhythmias/QT prolongation)	There is a small risk of altered electrical activity of the heart when taking hydroxyzine, which can lead to abnormal heart rhythm or even cause the heart to stop (cardiac arrest). The risk is mostly seen in patients who already have heart rhythm problems or have risk factors for these problems.	Hydroxyzine must not be taken by patients who already have disturbances of heart rhythm or are taking other medicines that can cause similar effects on the heart. It should be used with care if taking certain other medicines that slow the heart rate or decrease the level of potassium in the blood. Maximum daily doses must not be exceeded. Treatment with hydroxyzine should be stopped if signs or symptoms occur that may be associated with heart rhythm disturbances and the patients should seek immediate medical attention. Doctor should be promptly informed of any cardiac symptoms.
Use in patients with moderate or severe kidney impairment	Levels of drugs may increase too high as elimination rate of the drug is reduced.	Dose may need to be reduced in patients with poorly functioning kidneys.
Use in patients with liver (hepatic) impairment	Levels of drugs may increase too high as elimination rate of the drug is reduced.	Dose may need to be reduced in patients with poorly functioning liver.
Use in elderly	Hydroxyzine is not recommended in elderly patients. Elderly patients have greater risk of adverse reactions (e.g. anticholinergic effects, paradoxical central nervous system stimulation) and too high drug levels in blood.	In the elderly, it is advised to start with half the recommended dose due to the prolonged action. The lowest possible dose should be selected in the treatment of elderly patients. The maximum daily dose in elderly is 50 mg/day. The results and need for treatment should be continuously assessed.

Risk	What is known	Preventability
Use in patients with electrolyte imbalances (e.g. low levels of potassium or of magnesium in blood)	Electrolyte imbalance increases risk for changes in electrical activity of the heart and disturbances in heart rhythm.	Hydroxyzine must not be used in patients with significant electrolytes imbalance (low levels of potassium or of magnesium in blood). Simultaneous use of active substances that may cause electrolyte disturbances, such as certain type of diuretics (help rid body of salt (sodium) and water. should be avoided as they increase the risk of malignant arrhythmias.
Porphyria	Porphyrias are a group of metabolic disorders usually hereditary in nature. A number of drugs may cause a precipitous and dangerous rise in the level of porphyrins in blood. Hydroxyzine has been associated with acute attacks of porphyria. The symptoms of an acute attack are highly variable but the major characteristic of acute porphyria is neurologic.	Hydroxyzine must not be used in patients with porphyria.
Anticholinergic effects (e.g. dry mouth, problems with vision, fast or pounding heartbeat, difficulty passing water and constipation)	Hydroxyzine may cause anticholinergic effects especially in high doses. Elderly patients are more sensitive to anticholinergic effects than young adults as well as patients with certain medical conditions. Concomitant use of certain other drugs used e.g. for irritable bowel syndrome, asthma or incontinence may potentiate anticholinergic effects.	Caution is required in the treatment of elderly patients, patients with eye problems, difficulties to pass urine, reduced bowel movements, neurologic condition that causes muscle weakness (myasthenia gravis) or dementia. As high doses might result in dry mouth, good oral and dental hygiene are important. In order to avoid harmful interactions doctor and pharmacist should be informed of all concomitant medications.
Seizures (convulsions)	Convulsions have been reported in association with hydroxyzine therapy. Convulsions are more	Caution is required in the treatment of patients who are prone to seizures including

Risk	What is known	Preventability
	frequently reported in children than in adults.	patients with epilepsy.
Interaction with alcohol	Sedative effects of alcohol may be increased in concomitant use with hydroxyzine.	Alcohol should be avoided during hydroxyzine therapy.
Administration during pregnancy or breastfeeding	There are no or limited amount of data from the use of hydroxyzine in pregnant women. Hydroxyzine crosses the placental barrier. Adverse effects have been reported in new-born babies whose mothers have received hydroxyzine during pregnancy and/or birth. Animal studies have shown reproductive toxicity. Serious adverse effects have been observed in nursed new-born babies/infants whose mothers were treated with hydroxyzine.	Pregnant women must not use this medicine. Breastfeeding must be stopped if therapy with hydroxyzine is needed.
Effects on allergy tests	As hydroxyzine is so called antihistamine it relieves symptoms of allergic reactions and therefore may cause wrong results in allergy tests including certain asthma tests.	The treatment should be stopped at least 5 days before allergy testing or certain asthma tests.

Important potential risks

Risk	What is known (Including reason why it is considered a potential risk)
Effects on ability to drive and use machines	Hydroxyzine has moderate to major influence on the ability to drive and use machines. Patient's ability to perform activities requiring mental alertness or physical coordination such as operating machinery or driving a vehicle may be impaired during hydroxyzine therapy.
Problems caused by blood circulation problems in brains in patients with risk of stroke (Cerebrovascular events in patients with risk of stroke)	An approximately 3 times increased risk of events associated with blood circulation problems in brains have been observed in randomised, placebo-controlled clinical trials of some atypical antipsychotics in patients with dementia. The underlying mechanism for this is unknown. An increased risk with other

Risk	What is known (Including reason why it is considered a potential risk)
	antipsychotics, other patient population or hydroxyzine cannot be excluded. Hydroxyzine should be administered with caution in patients with a risk of stroke.

Missing information

Risk	What is known
Use in children under 5 years of age	Hydroxyzine Orion should not be used in children under 5 years of age.

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. The Summary of Product Characteristics and the Package leaflet for this medicinal product can be found in the national authority's web page.

This medicine has no additional risk minimisation measures.

VI.2.6 Planned post authorisation development plan (if applicable)

Not applicable.

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

Not applicable.