VI.2 Elements for a Public Summary

VI.2.1 Overview of disease epidemiology

Menopause is the time in most women's lives when menstrual periods stop permanently and the woman is no longer able to have children. Menopause typically occurs between 45 and 55 years of age, often defined as having occurred when a woman has not had any vaginal bleeding for a year. Menopause is coupled with a significant decrease in oestrogen levels and is usually a natural change. Before menopause, a woman's periods typically become irregular. During this time, women often experience hot flashes; these typically last from 30 seconds to ten minutes, and associated with shivering, sweating and reddening of the skin. Hot flashes often stop occurring after a year or two. Other symptoms may include vaginal dryness, trouble sleeping, cardiac complaints, vertigo and mood changes. Muscle pain, urinary tract disorders are also typical symptoms reported by menopausal women. The severity of symptoms varies between women.

VI.2.2 Summary of treatment benefits

The efficacy of Cimicifuga racemosa extract preparations on climacteric symptoms has now been demonstrated in several open and controlled studies that complied with state-of-the-art, evidence-based medicine and used validated rating scales for menopausal symptoms. Studies performed by Bionorica confirm that Cimicifuga racemosa can treat effectively menopausal complaints.

Klimadynon which contains Cimicifuga racemosa extract has been investigated in clinical trials up to 12 months and has been shown to be effective with no adverse effects or signs of intolerance.

The clinical safety of Klimadynon can be regarded as good. Considering the high number of Defined Daily Dosages (DDD) of Klimadynon, Klimadynon Uno FCT and Klimadynon oral drops marketed in the last years, the frequency of reported adverse drug reactions is very low. Thus, Klimadynon has a well-balanced risk-benefit ratio.

Overall, the good toxicological and safety profile of the Klimadynon, the proven efficacy of Cimicifuga in the indication targeted, coupled also with potential beneficial effects on bone turnover, establish a favourable benefit-risk ratio for the use of Klimadynon for the relief of menopausal complaints (such as hot flushes and profuse sweating) caused by menopause.

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
Skin reactions (urticaria, itching, exanthema); Facial oedema, peripheral oedema	Frequency: unknown In general, symptoms are expected to be of mild to moderate intensity. More pronounced symptoms may require extended medical treatment.	Patients who are hypersensitive (allergic) to the active substance or to any of the other ingredients must not take this medicinal product. At the first signs of a hypersensitivity/ allergic reaction this medicinal product must not be taken again.
<u>Gastrointestinal disorders:</u> e.g. dyspeptic disorders, diarrhoea	Frequency: not known. Gastrointestinal disorders are mostly of mild to moderate intensity and abate without further medical treatment in most cases.	This medicinal product contains lactose. Patients with rare hereditary problems of galactose intolerance, lactase deficiency or glucose-galactose malabsorption should not take this medicinal product.

Important potential risks

Risk	What is known (Including reason why it is considered a potential risk)
Liver toxicity (including hepatitis, jaundice, disturbances in the liver function tests)	Liver toxicity (including hepatitis, jaundice, disturbances in the liver function tests) is associated with the use of Cimicifuga containing products. The frequency is not known. Up to now, an association has not been adequately confirmed for this medicinal product. Patients with a history of liver disorder should take Klimadynon only after consultation with a physician. Patients should stop taking Klimadynon and consult their doctor immediately if they develop signs and symptoms suggestive of liver injury (tiredness, loss of appetite, yellowing of skin and eyes or severe upper stomach pain with nausea and vomiting or dark urine).
Possible hormonal or hormone-like activity of Cimicifuga racemosa on oestrogen receptors.	There is conflicting non-clinical data on potential hormonal or hormone-like activity of Cimicifuga racemosa on oestrogen receptors. Evidence from in-vitro and in-vivo pharmacological studies suggests that Cimicifuga extracts do not influence the latency or development of breast cancer. However, contradictory results have been obtained in other in-vitro experiments. Therefore, influence on breast cancer or other hormone-depending tumours cannot be completely excluded. Cimicifuga preparations should not be used together with oestrogens unless advised by a doctor. Patients who have been treated or who are undergoing treatment for breast cancer or other hormone-dependent tumours should not use Cimicifuga preparations without medical advice.

Missing information

None.

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 (PIL). 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.

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

Not applicable.