VI.2 Elements for a Public Summary

VI.2.1 Overview of disease epidemiology

Menopause is an event that typically occurs in women in midlife, during their late 40s or early 50s, and it signals the end of the fertile phase of a woman's life. This transition from a potentially reproductive to a non-reproductive state is the result of changes in female hormonal production by the ovaries. The menopause transition, and postmenopause itself, is at first a natural life change, not a disease state or a disorder. For some women, the accompanying signs and symptoms that can occur during the menopause transition years can significantly disrupt their daily activities and sense of well-being. Symptoms affect many women during the menopause transition. The duration of these symptoms varies, with a median of about 4 years, but may continue for as many as 12 years in a subgroup of women. Menopause is based on the natural or surgical cessation of estradiol and progesterone production by the ovaries, which are a part of the body's endocrine system of hormone production, in this case the hormones which make reproduction possible and influence sexual behavior. The official date of menopause is determined retroactively, once 12 months have passed

after the last appearance of menstrual blood. After menopause, estrogen continues to be produced at low levels in some tissues. However the dramatic fall in circulating estradiol levels at menopause impacts many tissues, from brain to bone.

Effects that are due to low estrogen levels (for example vaginal atrophy and skin drying) may continue into late age. Other symptoms, for example hot flashes and mood changes, have their highest prevalence around the time of the final menstrual period and diminish slowly thereafter.

One important consequence of the estrogen deficiency after menopause is a decrease in bone tissue, measured as a loss of bone mineral density.

VI.2.2 Summary of treatment benefits

Estrogen replacement therapy effectively reverses the changes related to postmenopausal estrogen depletion. In case of menopausal hormone depletion only manifests in signs and symptoms of vaginal atrophy, treatment can be efficiently accomplished by intravaginal application of preparations containing estradiol or estriol, which both have been proven to be effective and safe.

VI.2.3 Unknowns relating to treatment benefits

No limitations of the efficacy are expected in the target population.

VI.2.4 Summary of safety concerns

Important identified risks

There has not been identified any important risk.

Important potential risks

Risk	What is known (Including reason why it is considered a potential risk)
Endometrial hyperplasia	This risk is dependent on the duration of treatment with estrogens and also the dose administered. This risk has not been attributed to treatment with estriol by vaginal use. However, if continued treatment is required, periodical revisions are recommended.
Breast, uterine and ovarian cancer	Treatment with estrogens may increase the risk of breast cancer when the hormone in absorbed and goes into blood torrent. As Estriol 0.03 mg pessaries are administered directly in the vagina and have been studied that the amount that is absorbed shown to be almost negligible after repeated administration, such risk is highly unlikely to be produced.
Venous thromboembolic disorder, stroke and coronary artery disease	Treatment with estrogens may increase the risk of presenting with thrombosis, pulmonary embolism, stroke, myocardial infarction etc. when the hormone in absorbed and goes into blood torrent. As Estriol 0.03 mg pessaries are administered directly in the vagina and have been studied that the amount that is absorbed shown to be almost negligible after repeated administration, such risk is highly unlikely to be produced.
Fluid retention	Treatment with estrogens may increase the risk of fluid retention when the hormone in absorbed and goes into blood torrent. As Estriol 0.03 mg pessaries are administered directly in the vagina and have been studied that the amount that is absorbed shown to be almost negligible after repeated administration, such risk is highly unlikely to be produced.

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 information leaflet (PIL). The measures in these documents are known as routine risk minimisation measures.

The Summary of Product Characteristics and the package leaflet for Estriol 0,03 mg pessaries can be found on the webpage of the National Competent Authorities.

For this medicinal product there are no additional risk minimisation measures required.

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.