LÄKEMEDELSVERKET
SWEDISH MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

Utrogestan
(progesterone)

SE/H/2023/02/DC

This module reflects the scientific discussion for the approval of Utrogestan. The procedure was finalised on 2023-09-20. For information on changes after this date please refer to the module 'Update'.

Postadress/Postal address: P.O. Box 26, SE-751 03 Uppsala, SWEDEN
Besöksadress/Visiting address: Dag Hammarskjölds väg 42, Uppsala
Telefon/Phone: +46 (0)18 17 46 00 Fax: +46 (0)18 54 85 66
Internet: www.lakemedelsverket.se E-mail: registrator@lakemedelsverket.se

I. INTRODUCTION

Based on the review of the quality, safety and efficacy data, a marketing authorisation has been granted for Utrogestan, 400 mg, Vaginal capsule, soft.

The active substance is progesterone. A comprehensive description of the indication and posology is given in the SmPC.

For recommendations to the marketing authorisation not falling under Article 21a/22a/22 of Directive 2001/83/EC and conditions to the marketing authorisation pursuant to Article 21a/22a/ 22 of Directive 2001/83/EC to the marketing authorisation, please see section VI.

The application is an extension, new strength, of the previously authorised product Utrogestan, 200 mg, vaginal capsule, soft, marketed by Besins Healthcare Ireland Limited since 2019.

The application for Utrogestan, 400 mg, vaginal capsule, soft, is an application submitted according to Article 8(3) of Directive 2001/83/EC. The applicant applies through the Decentralised Procedure with Sweden acting as reference member state (RMS) and CY, FI, MT, and NO as concerned member states (CMS).

Potential similarity with orphan medicinal products
According to the application form and a check of the Community Register of orphan medicinal products there is no medicinal product designated as an orphan medicinal product for a condition relating to the indication proposed in this application.

II. QUALITY ASPECTS

II.1 Drug Substance

The structure of the drug substance has been adequately proven and its physico-chemical properties are sufficiently described.

The manufacture of the drug substance has been adequately described and satisfactory specifications have been provided for starting materials, reagents and solvents.

The drug substance specification includes relevant tests and the limits for impurities and degradation products have been justified. The analytical methods applied are suitably described and validated.

Stability studies confirm the retest period.

II.2 Medicinal Product

The medicinal product is formulated using excipients listed in section 6.1 in the Summary of Product Characteristics.

The manufacturing process has been sufficiently described and critical steps identified.

The tests and limits in the specification are considered appropriate to control the quality of the finished product in relation to its intended purpose.

Stability studies have been performed and data presented support the shelf life and special precautions for storage claimed in the Summary of Product Characteristics, sections 6.3 and 6.4.

III. NON-CLINICAL ASPECTS

Pharmacology
The pharmacology of progesterone is considered well-established. Progesterone is a natural endogenous hormone and is the most important hormone of the corpus luteum and the placenta. The product proposed for marketing has the same properties as endogenous progesterone with induction of a full secretory endometrium and gestagenic, antiestrogenic, slightly anti-androgenic and antialdosterone effects.

Pharmacokinetics
No non-clinical pharmacokinetics studies have been submitted. Considering the extensive clinical experience of progesterone, no studies are considered needed. The literature data provided by the Applicant is considered of limited relevance for the present Application.

Toxicology
No non-clinical studies have been submitted by the Applicant. The Applicant has made a summary of published literature regarding the toxicology of progesterone and this is considered sufficient for the present Application. The toxicology profile of progesterone is considered well established.

However, the references used in the toxicology section were not considered appropriate. Reference must be made to published scientific literature which means that the text should be freely available in the public domain and published by a reputable source, preferably peer reviewed. Thus, EPAR for EU marketing authorisations or similar summary reports from competent authorities inside and outside the EU which are made publicly available by competent authorities for reasons of transparency cannot be considered to meet the requirements. Therefore, the Applicant was asked to update the overview with appropriate references. In the response, appropriate references were included and the issue was thus considered resolved.

Environmental Risk Assessment (ERA)
The ERA submitted by the Applicant was not considered sufficient. The F-pen refinement provided was not considered acceptable. Therefore, as a first step, the Applicant was asked to provide with clear Phase I data for the 400mg line extension, which should include an experimentally determined octanol/water partitioning coefficient, Kow. If Fpen was refined, the correct data should be used for the refinement and should also take into account the exposure from previously approved strengths of Utrogestan.

In the D106 response, the Applicant provided with an updated ERA document. No experimentally determined octanol/water partitioning coefficient (Kow) has been provided. The Hensch 1995 reference (which has not been made available in full text) is a QSAR document and not considered sufficient. The Applicant provided a refined Fpen of 0.0000034. Using the (currently) derived Fpen in the PECsw calculation gives a PECsw of 0.0000136mg/l and the Applicant has converted this to 0.00136 µg/L. This is not correct, the conversion should be 0.0000136 mg/l = 0.0136 µg/L which is above the limit of 0.01 where a Phase II program should be performed.

Therefore, the Applicant was asked to provide with an experimenatally derived octanol/water partitioning coefficient (Kow), a correctly refined Fpen and an updated PECsw calculation. If the correctly derived PECsw is equal to or above 0.01 µg/L, a Phase II data package should be submitted which is in accordance with the relevant guidelines. If literature data was used, this data should be based on studies of sufficient quality and the information should be up to date. The Applicant was asked to make sure that all endpoints required in the guideline are covered.

In the D160 reponse, the Applicant has provided with a new reference for the octanol/water partitioning coefficient (Kow) which is based on a publication from Sharma et al. 2017. The paper briefly (and barely sufficiently) describes the methodology used, but since the reported value of 3.56

seems reasonable and near the value identified in other sources this issue is not further pursued at this time.

In the D106 and D160 responses, the Applicant refers to “sales forecast data for EU” which takes into account prevalence data. In the ERA, reference is made to attachment 2, but no such attachment is available. While the Applicant should clarify the reference to this data, it is not likely that this data will be considered sufficient. It is clearly stated in the ERA guideline that the Fpen can be refined by submitting European disease prevalence data for the sought indication(s) published by a reliable and independent source. No such prevalence data have been submitted.

The Applicant has also submitted “relevant environmental data” and based on the data calculated PEC/PNEC ratios for surface- and ground water. No fish data has been included with reference to a statement in Campbell 1998 regarding the role of the gestagen in normal fish development. This reference is in turn a reference from a book chapter (Scott AP. 1987. Reproductive endocrinology of fish. In Chester-Jones I, Ingleton PM, Phillips JG, eds, Fundamentals of Comparative Vertebrate Endocrinology. Plenum, New York, NY, USA). Since 1987 it has been made clear that progestins (including progesterone) are important endocrine disruptors in fish and amphibians at ng/ml levels (e.g. https://doi.org/10.1016/j.chemosphere.2017.04.021, DOI: 10.1002/etc.1754). Thus, the general statement from Campbell 1998 (i.e., Scott 1987) is not considered acceptable to justify the lack of fish studies.

In summary, the ERA provided by the Applicant is not considered sufficient. No appropriate prevalence data has been submitted to enable an Fpen refinement. Also, considering that progesterone is an endocrine active substance, a Phase II program should be made available irrespective of the quantity released into the environment. This is in accordance with the ERA Q&A document (EMA/CHMP/SWP/44609/2010 Rev. 1) as progesterone is considered a sexual endocrine disrupting compound. The literature data submitted is incomplete as no fish studies have been made available. Therefore, the Applicant should submit a complete Phase II data package which is in accordance with the relevant guidelines. If literature data is used, this data should be based on studies which are up to date and of sufficient quality. To assess the reliability and relevance of a study it is preferred if a standardized assessment method designed for toxicological/ecotoxicological studies is used, such as the Klimisch (Klimisch et al, 1997) or CRED method (Moermond et al, 2016). The Applicant was asked to make sure that all endpoints required in the guideline are covered.

In the D195 reponse, the Applicant provided a commitment letter ensuring that the requested Phase II data will be submitted. The Applicant committed to, within 3 months, provide an updated ERA, plus literature search or Phase II program, including a timetable stating when the data will be completed, and to submit a variation application when the data are completed. This was not considered as fully acceptable and the Applicant was asked to, within this procedure, provide with a timetable for submission of literature data and a timetable for submission of study data. When the data (literature or study data) is available, the Applicant should submit the data and an updated ERA as a variation application.

In the D205 reponse, an acceptable commitment letter was provided, see section VIII.2.

IV. CLINICAL ASPECTS

Pharmacokinetics

Pharmacokinetic properties of progesterone have been reviewed and data is based on literature search, no new clinical studies have been carried out. It appears that non-linear pharmacokinetics seems to occur in dose ranges between 300 mg to 600 mg progesterone given vaginally. This suggests that the absorption mechanism is saturated in the higher recommended clinical doses.

The pharmacokinetic properties of vaginally administered progesterone are well-characterised. Data

on the absorption, distribution and elimination of progesterone administered either by oral route or vaginally have been presented. Available studies show that within the recommended daily vaginal doses, plasma progesterone concentrations are relatively low and close to normal physiological levels during the luteal phase of menstrual cycle. Progesterone levels in uterus may exceed those in plasma after vaginal administration. The systemic levels of progesterone following vaginal administration at different dose levels is not considered predictive of efficacy. When given vaginally, the first-pass metabolism is avoided, and the metabolite profile is somewhat different than after oral administration. Kidneys are the main elimination route.

Pharmacodynamics
Utrogestan 400 mg vaginal capsule contains micronised progesterone which is equivalent to natural progesterone. Progesterone is a natural endogenous hormone and is the most important hormone of the corpus luteum and the placenta. It acts on the endometrium by converting the proliferating phase to the secretory phase. The product proposed for marketing has the same properties as endogenous progesterone with induction of a full secretory endometrium and gestagenic, antiestrogenic, slightly anti-androgenic and antialdosterone effects.

There are already on the market vaginal capsules containing progesterone marketed under the brand name Utrogestan®. In Sweden 200 and 300 mg vaginal capsules are approved, while other countries have a 100 mg vaginal capsule approved.

Clinical efficacy

Design and conduct of clinical studies
This application concerns a new strength, 400 mg, and a new indication for Utrogestan capsule. The initially proposed indication applied is: *Utrogestan is indicated in adults for the prevention of recurrent or threatened miscarriage in women with bleeding in the current pregnancy and a history of at least one or more previous miscarriages.* The recommended dose is 400 mg twice a day (morning and night). Treatment should be initiated during the first trimester of pregnancy, at first sign of vaginal bleeding (see Sections 4.2 and 4.4) and should continue to at least the 16th week of gestation.

Approximately 20% of pregnancies miscarry in the first trimester. Many women will experience some bleeding and/or pain in early pregnancy that does not cause miscarriage (Quenby 2021). Vaginal micronised progesterone is used empirically in women with recurrent miscarriage of <10 gestational weeks (NICE 2021, NICE 2019, Stephenson 2017). Progesterone supplementation has been used for several decades to prevent miscarriage although the exact mechanism by which progesterone may prevent pregnancy loss is not fully understood (Devall 2020).

The pharmacodynamic effects for threatened and recurrent miscarriage are that progesterone modulates maternal immune responses to protect the foetus, improves the utero-placental circulation, maintains cervical integrity throughout pregnancy, promotes myometrial relaxation, inhibits prostaglandin production, and possesses anti-inflammatory properties (Piette 2020, Romero 2018, Conde-Aguledo 2016).

Progesterone formulations have been widely used for the treatment of numerous gynecologic and obstetric indications, including the proposed indication of threatened miscarriage (BNF 2022), for more than 30 years.

The Applicant has in support of the present application submitted numerous published studies and meta-analyses adequately summarized in an extensive Clinical Overview. The research field is extensive as indicated by the long reference list and not all studies are in support of progesterone treatment in prevention of early miscarriage.

The most important studies/publications will be assessed in this Assessment Report together with the most up-to-date guidelines on progesterone in prevention of recurrent or threatened miscarriage. The

most important studies in support of the application are the PRISM study (Coomarasamy 2019) and the PROMISE study (Coomarasamy 2015).

The PRISM study
The PRISM study is a large clinical trial involving 4153 women, recruited at 48 hospitals in the United Kingdom. The women were recruited based on vaginal bleeding which occurred before 42 days versus after 42 days of estimated length of gestation. The clinical trial was designed to evaluate whether progesterone administration in women with vaginal bleeding in early pregnancy (with treatment up to 16 completed weeks of gestation) can prevent miscarriage and increase live births at ≥ 34 completed weeks of pregnancy by 5% compared to placebo. Women included in the study were randomized to administer either progesterone 400 mg vaginal capsule twice daily, in the morning and in the evening at bedtime, or matching placebo vaginal capsule.

The primary efficacy endpoint was live births at ≥ 34 completed weeks of pregnancy. A sensitivity analysis of the primary outcome that included all the participants was performed with the use of multiple imputation to account for missing data. Secondary efficacy endpoints included time from conception to the end of pregnancy, ongoing pregnancy at 12 weeks of gestation, miscarriage (pregnancy loss <24 weeks of gestation) and live birth <34 weeks of gestation.

The PROMISE study
The PROMISE study was conducted in 836 women with a history of unexplained recurrent miscarriage (≥3 consecutive or non-consecutive losses of 1st trimester pregnancy losses). A total of 1568 women were assessed for eligibility, and 836 of these women who conceived naturally within 1 year and remained willing to participate in the trial were randomized to administer either progesterone 400 mg vaginal capsule (404 women) twice daily in the morning and in the evening at bedtime, or matching placebo (432 women). The clinical trial was designed to evaluate whether progesterone supplementation in the first trimester of pregnancy increased live birth rate in women with a history of unexplained miscarriage.

The primary outcome was live birth rate after 24 completed weeks' gestation. The outcome was deemed significant if a 10% difference in live birth rate was achieved. Secondary outcomes included clinical pregnancy at 6-8 weeks, ongoing pregnancy with fetal heart activity at 12 weeks, and incidence of miscarriage.

Results - Efficacy data and additional analyses

The PRISM study

Demographic characteristics of included subjects showed a mean age of approximately 30 years of age in both progesterone and vehicle groups, the majority (77%) were below 35 years of age. Pregnancy history demonstrated that 55% (progesterone group) and 56% (placebo group) had no previous miscarriages at <24 weeks gestation. In the progesterone treatment group, 38% had 1-2 miscarriages, the corresponding figure was 39% in the placebo group, while 7% and 8% had three or more miscarriages in the progesterone and vehicle groups, respectively.

Most participants had completed ≥42 gestational days when recruited and had a singleton gestation (~97%).

The primary outcome demonstrated that the incidence of live birth was 75% in the progesterone group and 72% in the placebo group, with borderline significance (RR 1.03, 95% CI 1.00 to 1.07). The objective with the clinical trial was to evaluate whether progesterone used by women with vaginal bleeding in early pregnancy could prevent miscarriage and increase live births at ≥ 34 completed weeks of pregnancy by 5% compared to placebo. This goal was not reached. However, the 3% higher live birth in the progesterone treated women resulted in an additional 45 babies born compared with the placebo group, which is considered of clinical relevance.

The secondary endpoint ongoing pregnancy at week 12 was statistically significant in favour of progesterone treatment, 83% versus 80% in the placebo group. With a larger number of ongoing pregnancies at week 12, the odds ratio for an increased number of live births is positive. No other secondary endpoints investigated reached statistical significance.

To conclude, the PRISM study demonstrated that progesterone supplementation during the 1st trimester of pregnancy resulted in 45 additional live births compared with the placebo group. Investigation of pre-specified subgroup according to the number of miscarriages indicated an increased efficacy of progesterone in women with a history of miscarriage. The effect of progesterone differed according to the number of previous miscarriages, with largest efficacy noted in women with three or more miscarriages. However, a clinically relevant efficacy on prevention of miscarriages was already noted in women with one or more previous miscarriages.

The PROMISE study

Demographic characteristics of included subjects demonstrated a mean age of 32 years of age in both study groups, with a range of 28 to 36 years. Most included subjects were white with average BMI and were non-smokers. Gestation history demonstrated that included subjects had several previous miscarriages, 3-5 in the progesterone treatment group and 3-4 miscarriages in the placebo group. The median previous pregnancy loss in both groups was 3.

The follow-up rate for the primary outcome was 98.8%. In an intention to treat analysis, the live birth rate was 65.8% in the progesterone group and 63.3% in the placebo group (RR 1.04, 95% CI 0.94 to 1.15; rate difference, 2.5 percentage points; 95% CI, −4.0 to 9.0) which was not significant. Clinical pregnancy, ongoing pregnancy, miscarriage, and other secondary outcomes were statistically similar between the two groups.

To conclude, no significant effect of progesterone supplementation during the 1st trimester of pregnancy on the primary outcome live birth rate after 24 completed weeks' gestation was demonstrated in the PROMISE study.

Subgroup analysis

A sub-group analysis was performed in the PRISM study. All tests for subgroup by treatment group interaction were non-significant apart from the number of previous miscarriages. A significantly higher number of live births in the progesterone group than in the placebo group was demonstrated for those who had ≥3 miscarriages. The incidence among women who had ≥3 previous miscarriages was 72% and 57%, respectively (RR 1.28, 95% CI 1.08 to 1.51) (P = 0.007 for the interaction between trial group and the number of miscarriages).

A post-hoc subgroup analysis on the number of previous miscarriages, showed that progesterone was effective in preventing miscarriages in those with a history of ≥1 miscarriage (75% in the progesterone group v 70% in the placebo group, RR 1.09, 95% CI 1.03 to 1.15, P=0.01).

In the PROMISE study, no evidence of effect modification was identified in pre-specified subgroups, which were defined according to maternal age, number of previous miscarriages and presence or absence of polycystic ovaries. In the post-hoc subgroups, defined according to gestation at initiation of treatment, BMI and country, there was no evidence of effect modification.

Analysis performed across trials

Analysis of the PROMISE and PRISM live birth outcome (live birth >34 gestational weeks and live birth >24 gestational weeks, respectively) showed borderline significance. A subgroup analysis showed that the benefit of progesterone treatment was largest in the subgroup of women with ≥3 previous miscarriages.

Supportive evidence of efficacy

The UK National Institute for Care Excellence (NICE) provides guidelines on the management of miscarriage (NICE 2021). The NICE guideline is a detailed review of all existing published evidence on the use of progesterone for miscarriage. The essence of this guideline is that there is good evidence that 400 mg twice daily of micronised vaginal progesterone increases the number of live births in women with early pregnancy bleeding and a previous miscarriage. There was evidence of no benefit in women with early pregnancy bleeding but no previous miscarriage, nor in women with previous miscarriage but no early pregnancy bleeding in the current pregnancy.

Regarding safety, there was no evidence of harm to the mother or baby from the use of progesterone. Treatment should start as soon as possible in the proposed target population, women with early pregnancy bleeding and a previous miscarriage.

Furthermore, the Applicant has provided a synthesis of external evidence. Many clinical studies have been published, most of them are small with limited methodological quality as also pointed out by the Applicant. However, the outcomes of live birth rate and ongoing pregnancy rate were broadly consistent across the eight studies evaluating threatened miscarriage and the eight studies investigating recurrent miscarriage. The women who will benefit from progesterone therapy are those with the combined risk factors of early pregnancy bleeding and a history of miscarriage.

Conclusions on clinical efficacy
Several of the submitted placebo-controlled studies and systematic reviews have shown a clinically important effect of vaginal progesterone in the prevention of recurrent miscarriage in women with bleeding in the current pregnancy. The PRISM study showed that progesterone supplementation during the 1st trimester of pregnancy resulted in 45 additional live births compared with the placebo group. Investigation of pre-specified subgroup according to the number of miscarriages indicated largest efficacy of progesterone in women with three or more previous miscarriages.

There is an apparent lack of dose finding studies, but the proposed dose of 400 mg progesterone two times daily appears to be used in a large proportion of clinical studies and is also the dose usually recommended in clinical guidelines.

Clinical safety
In Sweden Utrogestan® 300 mg vaginal capsule is indicated in adult women for supplementation of the luteal phase during ART cycles. Furthermore, Utrogestan® 200 mg vaginal capsule is indicated for Supplementation of the luteal phase during ART cycles and for Prevention of preterm birth in women with a singleton pregnancy who have a short cervix (mid-trimester sonographic cervix ≤25 mm) and/or a history of spontaneous preterm birth.

The safety data provided by the Applicant in support of the application for Utrogestan 400 mg vaginal capsule originate from published metanalyses, systematic reviews, investigator-sponsored studies, company periodic safety update reports, and adverse events reported to the UK Regulatory Agency MHRA.

The worldwide cumulative exposure to progesterone in Utrogestan® of different strengths is overall considered extensive. In Sweden Utrogestan® 300 mg vaginal capsule is approved with posology 600 mg per day during ART up to week 12 of pregnancy. Similar posology is labeled for Utrogestan® 200 mg vaginal capsule when used during ART up to week 12 of pregnancy. The indication to prevent pre-term birth for Utrogestan® 200 mg vaginal capsule implies dosage of 200 mg progesterone once daily at bedtime.

The Applicant refers to the latest PSUR from 01-Jan-2021 to 31-Dec-2021 concerning adverse events of the product. No signals were identified which required further action, and the conclusion was that the safety profile of progesterone has not changed. In the SmPCs for Utrogestan® 200 mg and 300 mg, at frequencies that are reported as not known, are vaginal haemorrhage, vaginal discharge, and pruritus.

The safety of Utrogestan is considered benign and well established.

The Applicant has made a summary of published literature regarding safety of progesterone exposure during pregnancy, toxicity profile in relation to risk for hypospadias and congenital malformations, and last, health and developmental outcomes in children. No adverse effects in relation to progesterone have been noted.

The five most prevalent adverse reactions caused by progesterone are rash, dizziness, fatigue, headaches, and pruritus, evaluated by the UK regulatory agency (MHRA) (MHRA iDAP 2022).
The proposed SmPC for Utrogestan 400 mg vaginal capsule is more or less identical to Utrogestan® 200 mg or Utrogestan® 300 mg vaginal capsule with some exceptions due to different therapeutic indications. For comments on the SmPC see the appended SmPC document with RMS comments.

Risk Management Plan
The MAH has submitted a risk management plan, in accordance with the requirements of Directive 2001/83/EC as amended, describing the pharmacovigilance activities and interventions designed to identify, characterise, prevent, or minimise risks relating to Utrogestan.

Safety specification
Proposed safety concerns:

Summary of safety concerns	
Important identified risks	None
Important potential risks	None
Missing information	None

Pharmacovigilance Plan
Routine pharmacovigilance is suggested, and no additional pharmacovigilance activities are proposed by the applicant, which is endorsed.

Risk minimisation measures
Routine risk minimisation is suggested, and no additional risk minimisation activities are proposed by the applicant, which is endorsed.

Summary of the RMP
The submitted Risk Management Plan, version 6.0 signed May 2022 is considered acceptable.

The MAH shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the Marketing Authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:
- At the request of the RMS;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

If the dates for submission of a PSUR and the update of a RMP coincide, they can be submitted at the same time, but via different procedures.

V. USER CONSULTATION

A user consultation with target patient groups on the package information leaflet (PL) has been performed on the basis of a bridging report making reference to Utrogestan, soft vaginal capsules, SE/H/2023/01, earlier UK/H/5838/01/MR.

The bridging report submitted by the applicant has been found acceptable.

VI. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

There are no objections to approval of Utrogestan, from a non-clinical and clinical point of view. The product information is acceptable. The benefit/risk of Utrogestan 400 mg is considered positive, and the application is therefore recommended for approval.

List of recommendations not falling under Article 21a/22a/22 of Directive 2001/83/EC in case of a positive benefit risk assessment

Description	Due date
Environmental risk assessment Phase I: Conduct literature search and evaluate the data (to start in Q4 2023) Phase II: Submission (by variation) of an interim Phase II ERA Expert Report based on the relevant data obtained in Phase I. This interim report will contain an overview of the studies which need to be performed, determined from the results of the literature search performed in Phase I.	Q2 2024
Environmental risk assessment Perform remaining ERA studies with start in Q3 2024. Depending on the studies required, this step can take up to 3 years. The completed Phase II ERA Expert Report will be submitted by variation once the studies are completed.	By end of 2027

List of conditions pursuant to Article 21a/22a or 22 of Directive 2001/83/EC

N/A

VII. APPROVAL

The decentralised procedure for Utrogestan, 400 mg, vaginal capsule, soft was positively finalised on 2023-09-20.

LÄKEMEDELSVERKET
SWEDISH MEDICAL PRODUCTS AGENCY

Public Assessment Report – Update

Procedure number*	Scope	Product Information affected (Yes/No)	Date of end of procedure	Approval/ non approval	Summary/ Justification for refuse

*Only procedure qualifier, chronological number and grouping qualifier (when applicable)

Postadress/Postal address: P.O. Box 26, SE-751 03 Uppsala, SWEDEN
Besöksadress/Visiting address: Dag Hammarskjölds väg 42, Uppsala
Telefon/Phone: +46 (0)18 17 46 00 Fax: +46 (0)18 54 85 66
Internet: www.lakemedelsverket.se E-mail: registrator@lakemedelsverket.se