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Summary of risk management plan for Intrarosa (prasterone)

This is a summary of the risk management plan (RMP) for Intrarosa. The RMP details important risks of Intrarosa, how these risks can be minimised and how more information will be obtained about Intrarosa's risks and uncertainties (missing information).

Intrarosa's summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how Intrarosa should be used.

This summary of the RMP for Intrarosa should be read in the context of all this information including the assessment report of the evaluation and its plain-language summary, all which is part of the European Public Assessment Report (EPAR).

Important new concerns or changes to the current ones will be included in updates of Intrarosa's RMP.

I. The medicine and what it is used for

Intrarosa is authorised for treatment of vulvar and vaginal atrophy in postmenopausal women having moderate to severe symptoms (see SmPC for the full indication). It contains prasterone as the active substance and it is given intravaginally.

Further information about the evaluation of Intrarosa's benefits can be found in Intrarosa's EPAR, including in its plain-language summary, available on the EMA website, under the medicine's webpage.

II. Risks associated with the medicine and activities to minimise or further characterise the risks

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Important risks of Intrarosa, together with measures to minimise such risks and the proposed studies for learning more about Intrarosa's risks, are outlined below.

Measures to minimise the risks identified for medicinal products can be:

- Specific information, such as warnings, precautions, and advice on correct use, in the package leaflet and SmPC addressed to patients and healthcare professionals;
- Important advice on the medicine's packaging;
- The authorised pack size-the amount of medicine in a pack is chose so to ensure that the medicine is used correctly;
- The medicine's legal status- the way a medicine is supplied to the patient (e.g. with or without prescription) can help to minimize its risks.

Together, these measures constitute *routine risk minimisation* measures.

In addition to these measures, information about adverse reactions is collected continuously and regularly analyzed, so that immediate action can be taken as necessary. These measures constitute *routine pharmacovigilance activities*.

If important information that may affect the safe use of Intrarosa is not yet available, it is listed under 'missing information' below.

II.A List of important risks and missing information

Important risks for Intrarosa are risks that would need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely administered. Important risks can be regarded as identified or potential. Identified risks are concerns for which there is sufficient proof of a link with the use of Intrarosa. Potential risks are concerns for which an association with the use of this medicine is possible based on available data, but this association has not been established yet and needs further evaluation. Missing information refers to information on the safety of the medicinal product that is currently missing and would benefit to be collected.

List of important identified and potential risks and missing information	
Important identified risks	• Abnormal Pap smear (ASCUS).
Important potential risk	• Oestrogen-dependent cancers such as ovarian or breast cancer
Missing information	• Long-term use (after 12 months) • Use in women with active or past oestrogen-dependent malignant tumours (breast and endometrial cancer) • Use in women with gynecological findings (including uterine fibroids, abnormal Pap smear (ASCUS), untreated endometrial hyperplasia or undiagnosed genital bleeding) • Use in women with cardiovascular disease or

List of important identified and potential risks and missing information	
	uncontrolled hypertension (blood pressure above 140/90mmHg) • Use in women with current or previous thromboembolic disease (either arterial or venous) • Women with a current hormonal treatment (e.g. oestrogen alone or combined with progestogens or androgen treatment)

II.B Summary of important risks

Important identified risk	
Abnormal Pap smear (ASCUS)	
Risk minimisation measures	Routine risk minimisation measures *SmPC section 4.4* *PL section 2*
Additional pharmacovigilance activities	Additional pharmacovigilance activities: Drug utilization of Intrarosa (6.5mg prasterone pessaries) in European Countries. See section II.C of this summary for an overview of the post-authorisation development plan.

Important potential risk	
Oestrogen-dependent cancers such as ovarian or breast cancer	
Risk minimisation measures	Routine risk minimisation measures *SmPC section 4.3 and 4.4* *PL section 2*
Additional pharmacovigilance activities	Additional pharmacovigilance activities: Drug utilization of Intrarosa (6.5mg prasterone pessaries) in European Countries. See section II.C of this summary for an overview of the post-authorisation development plan.

Missing information
Long-term use (after 12 months)

Missing information	
Risk minimisation measures	Routine risk communication: *SmPC section 4.4.* *PL section 2*
Additional pharmacovigilance activities	Additional pharmacovigilance activities: Drug utilization of Intrarosa (6.5mg prasterone pessaries) in European Countries. See section II.C of this summary for an overview of the post-authorisation development plan.
Missing information	
Use in women with active or past oestrogen-dependent malignant tumours (breast and endometrial cancer)	
Risk minimisation measures	Routine risk minimisation measures: *SmPC section 4.3 and 4.4* *PL section 2*
Additional pharmacovigilance activities	Additional pharmacovigilance activities: Drug utilization of Intrarosa (6.5mg prasterone pessaries) in European Countries. See section II.C of this summary for an overview of the post-authorisation development plan.
Missing information	
Use in women with gynecological findings (including uterine fibroids, abnormal Pap smear (ASCUS), untreated endometrial hyperplasia or undiagnosed genital bleeding)	
Risk minimisation measures	Routine risk minimisation measures: *SmPC section 4.3 and 4.4* *PL section 2*
Additional pharmacovigilance activities	Additional pharmacovigilance activities: Drug utilization of Intrarosa (6.5mg prasterone pessaries) in European Countries. See section II.C of this summary for an overview of the post-authorisation development plan.
Missing information	
Use in women with cardiovascular disease or uncontrolled hypertension (blood pressure above 140/90mmHg)	

Missing information	
Risk minimisation measures	Routine risk minimisation measures: *SmPC section 4.4* *PL section 2*
Additional pharmacovigilance activities	Additional pharmacovigilance activities: Drug utilization of Intrarosa (6.5mg prasterone pessaries) in European Countries. See section II.C of this summary for an overview of the post-authorisation development plan.
Missing information	
Use in women with current or previous thromboembolic disease (either arterial or venous)	
Risk minimisation measures	Routine risk minimisation measures: *SmPC section 4.4* *PL section 2*
Additional pharmacovigilance activities	Additional pharmacovigilance activities: Drug utilization of Intrarosa (6.5mg prasterone pessaries) in European Countries. See section II.C of this summary for an overview of the post-authorisation development plan.
Missing information	
Women with a current hormonal treatment (e.g. oestrogen alone or combined with progestogens or androgen treatment)	
Risk minimisation measures	Routine risk minimisation measures: *SmPC section 4.4* *PL section 2*
Additional pharmacovigilance activities	Additional pharmacovigilance activities: Drug utilization of Intrarosa (6.5mg prasterone pessaries) in European Countries. See section II.C of this summary for an overview of the post-authorisation development plan.

II.C Post-authorisation development plan

II.C.1 Studies which are conditions of the marketing authorisation

The following study is a condition of the marketing authorisation:

Title

Drug utilization of Intrarosa (6.5mg prasterone pessaries) in European Countries.

Objectives

Among female patients initiating Intrarosa:

1. Describe their baseline and historical characteristics such as
   - Age
   - Indication (by ICD-10 code)
   - History or current:
     - oestrogen-dependent cancers such as ovarian or breast cancer
     - endometrial cancer
     - endometrial hyperplasia
     - abnormal Pap smear
     - deep venous thrombosis
     - pulmonary embolism
     - thrombophilic disorders
     - angina
     - myocardial infarction
     - acute liver disease
     - porphyria
   - Indication for use.

2. Estimate the proportion of patients that may have been prescribed Intrarosa outside of the specifications of the product label ('off-label use').

II.C.2 Other studies in post-authorisation development plan

Not applicable.