EU Risk Management Plan for Etonogestrel/Ethinylestradiol Leon Farma / Nilho / DONGARING 0,120 mg/0,015 mg per 24 uur, hulpmiddel voor vaginaal gebruik (etonogestrel/ethinylestradiol)

RMP version to be assessed as part of this application:

RMP Version number: 5.1

Data lock point for this RMP: 14-March-2025

Data of final sign-off: 02-April-2025

Rationale for submitting an updated RMP: This version 5.1 is submitted in response to the RMS comments

Summary of significant changes in this RMP:

- Part V: Risk minimisation measures: V.1. Routine Risk Minimisation Measures: Removal of additional risk minimisation measures
- Part V: Risk minimisation measures: V.2. Additional Risk Minimisation Measures: Specification from 'Educational materials for prescribers and patients' to 'Checklist for prescribers' and 'Patient information card'
- Part VII: Annexes: Annex 6 - Details of proposed additional risk minimisation activities: inclusion of key elements for the checklist for prescribers and the patient information card
- Part VI: Summary of the risk management plan - II.B Summary of important risks: updated accordingly

Other RMP versions under evaluation: Not applicable

Details of the currently approved RMP:

Version number: 4.0

Approved with procedure:

NL/H/3719/001/DC

NL/H/3720/001/DC

NL/H/3722/001/DC

NL/H/3723/001/DC

NL/H/3743/001/DC

Date of approval (opinion date): 18-May-2017

QPPV name:

Iván Arias García

PV Associate Director, EU-QPPV & UK-QPPV

CHEMO & XIROMED EU

QPPV signature:

Signed by:IVAN ARIAS
Signed at:2025-04-02 12:25:31 +02:00
Reason:I Signed this document

IVAN ARIAS

Table of contents

Table of contents 2
Part I: Product Overview 3
Part II: Safety Specification 5
Part II: Module SI - Epidemiology of the indication(s) and target population 5
Part II: Module SII - Non-clinical part of the safety specification 5
Part II: Module SIII - Clinical trial exposure 5
Part II: Module SIV - Populations not studied in clinical trials 5
Part II: Module SV - Post-Authorisation Experience 5
Part II: Module SVI - Additional EU requirements for the safety specification 5
Part II: Module SVII – Identified and potential risks 5
Part II: Module SVIII - Summary of safety concerns 6
Part III: Pharmacovigilance Plan (including post-authorisation safety studies) 6
III. 1 Routine pharmacovigilance activities 6
III. 2 Additional pharmacovigilance activities 6
III. 3 Summary Table of additional Pharmacovigilance activities 6
Part IV: Plans for post-authorisation efficacy studies 6
Part V: Risk minimisation measures (including evaluation of the effectiveness of risk minimisation activities) 7
V.1. Routine Risk Minimisation Measures 7
V.2. Additional Risk Minimisation Measures 8
V.3. Summary of risk minimisation measures 9
Part VI: Summary of the risk management plan 10
II.A List of important risks and missing information 11
II.B Summary of important risks 11
II.C Post-authorisation development plan 12
II.C.1 Studies which are conditions of the marketing authorisation 12
II.C.2 Other studies in post-authorisation development plan 12
Part VII: Annexes 13
Annex 1 – EudraVigilance Interface 14
Annex 2 – Tabulated summary of planned, ongoing, and completed pharmacovigilance study programme 14
Annex 3 - Protocols for proposed, on-going and completed studies in the pharmacovigilance plan 14
Annex 4 - Specific adverse drug reaction follow-up forms 14
Annex 5 - Protocols for proposed and on-going studies in RMP part IV 14
Annex 6 - Details of proposed additional risk minimisation activities (if applicable) 14
Annex 7 - Other supporting data (including referenced material) 15
Annex 8 – Summary of changes to the risk management plan over time 15

Part I: Product Overview

Table Part I.1 – Product Overview

Active substance(s) (INN or common name)	Etonogestrel and ethinylestradiol
Pharmacotherapeutic group(s) (ATC Code)	Other gynecologicals, Intravaginal contraceptives, vaginal ring with progestagen and estrogen (G02BB01)
Marketing Authorisation Holder(s) / Applicant	MAH(s): NL/H/3722/001: LABORATORIOS LEON FARMA, S.A. ARISTO PHARMA GMBH. LABORATORIOS CINFA, S.A. LABORATOIRE MAJORELLE S&R Farmaceutici S.p.A Pharmaceutical Works Polpharma SA LifeWell Pharmaceutical & Healthcare NL/H/3723/001: LABORATORIOS LEON FARMA, S.A. HEATON KS ORION PHARMA MEDINER Kft. HEATON ADAMED PHARMA, S.A. NL/H/3743/001: LABORATORIOS LEON FARMA, S.A. Q PHARMA LTD Applicant: Laboratorios Liconsa, S.A
Medicinal products to which this RMP refers	One (01)
Invented name(s) in the European Economic Area (EEA)	NL/H/3722/001: Etonogestrel/Ethinylestradiol Leon Farma 0,120 mg/0,015 mg per 24 uur, hulpmiddel voor vaginaal gebruik NL/H/3723/001: Nillho 0,120 mg/0,015 mg per 24 uur, hulpmiddel voor vaginaal gebruik NL/H/3743/001: DONGARING 0,120 mg/0,015 mg per 24 uur, hulpmiddel voor vaginaal gebruik
Marketing authorisation procedure(s)	Decentralised (NL/H/3722, 3723, 3743/001/DC)

Brief description of the product	Chemical class: Steroid and steroid derivatives Summary of mode of action: Etonogestrel is a 19-nortestosterone-derived progestagen and binds with high affinity to progesterone receptors in the target organs. Ethinylestradiol is an estrogen widely used in contraceptive products. The contraceptive effect of ring containing etonogestrel/ethinylestradiol is based on various mechanisms, the most important of which is the inhibition of ovulation. Important information about its composition: Not applicable
Hyperlink to the Product Information	Refer to section 1.3 of the dossier
Indication(s) in the EEA	Current: Contraception Proposed: Not Applicable
Dosage in the EEA	Current: The ring releases etonogestrel and ethinylestradiol at an average amount of 0.120 mg and 0.015 mg 120 micrograms and 15 micrograms, respectively per 24 hours, over a period of 3 weeks. Proposed: Not applicable
Pharmaceutical form(s) and strengths	Current: 120 micrograms / 15 micrograms per 24 hours, vaginal delivery system Proposed: Not applicable
Is/will the product be subject to additional monitoring in the EU?	No

Part II: Safety Specification

Part II: Module SI - Epidemiology of the indication(s) and target population

Not applicable for generic applications.

Part II: Module SII - Non-clinical part of the safety specification

Not applicable for generic applications.

Part II: Module SIII - Clinical trial exposure

Not applicable for generic applications.

Part II: Module SIV - Populations not studied in clinical trials

Not applicable for generic applications.

Part II: Module SV - Post-Authorisation Experience

Not applicable for generic applications.

Part II: Module SVI - Additional EU requirements for the safety specification

Not applicable for generic applications.

Part II: Module SVII – Identified and potential risks

Not applicable.

Part II: Module SVIII - Summary of safety concerns

Table SVIII.1 Summary of Safety Concerns

Summary of safety concerns	
Important identified risks	• Venous thromboembolism • Arterial thromboembolism
Important potential risks	• None
Missing information	• None

Part III: Pharmacovigilance Plan (including post-authorisation safety studies)

III. 1 Routine pharmacovigilance activities

Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection: None.

III. 2 Additional pharmacovigilance activities

Not applicable.

III. 3 Summary Table of additional Pharmacovigilance activities

Not applicable

Part IV: Plans for post-authorisation efficacy studies

Not applicable.

Part V: Risk minimisation measures (including evaluation of the effectiveness of risk minimisation activities)

Risk Minimisation Plan

V.1. Routine Risk Minimisation Measures

Table Part V.1: Description of routine risk minimisation measures by safety concern

Safety concern	**Routine risk minimisation activities**
Venous thromboembolic events (VTE)	Routine risk communication: *SmPC section 4.1, 4.3, 4.4, 4.6 and 4.8* *PL section 4* Routine risk minimisation activities recommending specific clinical measures to address the risk: *Highlighting the importance of taking into consideration the individual woman's current risk factors when prescribing in SmPC section 4.1* *Warning on the risk of VTE in SmPC section 4.3* *Warning on the risk of VTE, risk factors and symptoms of VTE in SmPC section 4.4* *Warning on the increased risk of VTE during the postpartum period in SmPC section 4.6* *Warning on the risk of blood clots, risk factors, symptoms, PL section 2* Other routine risk minimisation measures beyond the Product Information: *Prescription only medicine*
Arterial thromboembolism (ATE)	Routine risk communication: *SmPC section 4.3, 4.4 and 4.8* *PL section 4* Routine risk minimisation activities recommending specific clinical measures to address the risk: *Warning on the risk of ATE in SmPC section 4.3* *Warning on the risk of ATE, risk factors and symptoms of ATE in SmPC section 4.4* *Warning on the risk of blood clots in an artery, risk factors, symptoms in PL section 2* Other routine risk minimisation measures beyond the Product Information: *Prescription only medicine*

V.2. Additional Risk Minimisation Measures

Checklist for prescribers

Objectives: To help doctors to remind the most important risk factors to consider when discussing the most suitable contraceptive method.

Rationale for the additional risk minimisation activity: To increase the awareness of the risks of VTE and ATE and therefore minimise its occurrence.

Target audience and planned distribution path: The final form of the educational material intended for prescribers and also for patients use will be prepared by the MAH. The MAH of each country should agree with the Local Authorities the content, distribution, and necessity of implementation of the additional risk minimization measures.

Plans to evaluate the effectiveness of the interventions and criteria for success: Effectiveness will be measured by means of routine pharmacovigilance activities, especially through signal management and the criteria for judging the success of the proposed risk minimisation measures will be achieved if no disproportionate reporting rates are identified by the comparison of product information versus ICSRs.

Patient information card

Objectives: Provide patients with concise information on the important signs and symptoms of VTE or ATE and when to seek medical attention.

Rationale for the additional risk minimisation activity: To increase the awareness of the risks of VTE and ATE and therefore minimise its occurrence.

Target audience and planned distribution path: The final form of the educational material intended for patients use will be prepared by the MAH. The MAH of each country should agree with the Local Authorities the content, distribution, and necessity of implementation of the additional risk minimization measures.

Plans to evaluate the effectiveness of the interventions and criteria for success: Effectiveness will be measured by means of routine pharmacovigilance activities, especially through signal management and the criteria for judging the success of the proposed risk minimisation measures will be achieved if no disproportionate reporting rates are identified by the comparison of product information versus ICSRs.

V.3. Summary of risk minimisation measures

Table Part V.3: Summary table of pharmacovigilance activities and risk minimisation activities by safety concern

Safety concern	Risk minimisation measures	Pharmacovigilance activities
Venous thromboembolic events (VTE)	Routine risk minimisation measures: *SmPC section 4.1, 4.3, 4.4, 4.6 and 4.8* *PL section 4* Additional risk minimisation measures: *Checklist for Prescribers* *Patient Information Card*	Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection: None Additional pharmacovigilance activities: None
Arterial thromboembolism (ATE)	Routine risk minimisation measures: *SmPC section 4.3, 4.4 and 4.8* *PIL section 3 and 3* Additional risk minimisation measures: *Checklist for Prescribers* *Patient Information Card*	Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection: None Additional pharmacovigilance activities: None

Part VI: Summary of the risk management plan

Summary of risk management plan (RMP) for Etonogestrel/Ethinylestradiol Leon Farma / Nilho / DONGARING 0,120 mg/0,015 mg per 24 uur, hulpmiddel voor vaginaal gebruik (etonogestrel/ethinylestradiol)

This is a summary of risk management plan (RMP) for Etonogestrel/Ethinylestradiol Leon Farma / Nilho / DONGARING 0,120 mg/0,015 mg per 24 uur, hulpmiddel voor vaginaal gebruik. The RMP details important risks of Etonogestrel/Ethinylestradiol Leon Farma / Nilho / DONGARING 0,120 mg/0,015 mg per 24 uur, hulpmiddel voor vaginaal gebruik, how these risks can be minimised, and how more information will be obtained about Etonogestrel/Ethinylestradiol Leon Farma / Nilho / DONGARING 0,120 mg/0,015 mg per 24 uur, hulpmiddel voor vaginaal gebruik's risks and uncertainties (missing information).

Etonogestrel/Ethinylestradiol Leon Farma / Nilho / DONGARING 0,120 mg/0,015 mg per 24 uur, hulpmiddel voor vaginaal gebruik's summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how Etonogestrel/Ethinylestradiol Leon Farma / Nilho / DONGARING 0,120 mg/0,015 mg per 24 uur, hulpmiddel voor vaginaal gebruik should be used.

Important new concerns or changes to the current ones will be included in updates of Etonogestrel/Ethinylestradiol Leon Farma / Nilho / DONGARING 0,120 mg/0,015 mg per 24 uur, hulpmiddel voor vaginaal gebruik's RMP.

I. The medicine and what it is used for

Etonogestrel/Ethinylestradiol Leon Farma / Nilho / DONGARING 0,120 mg/0,015 mg per 24 uur, hulpmiddel voor vaginaal gebruik is authorised for contraception.

It contains etonogestrel and ethinylestradiol as active substances, and it is given by vaginal delivery system.

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

Important risks of Etonogestrel/Ethinylestradiol Leon Farma / Nilho / DONGARING 0,120 mg/0,015 mg per 24 uur, hulpmiddel voor vaginaal gebruik, together with measures to minimise such 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 chosen 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 minimise its risks.

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

In the case of Etonogestrel/Ethinylestradiol Leon Farma / Nilho / DONGARING 0,120 mg/0,015 mg per 24 uur, hulpmiddel voor vaginaal gebruik, these measures are supplemented with additional *risk minimisation measures* mentioned under relevant important risk, below.

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

II.A List of important risks and missing information

Important risks of Etonogestrel/Ethinylestradiol Leon Farma / Nilho / DONGARING 0,120 mg/0,015 mg per 24 uur, hulpmiddel voor vaginaal gebruik are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely taken. 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 Etonogestrel/Ethinylestradiol Leon Farma / Nilho / DONGARING 0,120 mg/0,015 mg per 24 uur, hulpmiddel voor vaginaal gebruik. 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 needs to be collected (e.g., on the long-term use of the medicine).

List of important risks and missing information	
Important identified risks	• Venous thromboembolism • Arterial thromboembolism
Important potential risks	• None
Missing information	• None

II.B Summary of important risks

Important identified risk: Venous thromboembolism	
Risk minimisation measures	Routine risk minimisation measures: *SmPC section 4.1, 4.3, 4.4, 4.6 and 4.8* *PL section 4* Additional risk minimisation measures: *Checklist for Prescribers* *Patient Information Card*

Important identified risk: Arterial thromboembolism	
Risk minimisation measures	Routine risk minimisation measures: *SmPC section 4.3, 4.4 and 4.8* *PL section 4* Additional risk minimisation measures: *Checklist for Prescribers* *Patient Information Card*

II.C Post-authorisation development plan

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

There are no studies which are conditions of the marketing authorisation or specific obligation of Etonogestrel/Ethinylestradiol Leon Farma / Nilho / DONGARING 0,120 mg/0,015 mg per 24 uur, hulpmiddel voor vaginaal gebruik.

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

There are no studies required for Etonogestrel/Ethinylestradiol Leon Farma / Nilho / DONGARING 0,120 mg/0,015 mg per 24 uur, hulpmiddel voor vaginaal gebruik.

Part VII: Annexes

Table of contents

Annex 1 – EudraVigilance Interface **14**
Annex 2 – Tabulated summary of planned, ongoing, and completed pharmacovigilance study programme **14**
Annex 3 - Protocols for proposed, on-going and completed studies in the pharmacovigilance plan **14**
Annex 4 - Specific adverse drug reaction follow-up forms **14**
Annex 5 - Protocols for proposed and on-going studies in RMP part IV **14**
Annex 6 - Details of proposed additional risk minimisation activities (if applicable) **14**
Annex 7 - Other supporting data (including referenced material) **15**
Annex 8 – Summary of changes to the risk management plan over time **15**

Annex 1 – EudraVigilance Interface

Not applicable.

Annex 2 – Tabulated summary of planned, ongoing, and completed pharmacovigilance study programme

Not applicable.

Annex 3 - Protocols for proposed, on-going and completed studies in the pharmacovigilance plan

Not applicable.

Annex 4 - Specific adverse drug reaction follow-up forms

Not applicable.

Annex 5 - Protocols for proposed and on-going studies in RMP part IV

Not applicable.

Annex 6 - Details of proposed additional risk minimisation activities (if applicable)

Checklist for Prescribers

Key elements:

A discussion of the suitability of etonogestrel/ethinylestradiol vaginal ring is listed within the checklist and the main points are presented below:

- List of conditions such as history of thromboembolic events, history of migraine with aura, diabetes mellitus with vascular complications, very high blood pressure or lipids, major surgery or a period of prolongated immobilization
- Clinical history including age, body mass index (BMI), blood pressure, medical conditions of close relatives, concomitant medicines that could increase the risk of thrombosis (e.g. corticosteroids, neuroleptics, antipsychotics, antidepressants, chemotherapy, etc.) and other medical condition

The checklist should be included in conjunction with the SmPC during combined contraceptive consultations.

Patient Information Card

Key elements:

The Patient Information card contains important information about combined hormonal contraceptives and the risk of blood clots, mentioned below:

- In which situations the risk of blood cloot is highest
- To seek medical attention when experiencing severe pain or swelling on legs, sudden unexplained breathlessness or rapid breathing, chest pain, pressure, heaviness, face, arm or leg weakness or numbness
- To watch out for symptoms of a blood clot just after an operation or long journey
- To inform the doctor if a surgery has been programmed

Annex 7 - Other supporting data (including referenced material)

Not applicable.

Annex 8 – Summary of changes to the risk management plan over time

Version	Approval date Procedure	Change
1.0	Approval date: not approved Procedures: NL/H/3719/001/DC NL/H/3720/001/DC NL/H/3722/001/DC NL/H/3723/001/DC NL/H/3743/001/DC	Initial application.
2.0	Approval date: not approved Procedures: NL/H/3719/001/DC NL/H/3720/001/DC NL/H/3722/001/DC NL/H/3723/001/DC NL/H/3743/001/DC	Included as additional risk minimisation measures a Checklist for Prescribers and a Patient Information Card for the identified risks VTE and ATE.
3.0	Approval date: not approved Procedures: NL/H/3719/001/DC NL/H/3720/001/DC NL/H/3722/001/DC NL/H/3723/001/DC NL/H/3743/001/DC	No changes are made in the safety concerns.
4.0	Approval date: 18-May-2017 Procedures: NL/H/3719/001/DC NL/H/3720/001/DC NL/H/3722/001/DC	Updated Annex 2 on request of CAs to include recent changes in Product Information of the reference product. - Section SVII.4.2: deleted interaction with antibiotics (penicillins, tetraciclyns) and added interaction between CHCs containing

	NL/H/3723/001/DC NL/H/3743/001/DC	ethinylestradiol with products containing ombatasvir/paritaprevir/ritonavir and dasabuvir. - For safety concern 'Unintended pregnancies', updated information on interactions (in 4.5. and 4.8) and posology (4.2) according to the updated SmPC, in tablets V.1, V.3 and VI.1.4.
5.0	Approval date: not approved Procedure: NL/H/3722/001/DC NL/H/3723/001/DC NL/H/3743/001/DC	This version 5.0 is submitted to follow the "Guideline on Good Pharmacovigilance Practices (GVP)" Module V Rev. 2 (28 March 2017), and the "Guidance on the format of the risk management plan (RMP) in the EU – in integrated format" Rev. 2.0.1 (31 October 2018) and to align the safety concerns with the Harmonisation of RMP (HaRP) Assessment Report for etonogestrel/ethinylestradiol. Summary of significant changes in this RMP: - Change in format following 'Guidance on the format of the risk management plan (RMP) in the EU – in integrated format', according to GVP Module V Rev.2. - Part II: Updated list of safety concerns to be aligned with HaRP Assessment
5.1	Approval date: pending Procedure: NL/H/3722/001/DC NL/H/3723/001/DC NL/H/3743/001/DC	This version 5.1 is submitted in response to the RMS comments. Summary of significant changes in this RMP: - Part V: Risk minimisation measures: V.1. Routine Risk Minimisation Measures: Removal of additional risk minimisation measures - Part V: Risk minimisation measures: V.2. Additional Risk Minimisation Measures: Specification from 'Educational materials for prescribers and patients' to 'Checklist for prescribers' and 'Patient information card' - Part VII: Annexes: Annex 6 - Details of proposed additional risk minimisation activities: inclusion of key elements for the checklist for prescribers and the patient information card - Part VI: Summary of the risk management plan - II.B Summary of important risks: updated accordingly