COLLEGE TER BEOORDELING VAN GENEESMIDDELEN

Public Assessment Report

Scientific discussion

Ethinylestradiol/Gestodeen Xiromed 0.02/0.075 mg and 0.03/0.075 mg, coated tablets (ethinylestradiol/gestodene)

NL/H/6415/001-002/DC

Date: 10 June 2025

This module reflects the scientific discussion for the approval of Ethinylestradiol/Gestodeen Xiromed 0.02/0.075 mg and 0.03/0.075 mg, coated tablets. The procedure was finalised at 13 August 2008 in Denmark (DK/H/1149/001-002/DC). After a transfer on 4 April 2025, the current RMS is the Netherlands. For information on changes after the finalisation date please refer to the 'steps taken after finalisation' at the end of this PAR.

List of abbreviations

ASMF	Active Substance Master File
CEP	Certificate of Suitability to the monographs of the European Pharmacopoeia
CHMP	Committee for Medicinal Products for Human Use
CMD(h)	Coordination group for Mutual recognition and Decentralised procedure for human medicinal products
CMS	Concerned Member State
EDMF	European Drug Master File
EDQM	European Directorate for the Quality of Medicines
EEA	European Economic Area
EMA	European Medicines Agency
ERA	Environmental Risk Assessment
ICH	International Conference of Harmonisation
MAH	Marketing Authorisation Holder
Ph.Eur.	European Pharmacopoeia
PL	Package Leaflet
RH	Relative Humidity
RMP	Risk Management Plan
RMS	Reference Member State
SmPC	Summary of Product Characteristics
TSE	Transmissible Spongiform Encephalopathy

I. INTRODUCTION

Based on the review of the quality, safety and efficacy data, the Member States have granted a marketing authorisation for of Ethinylestradiol/Gestodeen Xiromed 0.02/0.075 mg and 0.03/0.075 mg, coated tablets from Medical Valley Invest AB. The product is indicated for oral contraception.

Ethinylestradiol/Gestodeen Xiromed 0.02/0.075 mg and 0.03/0.075 mg, coated tablets are fixed-combination tablets of which combine potent synthetic derivatives of the natural estrogen estradiol and the progestogen gestodene. The tablets are monophasic oral contraceptives containing ethinylestradiol 20 micg/30 micg and gestodene 75 micg as active ingredients. The monophasic combination of ethinylestradiol and gestodene inhibits ovulation via a negative feedback mechanism on the hypothalamus, which alters the normal pattern of gonadotropin secretion of folliclestimulationg hormone and luteinizing hormone by the anterior pituitary. In addition, the combination oral contraceptive modifies cervical secretions, producing an unfavourable environment for implantation.

The product is indicated in women as oral hormonal contraceptive. The decision to prescribe Gestodene/Ethinylestradiol 75/20 Viatris and Gestodene/Ethinylestradiol 75/30 Viatris should take into consideration the individual woman's current risk factors, particularly those for venous thromboembolism (VTE), and how the risk of VTE with Gestodene / Ethinylestradiol 75/20 Viatris and Gestodene / Ethinylestradiol 75/30 Viatris compares with other CHCs (see sections 4.3 and 4.4 of the SmPC).

This repeat use procedure concerns a generic application claiming essential similarity with the reference products Meloden 75/20 micg coated tablets and Gynera 75/30 micg coated tablets by Schering. The reference products have been registered in Denmark since 1995 and 1988, respectively.

The marketing authorisation is granted based on article 10.1 of Directive 2001/83/EC.

II. QUALITY ASPECTS

II.1 Introduction

Each Ethinylestradiol/Gestodeen Xiromed 0.02/0.075 mg, coated tablet contains 75 micrograms gestodene and 20 micrograms ethinylestradiol.
Each Ethinylestradiol/Gestodeen Xiromed 0.03/0.075 mg, coated tablet contains 75 micrograms gestodene and 30 micrograms ethinylestradiol.

The tablets are white, round, biconvex sugar coated tablets, both sides are without imprinting. Ethinylestradiol/Gestodeen Xiromed is packed in blister packs (PVC/aluminium) in pack sizes of 1 x 21 tablets; 3 x 21 tablets, and 6 x 21 tablets. However, not all pack sizes may be marketed.

The excipients in the tablet core are: Magnesium stearate; povidone K-25; maize starch and lactose monohydrate.

The coating consists of: Povidone K-90; macrogol 6000; talc; calcium carbonate; sucrose and wax montan glycol.

Compliance with Good Manufacturing Practice
The RMS has been assured that acceptable standards of GMP (see Directive 2003/94/EC) are in place for this product type at all sites responsible for the manufacturing of the active substance as well as for the manufacturing and assembly of this product prior to granting its national authorisation.

II.2 Drug Substance

The active substance gestodene is not described in the European Pharmacopoeia. It is a white or yellowish crystalline powder. It is practically insoluble in water, soluble in methylene chloride, slightly soluble in ethanol and methanol. It is optically active. It has six asymmetric carbon atoms. It consists of only one crystalline form.

The documentation on the active substance is presented as a European Drug Master File/Active Substance Master File (DMF) (in CTD-format). The Applicant's Part of the DMF has been forwarded by the Applicant. The Applicant's and Restricted Part plus a LoA has been forwarded by the ASM.

The active substance ethinylestradiol is described in the European Pharmacopoeia. It is a white or slightly yellowish-white, crystalline powder. It is practically insoluble in water, freely soluble in alcohol. It dissolves in dilute alkaline solutions. It is optically active.
The manufacturer of the active substance has obtained a Certificate of Suitability, a copy of which is presented in the documentation.

Quality control of drug substance
The control tests and specifications for both drug substances gestodene and ethinylestradiol are adequately drawn up.

Stability of drug substance
Based on the stability data presented, appropriate retest periods have been set.

II.3 Medicinal Product

Pharmaceutical development
The finished product is white round biconvex coated tablets, to be marketed in PVC/Alu blister packaging. Each tablet core contains less than 5 % of the active substance gestodene and less than 5 % of the active substance ethinylestradiol.

The development of the product has been described, the choice of excipients is justified and their functions explained.

Quality control of drug product
The product specifications cover appropriate parameters for this dosage form. Validations of the analytical methods have been presented. Batch analysis has been performed on 6 batches of each 'strength'. The batch analysis results show that the finished products meet the specifications proposed.

Stability of drug product
The conditions used in the stability studies are according to the ICH stability guideline. The control tests and specifications for drug product are adequately drawn up.

The proposed shelf-life of 24 months with 'do not store above 30°C' for the drug product is considered acceptable.

II.4 Discussion on chemical, pharmaceutical and biological aspects

The following post-approval commitment was made:
- The Applicant commits to reconsider limits for total impurities in the shelf-life specification at the end of stability studies i.e. 36 months.

III. NON-CLINICAL ASPECTS

III.1 Ecotoxicity/environmental risk assessment (ERA)

The product is intended as a substitute for other identical products on the market. The approval of this product will not result in an increase in the total quantity of gestodene/ethinylestradiol released int the environment. It does not contain any component,

which results in an additional hazard to the environment during storage, distribution, use and disposal.

III.2 Discussion on the non-clinical aspects

This product is a generic formulation of Meloden and Gynera coated tablets, which are available on the European market. No new preclinical data have been submitted, and therefore the application has not undergone preclinical assessment. This is acceptable for this type of application since pharmacodynamic, pharmacokinetic and toxicological properties of gestodene and ethinylestradiol are well known. Overview based on literature review is, thus, appropriate.

IV. CLINICAL ASPECTS

IV.1 Introduction

Gestodene and ethinylestradiol are well-known active substances with established efficacy and tolerability.

IV.2 Pharmacokinetics

For this generic application, the MAH has submitted one single-dose bioequivalence study under fasting conditions in which the pharmacokinetic profile of the test product Ethinylestradiol/Gestodeen Xiromed 0.03/0.075 mg, coated tablet is compared with the pharmacokinetic profile of the reference product Moneva 75/30 micg coated tablets, Schering, France.

Bioequivalence study

The study was an open-label, randomized, two-treatment, two-sequence, two-period, two-way crossover, single-dose bioavailability study conducted under fasting conditions with a wash out period of 28 days between the two administrations. Gestodene is highly bound to SHBG which is why 28 days was chosen to allow SHBG to return to normal levels before Period 2. 2 tablets of Ethinylestradiol/Gestodeen 0.03/0.075 mg were administered in each period (~2x30 micg ethinylestradiol and 2x75 micg gestodene). 2 tablets were dosed to meet bioanalytial assay requirements although the product labelling specifies a dose of one tablet per day.

Blood samples were collected pre-dosing and at time points up to 96 hours for gestodene and up to 72 hours for ethinylestradiol post administration of a single-dose of 2x75 micg

gestodene/30 micg ethinylestradiol fixed combination tablets with 240 ml of water for the analyses of gestodene and ethinylestradiol.

48 healthy post-menopausal, non-smoking, Caucasian female subjects (49-63 years) were enrolled and participated in the study. 48 subjects completed the study. Statistical analysis was carried out on the first 46 subjects to complete the study according to study protocol.

The pharmacokinetic parameters calculated were AUC0-t, AUC0-∞, Cmax, tmax, Kel t½ el and residual area. Primary variables were AUC0-t, AUC0-∞ and Cmax.

The applicant would conclude bioequivalence if 90% CI were within 80-125% for ln-transformed AUC0-t, AUC0-inf and ln-transformed Cmax according to the study protocol.

Table 1. Pharmacokinetic parameters of gestodene under faster conditions.

Treatment N=46	**AUC_{0-t} (pg.h/mL)**	**$AUC_{0-\infty}$ (pg.h/mL)**	**C_{max} pg/mL)**	**t_{max} (h)**	**$t_{1/2}$ (h)**
Test	52794.80	57546.47	5662.99	0.894	25.87
Reference	52553.32	57701.88	5831.59	0.844	25.74
Ratio[1]	100.44%	99.94%	96.22%		
90% Geometric C.I.[2]	95.82% - 105.29%	95.49% - 104.59%	92.35% - 100.24%		
Intra-Subject CV	13.45%	13.00%	11.70%		

$AUC_{0-\infty}$ Area under the plasma concentration-time curve from time zero to infinity
AUC_{0-t} Area under the plasma concentration-time curve from time zero
C_{max} Maximum plasma concentration
t_{max} Time after administration when maximum plasma concentration occurs
$t_{1/2}$ Half-life

[1] *Calculated using least-squares means according to the formula* $e^{(Ethinylestradiol\text{-}Gestodene\ (A)\text{-}Moneva\ (B))} \times 100$

[2] *90% Geometric Confidence Interval using ln-transformed data*

Table 2. Pharmacokinetic parameters of ethinylestradiol under faster conditions.

Treatment N=46	AUC_{0-t} (pg.h/mL)	$AUC_{0-\infty}$ (pg.h/mL)	C_{max} pg/mL)	t_{max} (h)	$t_{1/2}$ (h)
Test	1367.86	1553.45	141.24	1.51	16.79
Reference	1281.11	1456.75	136.14	1.50	16.45
Ratio[1]	106.97%	107.02%	104.28%		
90% Geometric C.I.[2]	103.79% - 110.25%	104.06% - 110.07%	101.21% - 107.43%		
Intra-Subject CV	8.59%	7.99%	8.49%		

$AUC_{0-\infty}$	Area under the plasma concentration-time curve from time zero to infinity
AUC_{0-t}	Area under the plasma concentration-time curve from time zero
C_{max}	Maximum plasma concentration
t_{max}	Time after administration when maximum plasma concentration occurs
$t_{1/2}$	Half-life

[1] *Calculated using least-squares means according to the formula* $e^{(Ethinylestradiol\text{-}Gestodene\ (A)\text{-}Moneva\ (B))} \times 100$

[2] *90% Geometric Confidence Interval using ln-transformed data*

Conclusion on bioequivalence study

The 90% confidence intervals for the ln-transformed AUC0-t, AUC0-∞ and Cmax are within the acceptance range of 80-125%.

Based on the submitted bioequivalence study Ethinylestradiol/Gestodeen Xiromed 0.02/0.075 mg and 0.03/0.075mg, coated tablets are considered bioequivalent with Meloden 75/20 micg coated tablets and Gynera 75/30 micg coated tablets, respectively, with respect to rate and extent of absorption of gestodene and ethinylestradiol. Tolerability of the test product is acceptable and not significantly different from reference product.

The 0.02/0.075 mg strength is dose proportional with the 0.03/0.075 mg strength. The pharmacokinetics of the active substances are linear in the dose range. The results of the bioequivalence study performed with the 0.03/0.075 mg strength therefore apply to the 0.02/0.075 mg strength.

The RMS has been assured that the bioequivalence study has been conducted in accordance with acceptable standards of Good Clinical Practice (GCP, see Directive 2005/28/EC) and Good Laboratory Practice (GLP, see Directives 2004/9/EC and 2004/10/EC).

IV.3 Risk Management Plan

The combination gestodene/ethinylestradiol was first approved in 1995 (75/20 micg) and 1986 (75/30 micg), respectively, and there is now more than 10 years post-authorisation experience with the combination of active substances. The safety profile of gestodene/ethinylestradiol can be considered to be well established and no product specific pharmacovigilance issues were identified pre- or postauthorisation which are not adequately

covered by the current SPC. Additional risk minimization activities have not been identified for the reference medicinal product. The MAH has a pharmacovigilance system at their disposal, which is based on the current European legislation.

The Pharmacovigilance system described fulfils the requirements and provides adequate evidence that the applicant has the services of a qualified person responsible for pharmacovigilance and has the necessary means for the identification and notification of any a potential risks occurring either in the Community or in a third country.

V. USER CONSULTATION

SmPC and Package leaflet

The content of the SmPC and package leaflet approved during the decentralised procedure is in general in accordance with that accepted for Gestinyl (DK/H/0926/001-002/DC, Day 210: 26 January 2007), marketed by Stragen Nordic A/S.

Readability test

The package leaflet has been evaluated via a user consultation study in accordance with the requirements of Articles 59(3) and 61(1) of Directive 2001/83/EC. The language used for the purpose of user testing the package leaflet was Danish. The test consisted of a pilot test with 3 participants, followed by two rounds with 10 participants each. The questions covered the following areas sufficiently: traceability, comprehensibility and applicability.

The results show that the package leaflet meets the criteria for readability as set out in the Guideline on the readability of the label and package leaflet of medicinal products for human use.

VI. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

Ethinylestradiol/Gestodeen Xiromed 0.02/0.075 mg and 0.03/0.075 mg, coated tablets have a proven chemical-pharmaceutical quality and are generic forms of Meloden 75/20 micg coated tablets and Gynera 75/30 micg coated tablets by Schering. Meloden and Gynera are well-known medicinal products with an established favourable efficacy and safety profile.

Bioequivalence has been shown to be in compliance with the requirements of European guidance documents.

The MAH has provided written confirmation that systems and services are in place to ensure compliance with their pharmacovigilance obligations.

The SmPC, package leaflet and labelling are in the agreed templates and are in agreement with that accepted for Gestinyl (DK/H/0926/001-002/DC, Day 210: 26 January 2007), marketed by Stragen Nordic A/S.

Agreement between Member States was reached during a written procedure. There was no discussion in the CMD(h). The Concerned Member States, on the basis of the data submitted, considered that essential similarity has been demonstrated for Ethinylestradiol/Gestodeen Xiromed 0.02/0.075 mg and 0.03/0.075 mg with the reference product, and have therefore granted a marketing authorisation. The decentralised procedure was finalised on 13 August 2008. Ethinylestradiol/Gestodeen Xiromed 0.02/0.075 mg and Ethinylestradiol/Gestodeen Xiromed 0.03/0.075 mg was authorised in Denmark on 2 October 2008.

A European harmonised birth date has been allocated (1995-03-17 (0.02/0.075 mg) and 1986-07-09 (0.03/0.075 mg) and subsequently the first PSUR will be submitted with a DLP of 2009-03 (0.02/0.075 mg) and 2009-08 (0.03/0.075 mg), respectively, after which the PSUR submission cycle is 3 years.

The date for the first renewal will be: 13 August 2013.

STEPS TAKEN AFTER THE FINALISATION OF THE INITIAL PROCEDURE - SUMMARY

Procedure number	Scope	Product Information affected	Date of end of procedure	Approval/ non approval	Summary/ Justification for refuse
DK/H/1149/001-2/IB/001	Change in the name of the medicinal product - Name change only in CMS Belgium	No	30-04-2009	Approved	N.A.
DK/H/1149/001-2/IA/004	Submission of a new or updated Ph. Eur. Certificate of Suitability for an active substance or starting material/reagent/intermediate in the manufacturing process of the active substance - From a manufacturer currently approved	No	30-11-2009	Approved	N.A.
DK/H/1149/001-2/IB/002	Change in the shelf-life of the finished product - As packaged for sale	Yes	08-01-2010	Approved	N.A.
DK/H/1149/001-2/II/003	Batch size of API + API manufacturing process change	No	06-06-2010	Approved	N.A.
DK/H/1149/001-2/II/005	Minor changes brought to the manufacturing process and updates to comply with European Pharmacopeia Monograph of Gestodene newly published	No	06-06-2010	Approved	N.A.
DK/H/1149/001-2/IB/006/G	Change in the (invented) name of the medicinal product for Nationally Authorised Products + Introduction of, or changes to, a summary of pharmacovigilance system for medicinal products for human use which has been assessed by the relevant national competent authority/EMEA for another product of the same MAH +	No No	30-06-2011	Approved	N.A.

	Change(s) to an existing pharmacovigilance system as described in the detailed description of the pharmacovigilance system (DDPS). - Other change(s) to the DDPS that does not impact on the operation of the pharmacovigilance system (e.g. change of the major storage/archiving location, administrative changes, update of acronyms, naming changes of functions/procedures).	No			
DK/H/1149/001-2/IA/007	Submission of a new or updated Ph. Eur. certificate of suitability or deletion of Ph. Eur. certificate of suitability: -For an active substance -For a starting material/reagent/intermediate used in the manufacturing process of the active substance -For an excipient European Pharmacopoeial Certificate of Suitability to the relevant Ph. Eur. Monograph. - New certificate from an already approved manufacturer	No	01-07-2011	Approved	N.A.
DK/H/1149/001-2/R/001	Renewal	No	30-04-2012	Approved	N.A.
DK/H/1149/001-2/IA/009	Replacement or addition of a manufacturing site for part or all of the manufacturing process of the finished product - Secondary packaging site	No	07-05-2014	Approved	N.A.

DK/H/1149/001-2/IB/008	Change(s) in the Summary of Product Characteristics, Labelling or Package Leaflet of (union referral procedure) - The medicinal product is covered by the defined scope of the procedure	Yes	11-07-2014	Approved	N.A.
DK/H/1149/001-2/IA/011	Introduction of , or changes to, a summary of pharmacovigilance system for medicinal products for human use - Introduction of a summary of pharmacovigilance system, changes in QPPV (including contact details) and/or changes in the Pharmacovigilance System Master File (PSMF) location	No	16-07-2015	Approved	N.A.
DK/H/1149/001-2/II/010	Change(s) in the Summary of Product Characteristics, Labelling or Package Leaflet due to new quality, preclinical, clinical or pharmacovigilance data.	Yes	12-09-2015	Approved	N.A.
DK/H/1149/001-2/IA/012/G	Change in the name and/or address of: a manufacturer (including where relevant quality control testing sites) + Change in the manufacturer of a starting material/reagent/intermediate used in the manufacturing process of the active substance or change in the manufacturer (including where relevant quality control testing sites) of the active substance, where no Ph. Eur.	No No	27-11-2015	Approved	N.A.

	Certificate of Suitability is part of the approved dossier - Introduction of a new site of micronisation + Submission of a new or updated Ph. Eur. certificate of suitability or deletion of Ph. Eur. certificate of suitability: - For an active substance - For a starting material/reagent/intermediate used in the manufacturing process of the active substance - For an excipient European Pharmacopoeial Certificate of Suitability to the relevant Ph. Eur. Monograph. - New certificate from a new manufacturer (replacement or addition)	No			
DK/H/1149/001-2/IA/014	Introduction of , or changes to, a summary of pharmacovigilance system for medicinal products for human use - Introduction of a summary of pharmacovigilance system, changes in QPPV (including contact details) and/or changes in the Pharmacovigilance System Master File (PSMF) location	No	02-01-2016	Approved	N.A.
DK/H/1149/001-2/IB/013/G	Change in the manufacturing process of the finished product, including an intermediate used in the manufacture of the finished product: - Minor change in the	No	15-01-2016	Approved	N.A.

	manufacturing process + Change to in-process tests or limits applied during the manufacture of the finished product: - Deletion of a non-significant in-process test - Addition of a new test(s) and limits + Change in test procedure for the finished product: - minor change to the analytical methods	No No			
DK/H/1149/001-2/IA/015	Changes (Safety/Efficacy) to Human and Veterinary Medicinal Products - Other variation: Update of PI	Yes	22-06-2016	Approved	N.A.
DK/H/1149/001-2/IB/016	Change in the (invented) name of the medicinal product for Nationally Authorised Products	Yes	11-08-2016	Approved	N.A.
DK/H/1149/001-2/IB/017	Change in the re-test period/storage period or storage conditions of the active substance where no Ph. Eur. Certificate of Suitability covering the retest period is part of the approved dossier. - Re-test period/storage period: Extension or introduction of a re-test period/storage period supported by real time data	No	29-08-2016	Approved	N.A.
DK/H/1149/001-2/IB/018	Changes (Safety/Efficacy) to Human and Veterinary Medicinal Products - Other variation:	Yes	26-07-2017	Approved	N.A.

	Update of SmPC and PIL				
DK/H/1149/001-2/IA/019	Submission of a new or updated Ph. Eur. certificate of suitability or deletion of Ph. Eur. certificate of suitability: -For an active substance -For a starting material/reagent/intermediate used in the manufacturing process of the active substance -For an excipient European Pharmacopoeial Certificate of Suitability to the relevant Ph. Eur. Monograph. - Updated certificate from an already approved manufacturer	No	21-06-2018	Approved	N.A.
DK/H/1149/001-2/IA/020	Changes (Safety/Efficacy) to Human and Veterinary Medicinal Products - Other variation: Update of SmPC and PIL	Yes	13-01-2019	Approved	N.A.
DK/H/1149/001-2/II/021	Change(s) in the Summary of Product Characteristics, Labelling or Package Leaflet of generic medicinal products following assessment of the same change for the reference product - Implementation of change(s) which require to be further substantiated by new additional data to be submitted by the MAH (e.g. comparability)	Yes	22-05-2020	Approved	N.A.

DK/H/1149/001-2/IB/022	Changes (Safety/Efficacy) to Human and Veterinary Medicinal Products - Other variation: Update of the SmPC and PIL	Yes	13-12-2021	Approved	N.A.
DK/H/1149/001-2/IB/023	Change(s) in the Summary of product Characteristics, Labelling or Package Leaflet intended to implement the outcome of a procedure concerning PSUR or PASS, or the outcome of the assessment done by the competent authority under Articles 45 or 46 of Regulation 1901/2006: - Implementation of wording agreed by the competent authority	Yes	13-12-2021	Approved	N.A.
DK/H/1149/001-2/IA/024/G	Change to importer, batch release arrangements and quality control testing of the finished product - Addition of a manufacturer responsible for importation and/or batch release - Not including batch control/testing + Submission of a new or updated Ph. Eur. certificate of suitability or deletion of Ph. Eur. certificate of suitability: - For an active substance - For a starting material/reagent/intermediate used in the manufacturing process of the active substance - For an excipient	Yes No	13-03-2022	Approved	N.A.

	European Pharmacopoeial Certificate of Suitability to the relevant Ph. Eur. Monograph. - Updated certificate from an already approved manufacturer				
DK/H/1149/001-2/IA/025	Change(s) in the Summary of product Characteristics, Labelling or Package Leaflet intended to implement the outcome of a procedure concerning PSUR or PASS, or the outcome of the assessment done by the competent authority under Articles 45 or 46 of Regulation 1901/2006: - Implementation of wording agreed by the competent authority	Yes	02-03-2023	Approved	N.A.
DK/H/1149/001-2/IB/026	Change in the (invented) name of the medicinal product for Nationally Authorised Products	Yes	27-06-2024	Approved	N.A.
DK/H/1149/001-2/IA/027	Submission of a new or updated Ph. Eur. certificate of suitability or deletion of Ph. Eur. certificate of suitability: -For an active substance -For a starting material/reagent/intermediate used in the manufacturing process of the active substance -For an excipient European Pharmacopoeial Certificate of Suitability to the relevant Ph. Eur. Monograph. - New certificate from an already approved	No	15-09-2024	Approved	N.A.

	manufacturer				
DK/H/1149/001-2/IB/028	Change in the (invented) name of the medicinal product for Nationally Authorised Products	Yes	06-03-2025	Approved	N.A.
NL/H/6415/001-2/IA/029	Introduction of , or changes to, a summary of pharmacovigilance system for medicinal products for human use - Introduction of a summary of pharmacovigilance system, changes in QPPV (including contact details) and/or changes in the Pharmacovigilance System Master File (PSMF) location	No	17-04-2025	Approved	N.A.