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Public Assessment Report

Scientific discussion

Olseron 550 mg film-coated tablets
Naproxen Sodium

ES/H/1007/001/DC

Date of this report:	20/01/2026

This module reflects the scientific discussion for the approval of Olseron 550 mg film-coated tablets. The procedure was finalised at 14/01/2026. For information on changes after this date please refer to the module 'Update'.

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I INTRODUCTION

Based on the review of the quality, safety and efficacy data, the Member States have agreed to grant a marketing authorisation for Olseron 550 mg film-coated tablets.
The product is indicated in the symptomatic treatment of rheumatoid arthritis, osteoarthritis, acute gout attacks, ankylosing spondylitis, acute musculoskeletal disorders, primary dysmenorrhoea symptoms (For adults and adolescents aged 16 years and over).

A comprehensive description of the indications and posology is given in the SmPC.

II EXECUTIVE SUMMARY

II.1 Rationale for the product

Not applicable for generic products.

II.2 About the product

Naproxen sodium is a non-steroidal anti-inflammatory drug (NSAID) with analgesic, antiinflammatory and antipyretic action. Naproxen sodium is a propionic acid derivative chemically related to the arylacetic acid group. Naproxen sodium is a white to yellowish-white crystalline solid that is easily soluble in water at a neutral pH. Its anti-inflammatory effect has been confirmed even in adrenalectomised animals, which indicates that its action is not mediated through the pituitary–adrenal axis.
Like other non-steroidal anti-inflammatory agents, naproxen inhibits prostaglandin synthetase, although the exact mechanism of anti-inflammatory action is unknown for this type of product.

Pharmacotherapeutic group: anti-inflammatory and antirheumatic products, non-steroids. ATC code: M01AE02

Naproxen sodium is used for the symptomatic treatment of rheumatoid arthritis, osteoarthritis, acute gout attacks, ankylosing spondylitis, acute musculoskeletal disorders, primary dysmenorrhoea symptoms (For adults and adolescents aged 16 years and over).

II.3 General comments on the submitted dossier

This dossier concerns an application for marketing authorisation for Olseron 550 mg film-coated tablets according to Article 10(1) of Directive No 2001/83/EC.

European Reference Product (ERP)
The European Reference Product which is used in RMS and CMS NL, BE is Antalgin 550 mg film-coated tablets by Atnahs Pharma UK Limited, formally Roche Farma, registered since June 4th, 1987.

Assessment of similarity with authorised orphan medicinal product(s) under market exclusivity
Not applicable.

II.4 General comments on compliance with GMP, GLP, GCP and agreed ethical principles

The RMS has been assured that acceptable standards of GMP are in place for these product types at all sites responsible for the manufacture and assembly of this product.

For manufacturing sites within the Community, the RMS has accepted copies of current manufacturer authorisations issued by inspection services of the competent authorities as certification that acceptable standards of GMP are in place at those sites.

For manufacturing sites outside the Community, the RMS has accepted copies of current GMP Certificates as certification that acceptable standards of GMP are in place at the non-Community sites.

GMP active substance
Regarding the statement on GMP for the active substance a statement/declaration is provided from the manufacturer responsible for manufacture of the finished product and batch release situated in the EU.

GCP compliance
The study was conducted in accordance with Good Clinical Practice (GCP) standards. Monitoring reports and certificates of audits carried out by the Quality Assurance Unit are presented. The sites have been previously inspected by EU regulatory authorities.

III SCIENTIFIC OVERVIEW AND DISCUSSION

III.1 Quality aspects

The chemical-pharmaceutical documentation and Quality Overall Summary in relation to Olseron 550 mg film-coated tablets are of sufficient quality in view of the present European regulatory requirements.

Drug substance
The active substance naproxen sodium is described in the Ph.Eur. And the quality information is supported by a CEP issued by the EDQM.
The drug substance specification includes the tests prescribed by the Ph.Eur. Monograph and the CEP and suitable additional tests. The additional analytical methods applied are suitably described and validated.
The CEP includes a statement on the authorised re-test period and the container closure system.

Drug Product
The development of the product has adequately been performed and described.
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 control tests and limits in the specification are considered appropriate to control the quality of the finished product in relation to its intended purpose.
The limits for impurities and degradation products have been justified. The issue of nitrosamines is comprehensively and adequately addressed. The analytical methods applied are suitably described and validated.
Batch analysis has been performed on nine batches. The batch analysis results show that the finished products meet the specifications proposed.
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.
The conditions used in the stability studies are according to the ICH stability guidelines.

III.2 Non clinical aspects

Pharmacodynamic, pharmacokinetic and toxicological properties of naproxen sodium are well known. As naproxen sodium is a widely used, well-known active substance, the Applicant has not provided additional studies, and further studies are not required.

Environmental Risk Assessment (ERA)
Since Olseron 550 mg film-coated tablets is intended for generic substitution, this will not lead to an increased exposure to the environment. Additional ERA studies are therefore not deemed necessary.

III.3 Clinical aspects

For this generic application of an immediate release formulation, the MAH has submitted a bioequivalence study which is discussed below.

Pharmacokinetics

Biowaiver
N/A.

Bioequivalence studies
Study 16-522 (CEPHA s.r.o. study No.: CPA 491-16)

Clinical and analytical facilities
The clinical part of the study was performed at CEPHA s.r.o. Phase I Clinic, Komenského 19, CZ-323 00 Pilsen, Czech Republic. The analytical portion was conducted at KRKA, d. d., Novo Mesto, Pharmaceutical R&D, Bioanalytics Šmarješka cesta 6, 8501 Novo mesto, Slovenia.

Design
A randomized, two treatment, two period, two sequence, single dose, crossover bioequivalence study was carried out in fasting conditions in 24 subjects (12 male and 12 female). The medication was administered as a single dose by oral route with 240 mL of room temperature water after a fasting period for at least 10 hours prior to drug administration. There were two dosing periods, separated by a washout period of 7 days.

Analytical and statistical methods
The analytical method has been adequately validated and is considered acceptable for analysis of the plasma samples.
The 90% confidence interval (90% CI) of the ratio of the test formulation to the reference formulation for the log-transformed values of Cmax and AUC was calculated using an ANOVA model. This model included the covariates sequence, period, formulation and subject nested to sequence. Bioequivalence was defined when the 90% CI of the ratios (test/reference) for Cmax and AUC was in the range 80.00 -125.00%.
The methods used in this study for the pharmacokinetic calculations and statistical evaluation are considered acceptable.

Results
24 subjects were included in the study. 24 subjects were treated; 24 subjects completed the study and included in the statistical analysis according to the protocol.
The inclusion and exclusion criteria are considered acceptable for a bioequivalence study.

Descriptive statistics

Pharmacokinetic parameter	Arithmetic Means (±SD)	
	Test product	Reference product
AUC_t (h*µg/mL)	1138.53 (±181.86)	1150.88 (±152.06)
AUC_i (h*µg/mL)	1237.07 (±208.40)	1251.52 (±181.61)
C_{max} (µg/mL)	71.62 (±15.55)	75.05 (±11.53)
T_{max}[1] (h)	0.92 (0.50-3.00)	1.00 (0.50-1.67)

[1] Median (Min, Max)

Bioequivalence evaluation

Pharmacokinetic parameter	Geometric Mean Ratio Test/Ref	Confidence Intervals	CV%[1]
AUC_t	98.53%	95.15% - 102.03%	7.1%
C_{max}	94.10%	89.09% - 99.39%	11.1%

[1] Estimated from the Residual Mean Squares.

Based on the statistical analysis submitted by the Applicant, the test product is equivalent to the reference with respect to the extent and rate of absorption/exposure as the 90% confidence intervals (90% CI) for the ln-transformed Cmax and AUCt are within the acceptance range of 80.00-125.00%.

Pharmacodynamics/Clinical efficacy/Clinical safety

No new studies on pharmacodynamics, clinical efficacy or clinical safety have been submitted. Provided that bioequivalence with the reference product is demonstrated, additional data is not necessary.

Summary Pharmacovigilance system

The Applicant has submitted a signed Summary of the Applicant's and/or Proposed Future MAH's* Pharmacovigilance System. Provided that the Pharmacovigilance System Master File fully complies with the new legal requirements as set out in the Commission Implementing Regulation and as detailed in the GVP module, the RMS considers the Summary acceptable.>

* applicable in case the future MAH in RMS/CMSs will be different from the applicant

Risk Management Plan

The MAH has submitted a risk management plan (version 2.0, 15 March 2022), 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 Olseron 550 mg film-coated tablets.

There are neither proposed additional pharmacovigilance activities nor proposed additional risk minimisation measures planned for Olseron 550 mg film-coated tablets.

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.

Periodic Safety Update Report (PSUR)
With regard to PSUR submission, the MAH should take the following into account:

- For medicinal products authorized under the legal basis of Article 10(1) or Article 10a of Directive 2001/83/EC, no routine PSURs need to be submitted, unless otherwise specified in the EURD list.

Common renewal date
Five years after the finalization of the marketing authorisation procedure.

IV BENEFIT RISK ASSESSMENT

This application concerns a generic medicinal product referencing Antalgin 550 mg film-coated tablets. Bioequivalence between the test and reference product has been adequately demonstrated. No clinically relevant differences in efficacy or safety are anticipated in the proposed indication.

V RECOMMENDATIONS AND CONDITIONS FOR MARKETING AUTHORISATION AND PRODUCT INFORMATION

V.1 List of recommendations not falling under Article 21a/22 of Directive 2001/83/EC

Description	Due date

V.2 List of conditions pursuant to Article 21a or specific obligations pursuant to Article 22 of Directive 2001/83/EC

- **<Additional risk minimisation measures (including educational material)>**

The educational material should contain the following key elements:

-

- **<Obligation to conduct post-authorisation measures in accordance with Article 21a of Directive 2001/83>**

The MAH shall complete, within the stated timeframe, the below measures:

Description	Due date

- **<Specific obligation to complete post-authorisation measures for <the marketing authorisation under exceptional circumstances in accordance with Article 22 of Directive 2001/83/EC>**

<This being a marketing authorisation under exceptional circumstances and pursuant to Article 22 of Directive 2001/83/EC, the MAH shall complete, within the stated timeframe, the following measures:>

Description	Due date

V.3 Summary of Product Characteristics (SmPC)

The approved SmPC is available in the MRI Product Index.

V.4 Package Leaflet (PL)

V.4.1 Package Leaflet

The approved PL is available in the MRI Product Index.

V.4.2 Assessment of User Testing

No full user consultation with target patient groups on the package leaflet has been performed on the basis of a bridging report making reference to Naproxen Generis 550 mg film-coated tablets. The bridging report submitted by the applicant has been found acceptable.

V.5 Labelling

The approved Labelling is available in the MRI Product Index.

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
-	-	-	-	-	-