

Public Assessment Report

Scientific discussion

Pomalidomide Devatis 1 mg, 2 mg, 3 mg and 4 mg, hard capsules (pomalidomide)

NL/H/5818/001-004/DC

Date: 17 September 2025

This module reflects the scientific discussion for the approval of Pomalidomide Devatis 1 mg, 2 mg, 3 mg and 4 mg, hard capsules. The procedure was finalised on 7 November 2024. For information on changes after this 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 Pomalidomide Devatis 1 mg, 2 mg, 3 mg and 4 mg, hard capsules, from Devatis GmbH.

The product in combination with bortezomib and dexamethasone is indicated in the treatment of adult patients with multiple myeloma who have received at least one prior treatment regimen including lenalidomide.

The product in combination with dexamethasone is indicated in the treatment of adult patients with relapsed and refractory multiple myeloma who have received at least two prior treatment regimens, including both lenalidomide and bortezomib, and have demonstrated disease progression on the last therapy.

A comprehensive description of the up-to-date indications and posology is given in the SmPC.

The marketing authorisation has been granted pursuant to Article 10(1) of Directive 2001/83/EC, which concerns a generic application.

In this decentralised procedure, essential similarity is proven between the new product and the innovator product Imnovid 1 mg, 2 mg, 3 mg and 4 mg, hard capsules, which has been registered in the EEA via a centralised procedure (EU/1/13/850) since 5 August 2013.

The concerned member states (CMS) involved in this procedure were Austria, Denmark, Finland, Germany, Norway and Sweden.

Similarity assessment

According to Article 8(1) of Regulation (EC) No 141/2000, no marketing authorisation can be granted for a product similar to an orphan medicinal product for a period of ten years, when this concerns a similar medicinal product with the same therapeutic indication (treatment of multiple myeloma). The MAH has provided a similarity assessment between Pomalidomide Devatis and the current orphan products authorised in the EU. These orphan products are:

Indicated for the treatment of multiple myeloma:

- Abecma (idecabtagene vicleucel), Bristol-Myers Squibb Pharma EEIG, EU/1/21/1539 orphan designation number EU/3/17/1863
- Blenrep (belantamab mafodotin), GlaxoSmithKline (Ireland) Limited, EU/1/20/1474 orphan designation number EU/3/17/1925
- Carvykti (ciltacabtagene autoleucel), Janssen-Cilag International NV, EU/1/22/1648 orphan designation number EU/3/20/2252
- Darzalex (daratumumab), Janssen-Cilag International NV, EU/1/16/1101 orphan designation number EU/3/13/1153
- Farydak (panobinostat), zr pharma& GmbH, EU/1/15/1023 orphan designation number EU/3/12/1063

- Kyprolis (carfilzomib), Amgen Europe B.V., EU/1/15/1060
orphan designation number EU/3/08/548
- Ninlaro (ixazomib), Takeda Pharma A/S, EU/1/16/1094
orphan designation number EU/3/11/899
- Talvey (talquetamab), Janssen-Cilag International NV, EU/1/23/1748
orphan designation number EU/3/21/2486

The assessment included the comparison of the therapeutic indication, mechanism of action and principal (molecular) structure. The similarity assessment report was completed in August 2024. After consideration of the MAH arguments, Pomalidomide Devatis is not considered similar to the orphan products with regard to the mechanism of action and principal molecular structure.

Therefore, with reference to Article 8 of Regulation (EC) No. 141/2000, the existence of any market exclusivity for Abecma, Blenrep, Carvykti, Darzalex, Farydak, Kyprolis, Ninlaro and Talvey does not prevent the granting of the marketing authorisation of Pomalidomide Devatis.

II. QUALITY ASPECTS

II.1 Introduction

Pomalidomide Devatis is a hard capsule. Each capsule contains as active substance 1 mg, 2 mg, 3 mg or 4 mg pomalidomide.

The 1 mg hard capsule has an opaque dark blue cap and opaque ivory body imprinted with "1 mg" in black. The capsule has a length of 14 mm.

The 2 mg hard capsule has an opaque dark blue cap and opaque light orange body imprinted with "2 mg" in white. The capsule has a length of 14 mm.

The 3 mg hard capsule has an opaque dark blue cap and opaque light green body imprinted with "3 mg" in white. The capsule has a length of 18 mm.

The 4 mg hard capsule has an opaque dark blue cap and opaque light blue body imprinted with "4 mg" in white. The capsule has a length of 18 mm.

The excipients are:

Capsule contents (for all four strengths) - lactose, pregelatinised starch (maize) and sodium stearyl fumarate

Capsule shell

1 mg hard capsule - gelatine, titanium dioxide (E171, indigotine (E132), yellow iron oxide (E172), erythrosine (E127) and black ink (shellac, black iron oxide (E172), propylene glycol and ammonium hydroxide)

2 mg hard capsule - gelatine, titanium dioxide (E171, indigotine (E132), yellow iron oxide (E172), erythrosine (E127 and white ink (shellac, titanium dioxide (E171) and propylene glycol (E1520))

3 mg hard capsule - gelatine, titanium dioxide (E171, indigotine (E132), yellow iron oxide (E172), black iron oxide (E172), patent blue V (E131), erythrosine (E127) and white ink (shellac, titanium dioxide (E171) and propylene glycol (E1520))

4 mg hard capsule - gelatine, titanium dioxide (E171, indigotine (E132), yellow iron oxide (E172), patent blue V (E131), erythrosine (E127) and white ink (shellac, titanium dioxide (E171) and propylene glycol (E1520))

The capsules are packed in polyvinyl chloride (PVC)/polychlorotrifluoroethylene (PCTFE) - aluminium blisters packs.

II.2 Drug Substance

The active substance is pomalidomide, an established active substance not described in the European or Pharmacopoeia of a member state. The active substance is a yellow to dark yellow white powder and is practically insoluble in water. The active substance is chiral and is a racemic mixture. The active substance exists in one polymorphic form.

The Active Substance Master File (ASMF) procedure is used for the active substance. The main objective of the ASMF procedure, commonly known as the European Drug Master File (EDMF) procedure, is to allow valuable confidential intellectual property or 'know-how' of the manufacturer of the active substance (ASM) to be protected, while at the same time allowing the applicant or marketing authorisation holder (MAH) to take full responsibility for the medicinal product, the quality and quality control of the active substance. Competent Authorities/EMA thus have access to the complete information that is necessary to evaluate the suitability of the use of the active substance in the medicinal product.

Manufacturing process

The manufacturing process is covered by the ASMF. Starting materials are used in two chemical reactions and one purification step. The resulting product is dried and micronised. Adequate specifications have been adopted for starting materials, solvents and reagents. The active substance has been adequately characterised and the manufacturing process is described in sufficient detail. Particle size is controlled through the drug substance specifications.

Quality control of drug substance

The active substance specification is considered adequate to control the quality. Batch analytical data demonstrating compliance with this specification have been provided for three batches.

Stability of drug substance

Stability data on the active substance have been provided for six batches in accordance with applicable European guidelines demonstrating the stability of the active substance for 60 months when stored under the stated conditions.

II.3 Medicinal Product

Pharmaceutical development

The product is an established pharmaceutical form and its development is adequately described in accordance with the relevant European guidelines. The choice of excipients is justified, and their functions are explained. The choices of packaging and manufacturing process are adequately justified based on the dosage form. Comparative dissolution studies have been performed at 3 pH values (1.2, 4.5 and 6.8) in support of bioequivalence and the biowaiver of strengths which is acceptable. The QC dissolution method has been justified and discriminatory power has been sufficiently demonstrated. The optimal composition and manufacturing process parameters have been adequately investigated. The pharmaceutical development of the product is acceptable.

Manufacturing process

The manufacturing process consists of blending, followed by capsule filling and packaging. The process has been validated according to relevant European/ICH guidelines. The product is manufactured by well-known manufacturing techniques. Process validation data on the product have been presented for four batches per strength, in accordance with the relevant European guidelines.

Control of excipients

The excipients comply with Ph.Eur. and in-house requirements. These specifications are acceptable.

Quality control of drug product

The finished product specifications are adequate to control the relevant parameters for the dosage form. The specification includes tests for appearance, identification (HPLC and UV), water content, assay, uniformity of dosage units (content uniformity), dissolution, related substances and microbiological controls. Limits in the specification have been justified and are considered appropriate for adequate quality control of the product. An adequate nitrosamines risk evaluation report has been provided. No risk for presence of nitrosamines in the drug product was identified.

Satisfactory validation data for the analytical methods have been provided.

Batch analytical data from three to four batches per strength from the proposed production site have been provided, demonstrating compliance with the release specification.

Stability of drug product

Stability data on the product have been provided for three batches per strength stored at 25°C/ 60% RH (36 or 24 months) and 40°C/75% RH (6 months). The stability was tested in accordance with applicable European guidelines. Photostability studies were performed in

accordance with ICH recommendations and showed that the product is photostable. On basis of the data submitted, a shelf life was granted of 36 months. No specific storage conditions needed to be included in the SmPC or on the label.

Specific measures concerning the prevention of the transmission of animal spongiform encephalopathies

Scientific data and/or certificates of suitability issued by the EDQM for excipient lactose have been provided and compliance with the Note for Guidance on Minimising the Risk of Transmitting Animal Spongiform Encephalopathy Agents via medicinal products has been satisfactorily demonstrated.

II.4 Discussion on chemical, pharmaceutical and biological aspects

Based on the submitted dossier, the member states consider that Pomalidomide Devatis has a proven chemical-pharmaceutical quality. Sufficient controls have been laid down for the active substance and finished product.

No post-approval commitments were made.

III. NON-CLINICAL ASPECTS

III.1 Ecotoxicity/environmental risk assessment (ERA)

Since Pomalidomide Devatis is intended for generic substitution, this will not lead to an increased exposure to the environment. An environmental risk assessment was therefore not deemed necessary.

III.2 Discussion on the non-clinical aspects

This product is a generic formulation of Imnovid which is available on the European market. Reference was made to the preclinical data obtained with the innovator product. A non-clinical overview on the pharmacology, pharmacokinetics and toxicology has been provided, which was based on up-to-date and adequate scientific literature. The overview justifies why there is no need to generate additional non-clinical pharmacology, pharmacokinetics and toxicology data. Therefore, the member states agreed that no further non-clinical studies are required.

IV. CLINICAL ASPECTS

IV.1 Introduction

Pomalidomide is a well-known active substance with established efficacy and tolerability. A clinical overview has been provided, which is based on scientific literature. The member states

agreed that no further clinical studies are required, besides one bioequivalence study for the 4 mg strength, which is discussed below. In addition, a biowaiver was requested for the lower strengths 1 mg, 2 mg and 3 mg.

IV.2 Pharmacokinetics

The MAH conducted a bioequivalence study in which the pharmacokinetic profile of the test product Pomalidomide Devatis 4 mg, hard capsules (Deva Holding A.S., Turkey) was compared with the pharmacokinetic profile of the reference product Imnovid 4 mg, hard capsules (Celgene Europe B.V., the Netherlands).

The choice of the reference product in the bioequivalence study has been justified by comparison of dissolution study results and composition. The formula and preparation of the bioequivalence batch was identical to the formula proposed for marketing.

Biowaiver

The following general requirements were met for the waiver for additional strength, according to the EMA Bioequivalence guideline:

- a. All strengths are manufactured by the same process
- b. The qualitative composition of the different strengths is the same
- c. The composition of the strengths are quantitatively proportional, i.e. the ratio between the amount of each excipient to the amount of active substance(s) is the same for all strengths

The dissolution was investigated according to the EMA Bioequivalence guideline. The calculated f_2 similarity factor values for the 1 mg, 2 mg and 3 mg strengths, each of them compared to the 4 mg strength at three pH values (pH 1.2, pH 4.5 and pH 6.8), were within criteria (>50%). An f_2 value between 50 and 100% suggests that the dissolution profiles of the two compared dissolution profiles are similar.

Bioequivalence study

Design

A single-dose, randomised, two-period, two-treatment, two-sequence, crossover bioequivalence study was carried out under fasted conditions in 24 healthy male subjects, aged 23-44 years. Each subject received a single dose (4 mg) of one of the two pomalidomide formulations. The tablet was orally administered with 240 ml water after an overnight fast of 10 hours. There were two dosing periods, separated by a washout period of 15 days.

Blood samples were collected pre-dose and at 0.5, 1, 1.33, 1.66, 2, 2.33, 2.66, 3, 3.5, 4, 5, 6, 8, 10, 12, 16, 24 and 48 hours after administration of the products.

The design of the study is acceptable.

Analytical/statistical methods

The analytical method has been adequately validated and is considered acceptable for analysis of the plasma samples. The methods used in this study for the pharmacokinetic calculations and statistical evaluation are considered acceptable.

Results

A total of 24 subjects were enrolled in the study. One subject was withdrawn due to an AE (adverse event) before the second dosing period (increased bilirubin level). In total, 23 subjects were eligible for pharmacokinetic analysis.

Table 1. Pharmacokinetic parameters (non-transformed values; arithmetic mean \pm SD, t_{max} (median, range)) of pomalidomide, 4 mg under fasted conditions.

Treatment N=23	AUC _{0-t} (ng.h/mL)	AUC _{0-∞} (ng.h/mL)	C _{max} (ng/mL)	t _{max} (h)
Test	608.5 \pm 157.8	633.4 \pm 159.0	68.6 \pm 13.7	2.33 (1.00 - 4.00)
Reference	611.8 \pm 138.7	629.3 \pm 136.3	64.5 \pm 10.9	2.33 (1.00 - 5.00)
*Ratio (90% CI)	0.99 (0.93 – 1.06)	-	1.06 (0.98 -1.14)	-
AUC_{0-∞} 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 to t = 48 hours C_{max} Maximum plasma concentration t_{max} Time after administration when maximum plasma concentration occurs CI Confidence interval				

**In-transformed values*

Conclusion on bioequivalence study:

The 90% confidence intervals calculated for AUC_{0-t}, AUC_{0-∞} and C_{max} are within the bioequivalence acceptance range of 0.80 – 1.25. Based on the submitted bioequivalence study Pomalidomide Devatis 4 mg, hard capsules is considered bioequivalent with Imnovid 4 mg, hard capsules.

The MEB 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).

The biowaiver of strengths is acceptable. The results of the BE study with 4 mg formulation can be extrapolated to other strengths 1 mg, 2 mg and 3 mg, according to conditions in Guideline on the Investigation of Bioequivalence CPMP/EWP/QWP/1401/98 Rev. 1/Corr*, section 4.1.6.

IV.3 Risk Management Plan

The MAH has submitted a risk management plan (RMP), 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 Pomalidomide Devatis. At the time of approval, the most recent version of the RMP was version 0.3 dated 11 September 2024.

Table 2. Summary table of safety concerns as approved in RMP

Important identified risks	-Teratogenicity -Severe infection due to neutropenia and pancytopenia -Thrombocytopenia and bleeding -Cardiac failure -Non-melanoma skin cancer
Important potential risks	-Cardiac arrhythmia -Other second primary malignancies
	-None

The routine pharmacovigilance and risk minimisation measures, the safety information and the product information are aligned to the reference medicinal product Imnovid and are acceptable.

At the time of approval of this product, it was considered that a pregnancy prevention programme (PPP) should be implemented and monitored as additional pharmacovigilance activity to investigate risks of teratogenicity, in line with the reference product.

Besides routine risk minimisation measures, the MAH provided additional risk minimisation measures (aRMM) for all the safety concerns as mentioned in Table 2, in a controlled access program. The aRMM consist of HCP Educational Materials and Patient Educational Materials. The educational Healthcare Professional's Kit must contain the following key elements:

- Educational Healthcare Professional brochure
- Educational brochures for patients
- Patient card
- Risk awareness forms
- Information where to find the latest Summary of Product Characteristics (SmPC)

Overall, the safety specification, additional pharmacovigilance activities and additional risk minimisation measures are considered to be in line with the RMP of the reference product Imnovid (version 17.0) and are acceptable.

The MAH shall implement and monitor a PPP in each member state. Details of the PPP should be agreed with the national competent authorities in each member state and put in place prior to the launch of the medicinal product. Safety updates will be submitted with future PSURs (as required per EURD list).

The MAH shall agree on the details and the implementation of the controlled access programme in each member state prior to launch of the medicinal product.

The MAH shall agree the final text of the contents of the Educational Healthcare Professional's Kit with the national competent authority in each member state prior to launch of the medicinal product and ensure that the materials contain all key elements.

IV.4 Discussion on the clinical aspects

For this authorisation, reference is made to the clinical studies and experience with the innovator product Imnovid. The MAH demonstrated through a bioequivalence study that the pharmacokinetic profile of the product is similar to the pharmacokinetic profile of this reference product. Risk management is adequately addressed. This generic medicinal product can be used instead of the reference product.

V. USER CONSULTATION

A user consultation with target patient groups on the package leaflet (PL) has been performed on the basis of a bridging report making reference for the content to Imnovid 1 mg, 2 mg, 3 mg and 4 mg, hard capsules (EU/1/13/850/001-008). The PL of Pomalidomide Devatis covers all four strengths, as the key safety information is identical for all four strengths. This is in accordance with the PL of the reference product Imnovid 1 mg, 2 mg, 3 mg and 4 mg hard capsules. For the layout reference is made to Lenalidomide Devatis 2.5 mg, 5 mg, 7.5 mg, 10 mg, 15 mg, 20 mg and 25 mg, hard capsules (NL/H/4989/001-007/DC).

The bridging report submitted by the MAH has been found acceptable; bridging is justified for both content and layout of the leaflet.

VI. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

Pomalidomide Devatis 1 mg, 2 mg, 3 mg and 4 mg, hard capsules have a proven chemical-pharmaceutical quality and are generic forms of Imnovid 1mg, 2 mg, 3 mg and 4 mg, hard capsules. Imnovid is a well-known medicinal product with an established favourable efficacy and safety profile.

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

The Board followed the advice of the assessors.

There was no discussion in the CMD(h). Agreement between member states was reached during a written procedure. The member states, on the basis of the data submitted, considered that essential similarity has been demonstrated for Pomalidomide Devatis with the reference product, and have therefore granted a marketing authorisation. The decentralised procedure was finalised with a positive outcome on 7 November 2024.

**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
NL/H/5818/001-004/IB/001	Change in the specification parameters and/or limits of the immediate packaging of the finished product - Other variation	No	16 July 2025	Approved	N.A.