COLLEGE TER BEOORDELING VAN GENEESMIDDELEN

Public Assessment Report

Scientific discussion

Plerixafor Vivanta 20 mg/ml, solution for injection (plerixafor)

NL/H/5513/001/DC

Date: 28 October 2025

This module reflects the scientific discussion for the approval of Plerixafor Vivanta 20 mg/ml, solution for injection. The procedure was finalised on 8 November 2023. 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
G-CSF	Granulocyte-Colony Stimulating Factor
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 Plerixafor Vivanta 20 mg/ml, solution for injection, from Vivanta Generics s.r.o.

The product is indicated for:
Adult patients
in combination with granulocyte-colony stimulating factor (G-CSF) to enhance mobilisation of haematopoietic stem cells to the peripheral blood for collection and subsequent autologous transplantation in adult patients with lymphoma or multiple myeloma whose cells mobilise poorly.

Paediatric patients (1 to less than 18 years):
in combination with G-CSF to enhance mobilisation of haematopoietic stem cells to the peripheral blood for collection and subsequent autologous transplantation in children with lymphoma or solid malignant tumours, either:

- pre-emptively, when circulating stem cell count on the predicted day of collection after adequate mobilisation with G-CSF (with or without chemotherapy) is expected to be insufficient with regards to desired hematopoietic stem cells yield, or
- who previously failed to collect sufficient haematopoietic stem cells.

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 Mozobil 20 mg/ml, solution for injection, which has been registered in the EEA by Genzyme Europe B.V. via a centralised procedure (EU/1/09/537/001) since 31 July 2009.

The concerned member states (CMS) involved in this procedure were Croatia and Germany.

II. QUALITY ASPECTS

II.1 Introduction

Plerixafor Vivanta is a solution for injection. It is a clear colourless to pale yellow colour solution, with a pH of 6.0-7.5. It has an osmolality of 260-320 mOsmol/kg and is free from visible particulate matter.

Each ml solution for injection contains as active substance 20 mg plerixafor. Each vial contains 24 mg plerixafor in 1.2 ml solution for injection.

The excipients are sodium chloride, hydrochloric acid (pH adjustment), sodium hydroxide (pH adjustment) and water for injection.

The solution is packed in 2 ml clear type-I glass vial having chlorobutyl rubber stopper with aluminium flip-off seal.

II.2 Drug Substance

The active substance is plerixafor and not described in the European Pharmacopoeia (Ph.Eur.). Plerixafor is a white to off-white crystalline solid. It is freely soluble in ethanol (95%), slightly soluble in water and insoluble in acetone. Although polymorphism is known for plerixafor, it is not relevant for the current drug product as it concerns a solution..

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 consists of three chemical steps and one purification step.
In the (publicly accessible) EPAR for Mozobil (link to: https://www.ema.europa.eu/en/documents/overview/mozobil-epar-medicine-overview_en.pdf) in principle the same synthesis route is followed.
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. The drug substance is hygroscopic. The four additional precautionary measures are considered acceptable.

Quality control of drug substance

The active substance specification is established in-house by the ASMF-holder and is considered adequate to control the quality of the drug substance. All analytical procedures are adequately described. Micro-biological methods have been sufficiently verified.
Batch analytical data demonstrating compliance with this specification have been provided for three production batches.

Stability of drug substance

Stability data on the active substance have been provided for three production scaled batches in accordance with applicable European guidelines. Based on the data submitted, a retest period could be granted of 48 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.

Manufacturing process

The manufacturing process consists of compounding, mixing, filtration, filling/stopping/and sealing, external vial washing, terminal sterilisation, optical inspection before/after terminal sterilisation and packing. The process has been validated according to relevant European/ICH guidelines. Process validation data on the product have been presented for three batches in accordance with the relevant European guidelines.

Control of excipients

All excipients comply with the specifications of Ph. Eur. These specifications are acceptable.

Microbiological attributes

All involved sterilisation processes have been described and validated. The provided data on container closure system, including data on the chosen rubber stopper, and microbial attributes are considered adequate.

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, HPLC identification, pH, osmolality, foreign and particulate contamination, extractable volume, HPLC assay, HPLC related substances, bacterial endotoxins test, sterility test, colour absorbance at 420 nm and % transmittance at 650 nm. Limits in the specification have been justified and are considered appropriate for adequate quality control of the product. Adequate data/discussion is provided for limitation of genotoxic impurities and elemental impurities. 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 batches have been provided, demonstrating compliance with the specification.

Stability of drug product

Stability data on the product have been provided from three batches stored at 25°C/ 60% RH (36 months) and 40°C/75% RH (6 months) in accordance with applicable European guidelines. The drug product manufacturer has restricted the shelf-life of drug product to 24 months to ensure better quality of the drug product.

The product has been subjected to photostability evaluation. Based on the study, it is concluded that Plerixafor is not affected when exposed to light.

In addition, the product has been subjected to freeze thaw study evaluation at -20°C and 40°C/75% RH. Based on the study, it is concluded that Plerixafor is not affected when exposed to temperature cycling.
Based on these data, the proposed pack is suitable for its intended use.

On basis of the data submitted, a shelf life of the unopened vial was granted of 2 years. The labelled storage conditions are: "Store below 25°C".
After opening of the vial, and after transfer to a sterile syringe, chemical and physical in-use stability has been demonstrated for seven days at room temperature (20 - 25°C) and at 2 - 8°C.

From a microbiological point of view the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at room temperature (20°C – 25°C), unless withdrawal has taken place in controlled and validated aseptic conditions.

Specific measures concerning the prevention of the transmission of animal spongiform encephalopathies
There are no substances of ruminant animal origin present in the product nor have any been used in the manufacturing of this product, so a theoretical risk of transmitting TSE can be excluded.

II.4 Discussion on chemical, pharmaceutical and biological aspects

Based on the submitted dossier, the member states consider that Plerixafor Vivanta 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 Plerixafor Vivanta 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 Mozobil 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

Plerixafor 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.

IV.2 Pharmacokinetics

Plerixafor Vivanta 20 mg/ml, solution for injection is a parenteral formulation and therefore fulfils the exemption mentioned in the Note for Guidance on bioequivalence "5.1.6 parenteral solutions", which states that a bioequivalence study is not required if the product is administered as an aqueous intravenous solution containing the same active substance in the same concentration as the currently authorised reference medicinal product (NfG CPMP/EWP/QWP 1401/98). The quantitative composition of Plerixafor Vivanta is entirely the same as the originator. Therefore, it may be considered as therapeutic equivalent, with the same efficacy/safety profile as known for the active substance of the reference medicinal product. The current product can be used instead of its reference product.

IV.3 Risk Management Plan

The MAH has submitted a risk management plan, 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 Plerixafor Vivanta. At the time of approval, the most recent version of the RMP was version 1.0 dated 12 August 2021.

Table 1. Summary table of safety concerns as approved in RMP

Important identified risks	Splenomegaly and splenic rupture
Important potential risks	• Interstitial lung disease • Myocardial infarction • Tumour cell mobilisation • Drug level NOS increased • Anxiety, hallucination (including hallucination, visual hallucination, and auditory hallucination) • Effect on embryo-foetal development (including teratogenicity and foetal growth restriction)

Missing information	Safety profile in paediatric under 2 years of age

The member states agreed that routine pharmacovigilance activities and routine risk minimisation measures are sufficient for the risks and areas of missing information.

IV.4 Discussion on the clinical aspects

For this authorisation, reference is made to the clinical studies and experience with the innovator product Mozobil. No new clinical studies were conducted. 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 to Mozobil 20 mg/ml, solution for injection, EMEA/H/C/001030. 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

Plerixafor Vivanta 20 mg/ml, solution for injection has a proven chemical-pharmaceutical quality and is a generic form of Mozobil 20 mg/ml, solution for injection. Mozobil is a well-known medicinal product with an established favourable efficacy and safety profile.

Since both the reference and current product are intended for parenteral use, no bioequivalence study is deemed necessary. A biowaiver has been granted.

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 Plerixafor Vivanta with the reference product, and have therefore granted a marketing authorisation. The decentralised procedure was finalised with a positive outcome on 8 November 2023.

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/5513/001 /IB/001/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 us • Introduction of a summary of pharmacovigilance system, changes in QPPV (including contact details) and/or changes in the Pharmacovigilance System Master File (PSMF) location	Yes No	6-11-2024	Approved	N.A.