COLLEGE TER BEOORDELING VAN GENEESMIDDELEN

Public Assessment Report

Scientific discussion

Irinotecan Glenmark 20 mg/ml, concentrate for solution for infusion (irinotecan hydrochloride trihydrate)

NL/H/5626/001/DC

Date: 24 November 2025

This module reflects the scientific discussion for the approval of Irinotecan Glenmark 20 mg/ml concentrate for solution for infusion. The procedure was finalised on 4 January 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 Irinotecan Glenmark 20 mg/ml concentrate for solution for infusion, from Glenmark Pharmaceuticals s.r.o.

The product is indicated for the treatment of patients with advanced colorectal cancer:

- in combination with 5-fluorouracil and folinic acid in patients without prior chemotherapy for advanced disease,
- as a single agent in patients who have failed an established 5-fluorouracil containing treatment regimen.

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 Campto 20 mg/ml, concentrate for solution for infusion (NL RVG 22820) which has been registered in the Netherlands by Pfizer B.V. since 1998 (original product).

The concerned member state (CMS) involved in this procedure was Italy.

II. QUALITY ASPECTS

II.1 Introduction

Irinotecan Glenmark is a pale yellow colour clear aqueous solution.

One ml of concentrate contains 20 mg irinotecan hydrochloride trihydrate equivalent to 17,33 mg irinotecan.

The excipients are: sorbitol (E420), lactic acid (E270), sodium hydroxide (E524; for pH-adjustment), hydrochloric acid (E507; for pH-adjustment) and water for injections.

The concentrate for solution for infusion is packed in type-1 glass vials with 20 mm bromo butyl rubber stopper with dark blue colour seal for 2 ml, 15 ml and 25 ml.

II.2 Drug Substance

The active substance is irinotecan hydrochloride trihydrate, an established active substance described in the European Pharmacopoeia (Ph.Eur.). The active substance is a pale yellow to yellow crystalline powder, sparingly soluble in water, in ethanol (96%) and in methanol.

Irinotecan hydrochloride trihydrate shows polymorphism. For this product, a specific polymorphic form is consistently produced.

The CEP procedure is used for the active substance. Under the official Certification Procedures of the EDQM of the Council of Europe, manufacturers or suppliers of substances for pharmaceutical use can apply for a certificate of suitability concerning the control of the chemical purity and microbiological quality of their substance according to the corresponding specific monograph, or the evaluation of reduction of Transmissible Spongiform Encephalopathy (TSE) risk, according to the general monograph, or both. This procedure is meant to ensure that the quality of substances is guaranteed and that these substances comply with the Ph.Eur.

Manufacturing process
A CEP has been submitted; therefore no details on the manufacturing process have been included.

Quality control of drug substance
The active substance specification is considered adequate to control the quality and is in line with the CEP with additional tests for polymorphism, residual solvents (besides the required test for chloroform from the CEP), microbial limits and bacterial endotoxins. The specification is acceptable in view of the various European guidelines. Batch analytical data demonstrating compliance with this specification have been provided for three batches.

Stability of drug substance
The active substance is stable for 48 months when stored under the stated conditions. Assessment thereof was part of granting the CEP (and has been granted by the EDQM).

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 explained. A Quality Target Product Profile (QTPP) has been provided, critical quality attributes of the drug product were defined and a risk assessment on the formulation and manufacturing process parameters on the defined drug product quality attributes was provided according to the principles of ICH Q8.

Manufacturing process
The manufacturing process has been validated according to relevant European/ICH guidelines. Process validation data on the product have been presented for eleven batches (three exhibit batches of 2 ml, 5 ml and 15 ml fill volume and two exhibit batches of 25 ml fill volume) in accordance with the relevant European guidelines.

Control of excipients
The excipients comply with Ph. Eur. requirements. These specifications are acceptable.

Microbiological attributes
The drug substance is packed in the packaging stated on the CEP. Container closure system is identical to global markets.

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 description, identity, pH, colour of solution, light transmission, extractable volume, particulate contamination sub-visible and visible particles, bacterial endotoxins, sterility, assay, related substances, osmolality and clarity of solution. 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 twelve batches (three commercial minimum scale batches of the 2 ml and 5 ml, four commercial minimum scale batches of the 15 ml and two commercial minimum scale batches of the 25 ml) from the proposed production site have been provided, demonstrating compliance with the specification.

Stability of drug product
Stability data on the product have been provided for twelve batches ((3x 2 ml and 5 ml, 4x 15 ml, 2x 25 ml) stored at 25°C/ 60% RH (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 packed in the amber coloured vials is stable when exposed to light. On basis of the data submitted, a shelf life was granted of two years. The labelled storage conditions are 'This medicinal product does not require any special storage conditions'.

In-use stability data have been provided demonstrating that the product remains stable for 28 days following dilution, when stored in low-density polyethylene (LDPE) or polyvinyl chloride (PVC) containers between 5°C and 30°C, protected from light.

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 Irinotecan Glenmark has a proven chemical-pharmaceutical quality. Sufficient controls have been laid down for the active substance and finished product.

The following post-approval commitment was made:

- The MAH commits to conduct long-term stability studies (at 25°C ± 2°C and 60% ± 5% RH) of Irinotecan 20 mg/ml concentrate for solution for infusion (2 ml fill, 5 ml fill, 15 ml fill and 25 ml fill), on a minimum of one marketed production batch per year in the marketing packaging material.

III. NON-CLINICAL ASPECTS

III.1 Ecotoxicity/environmental risk assessment (ERA)

Since Irinotecan Glenmark 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 Campto 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

Irinotecan hydrochloride trihydrate 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

Irinotecan Glenmark 20 mg/ml concentrate for solution for infusion 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 Irinotecan Glenmark 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 Irinotecan Glenmark. At the time of approval, the most recent version of the RMP was version 1.0 dated 4 October 2022.

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

Important identified risks	• Delayed diarrhoea • Acute and severe cholinergic syndrome • Interstitial lung disease • Myocardial ischaemic events • Blood disorders including neutropenia, thrombocytopenia, anaemia and febrile neutropenia • Infections • Drug toxicity in patients with reduced uridine diphosphate glucuronosyltransferase activity
Important potential risks	• Drug interaction with CYP3A inducers • Drug interaction with CYP3A inhibitors • Interaction between Irinotecan and neuromuscular blocking agents • Interaction between irinotecan and oral anticoagulant • Use in elderly population • Use in patients with bowel obstruction
Missing information	• Use in patients with impaired renal function • Use in Pregnancy and lactation • Effect on fertility

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 Campto. 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

The package leaflet (PL) 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 PL was English.

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 Irinotecan Koanaa 20 mg/ml, concentrate for solution or infusion, RVG 119107. 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

Irinotecan Glenmark 20 mg/ml concentrate for solution for infusion has a proven chemical-pharmaceutical quality and is a generic form of Campto 20 mg/ml, concentrate for solution for infusion. Campto 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 Irinotecan Glenmark with the reference product, and have therefore granted a marketing authorisation. The decentralised procedure was finalised with a positive outcome on 4 January 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
N.A.	N.A.	N.A.	N.A.	N.A.	N.A.