



Medicines & Healthcare products
Regulatory Agency

Public Assessment Report

National Procedure

**Enrylaze 10 mg/0.5 mL solution for
injection/infusion**

crisantaspase

PLGB 31626/0007

JAZZ PHARMACEUTICALS UK LIMITED

LAY SUMMARY

Enrylaze 10 mg/0.5 mL solution for injection/infusion crisantaspase

This is a summary of the Public Assessment Report (PAR) for Enrylaze 10 mg/0.5 mL solution for injection/infusion. It explains how this product was assessed and its authorisation recommended, as well as its conditions of use. It is not intended to provide practical advice on how to use this product.

This product will be referred to as Enrylaze in this lay summary for ease of reading.

This product has been authorised by the Medicines and Healthcare products Regulatory Agency (MHRA) for Great Britain (consisting of England, Scotland and Wales). In coming to its decision, MHRA has relied on a European Commission (EC) decision on 15/09/2023 (EMA/H/C/005917/0000), in accordance with the advice from the Committee for Medicinal Products for Human Use (CHMP). This is known as the EC Decision Reliance Procedure.

This application was approved under Regulation 50 of the Human Medicines Regulation 2012, as amended (previously Article 8.3 of Directive 2001/83/EC, as amended).

For practical information about using Enrylaze, patients should read the Patient Information Leaflet (PIL) or contact their doctor or pharmacist.

What is Enrylaze and what is it used for?

Enrylaze contains the active substance recombinant crisantaspase. It is a medicine used alongside other medicines to treat acute lymphoblastic leukaemia (ALL) and lymphoblastic lymphoma (LBL). Enrylaze can be given to patients aged 1 months of age or older.

How does Enrylaze work?

Enrylaze works by decreasing the amount of a protein called asparagine. This protein is needed by the ALL and LBL cancer cells to survive.

How is Enrylaze used?

The pharmaceutical form of this medicine is solution for injection/infusion, and the route of administration is by an infusion into the patient's veins over a 2-hour period, or an injection into the patient's muscle, several injection sites may be used (intramuscular, intravenous).

The dosage and how this medicine is administered may vary depending on the patient's condition, body surface area and response to therapy.

For further information on how Enrylaze is used, refer to the PIL and Summary of Product Characteristics (SmPC) available on the Medicines and Healthcare products Regulatory Agency (MHRA) website.

This medicine can only be obtained with a prescription.

The patient should ask the administering healthcare practitioner if they have any questions concerning their medicine.

What benefits of Enrylaze have been shown in studies?

The benefits of Enrylaze were evaluated in a study involving adults and children with ALL or LBL who had developed hypersensitivity or silent inactivation following use of E. coli-derived asparaginase. The study did not compare Enrylaze with other medicines or placebo (a dummy treatment).

In this study, 90% (44 out of 49) of patients given Enrylaze by injection achieved nadir serum asparaginase activity (NSAA) levels ≥ 0.1 U/mL (a measure corresponding to the complete depletion of blood asparagine) after 72 hours of receiving a first course of treatment; 96% (47 out of 49) achieved NSAA levels ≥ 0.1 U/mL after 48 hours.

For those patients given Enrylaze by infusion, 40% (20 out of 50) achieved NSAA levels ≥ 0.1 U/mL after 72 hours of receiving a first course of treatment; 90% (53 out of 59) achieved NSAA levels ≥ 0.1 U/mL after 48 hours.

What are the possible side effects of Enrylaze?

For the full list of all side effects reported with this medicine, see Section 4 of the PIL or the SmPC available on the MHRA website.

If a patient gets any side effects, they should talk to their doctor, pharmacist or nurse. This includes any possible side effects not listed in the product information or the PIL that comes with the medicine. Patients can also report suspected side effects themselves, or a report can be made on their behalf by someone else who cares for them, directly via the Yellow Card scheme at <https://yellowcard.mhra.gov.uk> or search for 'MHRA Yellow Card' online. By reporting side effects, patients can help provide more information on the safety of this medicine.

Why was Enrylaze approved?

MHRA decided that the benefits are greater than the risks and recommended that this medicine can be approved for use.

What measures are being taken to ensure the safe and effective use of Enrylaze?

As for all newly-authorised medicines, an Risk Management Plan (RMP) has been developed for Enrylaze. The RMP details the important risks of Enrylaze, how these risks can be minimised, any uncertainties about Enrylaze (missing information), and how more information will be obtained about the important risks and uncertainties.

There are no safety concerns associated with use of Enrylaze.

The information included in the SmPC and the PIL is compiled based on the available quality, non-clinical and clinical data, and includes appropriate precautions to be followed by healthcare professionals and patients. Side effects of Enrylaze are continuously monitored and reviewed including all reports of suspected side-effects from patients, their carers, and healthcare professionals.

An RMP and a summary of the pharmacovigilance system have been provided with this application and are satisfactory.

Other information about Enrylaze

A marketing authorisation was granted in Great Britain on 30 January 2024.

The full PAR for Enrylaze follows this summary.

This summary was last updated in April 2024.

TABLE OF CONTENTS

I.	INTRODUCTION	6
II.	PRODUCT INFORMATION	7
III.	QUALITY ASPECTS	7
IV.	NON-CLINICAL ASPECTS	7
V.	CLINICAL ASPECTS	7
VI.	RISK MANAGEMENT PLAN (RMP)	7
VII.	USER CONSULTATION	7
VIII.	OVERALL CONCLUSION, BENEFIT/RISK AND RECOMMENDATION	7
	TABLE OF CONTENT OF THE PAR UPDATE	9

I. INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the Medicines and Healthcare products Regulatory Agency (MHRA) considered that the application for Enrylaze 10 mg/0.5 mL solution for injection/infusion (PLGB 31626/0007) could be approved.

The product is approved for the following indications:

As a component of a multi-agent chemotherapeutic regimen for the treatment of acute ALL and LBL in adult and paediatric patients (1 month and older) who developed hypersensitivity or silent inactivation to *E. coli*-derived asparaginase.

crisantaspase is a protein made in the laboratory by recombinant DNA technology.

Asparaginase is an enzyme that catalyses the conversion of the amino acid L-asparagine into L-aspartic acid and ammonia. The pharmacological effect of Enrylaze is based on the killing of leukemic cells due to depletion of plasma asparagine. Leukemic cells with low expression of asparagine synthetase have a reduced ability to synthesize asparagine, and therefore is dependent on an exogenous source of asparagine for survival.

This product has been authorised by MHRA for Great Britain (consisting of England, Scotland and Wales). In coming to its decision, MHRA has relied on a European Commission (EC) decision on 15/09/2023 (EMA/H/C/005917/0000), in accordance with the advice from the Committee for Medicinal Products for Human Use (CHMP). For the scientific discussion of the quality, non-clinical and clinical assessment conducted by the European Medicines Agency (EMA), please refer to the European Public Assessment Report, available on the EMA website.

This application was approved under Regulation 50 of the Human Medicines Regulation 2012, as amended (previously Article 8.3 of Directive 2001/83/EC, as amended).

In line with the legal requirements for children's medicines, the application included a licensing authority decision on the agreement of a paediatric investigation plan (PIP) *MHRA-100741-PIP01-22*.

At the time of the submission of the application the PIP was not yet completed as some measures were deferred.

The licensing authority issued an opinion on compliance of the PIP *MHRA-100741-PIP01-22-C*.

The MHRA has been assured that acceptable standards of Good Manufacturing Practice (GMP) are in place for this product at all sites responsible for the manufacture, assembly and batch release of this product.

A Risk Management Plan (RMP) and a summary of the pharmacovigilance system have been provided with this application and are satisfactory.

A marketing authorisation was granted on 30 January 2024.

II. PRODUCT INFORMATION**SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)**

The SmPC is in line with current guidelines and was satisfactory.

PATIENT INFORMATION LEAFLET (PIL)

The PIL is in line with current guidelines and is satisfactory.

LABEL

The labelling is in line with current guidelines and is satisfactory.

III. QUALITY ASPECTS

MHRA considered that the quality data submitted for this application is satisfactory.

The grant of a marketing authorisation was recommended.

IV. NON-CLINICAL ASPECTS

MHRA considered that the non-clinical data submitted for this application is satisfactory.

The grant of a marketing authorisation was recommended.

V. CLINICAL ASPECTS

MHRA considered that the clinical data submitted for this application is satisfactory.

The grant of a marketing authorisation was recommended.

VI. RISK MANAGEMENT PLAN (RMP)

The applicant has submitted an RMP, in accordance with the requirements of Regulation 182 of The Human Medicines Regulation 2012, as amended. The applicant proposes only routine pharmacovigilance and routine risk minimisation measures for all safety concerns. This is acceptable.

VII. USER CONSULTATION

A full colour mock-up of the Patient Information Leaflet (PIL) was provided with the application in accordance with legal requirements, including user consultation.

VIII. OVERALL CONCLUSION, BENEFIT/RISK AND RECOMMENDATION

The quality of the product is acceptable. The non-clinical and clinical data submitted have shown the positive benefit/risk of this product as a component of a multi-agent chemotherapeutic regimen for the treatment of acute ALL and LBL in adult and paediatric patients (1 month and older) who developed hypersensitivity or silent inactivation to E. coli-derived asparaginase.

Recommendations for future quality development the following post-authorisation measures are in place:

1. The applicant should commit to develop a new HCP test method or, alternatively, to revalidate the current HCP method as recommended in Ph. Eur. 2.6.34.

2. Concerning the method description for determination of catalytic efficiency, the applicant should commit to include additional controls to assure method validity and to comply with GMP requirements with respect to trending.
3. The applicant should commit to perform supplemental validation of the analytical method for Protein Concentration.
4. The applicant should commit to perform an evaluation of a potential potency assay method optimisation.
5. The applicant should commit to re-evaluate the requirement for conducting a stressed sample routine test for active substance release once batch data from a sufficient number of batches are available.
6. The applicant should commit to adjust the fill weight target and change the extractable volume acceptance criterion to comply with Ph. Eur. requirements via a post-approval variation application.

The Summaries of Product Characteristics (SmPCs), Patient Information Leaflet (PIL) and labelling are satisfactory.

In accordance with legal requirements, the current approved UK versions of the SmPC and PIL for this product are available on the MHRA website.

IX. TABLE OF CONTENT OF THE PAR UPDATE

Steps taken after the initial procedure with an influence on the Public Assessment Report (non-safety variations of clinical significance).

Please note that only non-safety variations of clinical significance are recorded below and in the annexes to this PAR. The assessment of safety variations, where significant changes are made, are recorded on the MHRA website or European Medicines Agency (EMA) website. Minor changes to the marketing authorisation are recorded in the current SmPCs and/or PIL available on the MHRA website.

Application type	Scope	Product information affected	Date of grant	Outcome	Assessment report attached Y/N

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