Medicines & Healthcare products Regulatory Agency

MHRA

Public Assessment Report

National Procedure

Minjuvi 200 mg powder for concentrate for solution for infusion

PLGB 42338/0016

tafasitamab

INCYTE BIOSCIENCES UK LIMITED

LAY SUMMARY

Minjuvi 200 mg powder for concentrate for solution for infusion tafasitamab

This is a summary of the Public Assessment Report (PAR) for Minjuvi 200 mg powder for concentrate for solution for 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 Minjuvi in this lay summary for ease of reading.

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

What is Minjuvi and what is it used for?
This product has been authorised by MHRA for Great Britain (consisting of England, Scotland and Wales). This procedure relies on a European Commission (EC) decision on 26 August 2021 (EMEA/H/C/ 005436/0000), in accordance with the advice from the Committee for Medicinal Products for Human Use (CHMP). This is known as the EC Decision Reliance Procedure.

Minjuvi is used to treat adults with a cancer of B cells called diffuse large B-cell lymphoma.

How does Minjuvi work?
MINJUVI is used to treat adults with a cancer of B cells called diffuse large B-cell lymphoma. It is used when the cancer has come back after, or not responded to, previous treatment, if patients cannot be treated with a stem cell transplant instead.

MINJUVI contains the active substance tafasitamab. This is a type of protein called a monoclonal antibody designed to kill cancer cells. This protein acts by attaching to a specific target on the surface of a type of white blood cell called B cells or B lymphocytes. When tafasitamab sticks to the surface of these cells, the cells die.

How is Minjuvi used?
The pharmaceutical form of this medicine is powder for concentrate for solution and the route of administration is infusion.

The recommended dose of Minjuvi is 12 mg per kg body weight administered as an intravenous infusion according to the following schedule:
- Cycle 1: infusion on day 1, 4, 8, 15 and 22 of the cycle.
- Cycles 2 and 3: infusion on day 1, 8, 15 and 22 of each cycle.
- Cycle 4 until disease progression: infusion on day 1 and 15 of each cycle.

Each cycle has 28 days.

In addition, patients should self-administer lenalidomide capsules at the recommended starting dose of 25 mg daily on days 1 to 21 of each cycle. The starting dose and subsequent dosing may be adjusted according to the lenalidomide Summary of Product Characteristics (SmPC).

Minjuvi plus lenalidomide in combination is given for up to twelve cycles.

For further information on how Minjuvi is used, refer to the PIL and 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 the medicine.

What are the possible side effects of Minjuvi?
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 behalf of someone else they care for, directly via the Yellow Card scheme at www.mhra.gov.uk/yellowcard or search for 'MHRA Yellow Card' online. By reporting side effects, patients can help provide more information on the safety of this medicine.

The most common side effects with Minjuvi (which may affect more than 1 in 10 people) are a reduced number of some types of blood cells in your body, such as white blood cells called neutrophils (possible symptoms: fever of 38 °C or above, or any symptoms of an infection), platelets (possible symptoms: unusual bruising or bleeding without or on only minor injury), red blood cells (possible symptoms: pale skin or lips, tiredness, shortness of breath); bacterial, viral or fungal infections such as respiratory tract, infections, bronchitis, lung inflammation, urinary tract infections; rash; low blood potassium level in tests; muscle cramps; back pain; swelling of arms and/or legs due to build-up of fluid; weakness, tiredness, feeling generally unwell; fever; diarrhoea; constipation; abdominal pain; nausea; vomiting; cough, shortness of breath; and decreased appetite.

Why was Minjuvi approved?
MHRA decided that the benefits are greater than the risks and recommended that this medicine/these medicines can be approved for use.

Minjuvi has been authorised with a Conditional Marketing Authorisation (CMA). CMAs are intended for medicinal products that fulfil an unmet medical need, such as for serious and life-threatening diseases where no satisfactory treatment methods are available or where the product offers a major therapeutic advantage. CMAs may be granted where comprehensive clinical data is not yet complete, but it is judged that such data will become available soon. Adequate evidence of safety and efficacy to enable the MHRA to conclude that the benefits are greater than the risks is required. Any new information on Minjuvi will be reviewed every year and this report will be updated as necessary.

Minjuvi has been authorised as a GB Orphan medicine. Orphan medicines are intended for use against rare conditions that are life-threatening or chronically debilitating. To qualify as an orphan medicine, certain criteria, for example concerning the rarity of the disease and the lack of currently available treatments, must be fulfilled.

What measures are being taken to ensure the safe and effective use of Minjuvi?
A Risk Management Plan (RMP) has been developed to ensure that Minjuvi is used as safely as possible. Based on this plan, safety information has been included in the SmPC and the

PIL, including the appropriate precautions to be followed by healthcare professionals and patients.

Known side effects are continuously monitored. Furthermore, new safety signals reported by patients/healthcare professionals will be monitored and reviewed continuously.

The mandatory post-authorisation safety studies required for the European authorisation are feasible and likely to generate data relevant to the GB population.

Other information about Minjuvi
A marketing authorisation was granted in Great Britain (consisting of England, Scotland and Wales) on 8 October 2021

The full PAR for Minjuvi follows this summary.

This summary was last updated in December 2021.

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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 Minjuvi 200 mg powder for concentrate for solution for infusion (PLGB 42338/0016) could be approved.

The product is approved for the following indication:
Minjuvi is indicated in combination with lenalidomide followed by Minjuvi monotherapy for the treatment of adult patients with relapsed or refractory diffuse large B cell lymphoma (DLBCL) who are not eligible for autologous stem cell transplant (ASCT).

The name of the active substance is tafasitamab.
Tafasitamab is an Fc-enhanced monoclonal antibody that targets the CD19 antigen expressed on the surface of pre-B and mature B lymphocytes. Upon binding to CD19, tafasitamab mediates B-cell lysis through engagement of immune effector cells like natural killer cells, γδ T cells and phagocytes, and through direct induction of cell death (apoptosis).

The Fc modification results in enhanced antibody-dependent cellular cytotoxicity and antibody dependent cellular phagocytosis.

This product has been authorised by MHRA for Great Britain (consisting of England, Scotland and Wales). This procedure relies on a European Commission (EC) decision on 26 August 2021 (EMEA/H/C/005436/0000), 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 submitted under Regulation 50 of the Human Medicines Regulation 2012, as amended (previously Article 8(3) of Directive 2001/83/EC, as amended).

This application was evaluated for fulfilment of orphan designation criteria and was examined by the Commission on Human Medicines (CHM) in September 2020. It was concluded that fulfilment of the criteria for approval as an orphan medicinal product was satisfactorily demonstrated. Please see Annex 1 for a summary of the orphan.

In line with the legal requirements for children's medicines, the application included a licensing authority decision on the agreement of a full product-specific waiver (P/0294/2019).

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 8 October 2021.

II. ASSESSOR'S COMMENTS ON THE PRODUCT INFORMATION

SUMMARY OF PRODUCT CHARACTERITICS (SmPC)

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

PATIENT INFORMATION LEAFLET

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
This application was assessed by CHMP in the Centralised procedure and a positive opinion was adopted. There are no additional GB-specific concerns and approval of this application is recommended from a quality perspective.

IV. NON-CLINICAL ASPECTS
This application was assessed by CHMP in the Centralised procedure and a positive opinion was adopted. There are no additional GB-specific concerns and approval of this application is recommended from a non-clinical perspective.

V. CLINICAL ASPECTS
This application was assessed by CHMP in the Centralised procedure and a positive opinion was adopted. There are no additional GB-specific concerns and approval of this application is recommended from a clinical perspective.

The grant of a marketing authorisation is 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
The results of the user consultation with target patient groups on the package leaflet submitted by the applicant show that the package leaflet meets the criteria for readability as set out in the Guideline on the readability of the label and package leaflet of medicinal products for human use.

VIII. OVERALL CONCLUSION, BENEFIT/RISK AND RECOMMENDATION
The quality of the product is acceptable, and no new non-clinical or clinical safety concerns have been identified. The benefit/risk balance is, therefore, considered to be positive.

Minjuvi has been authorised with a Conditional Marketing Authorisation (CMA). The Marketing Authorisation Holder shall complete, within the stated timeframe, the following measures:

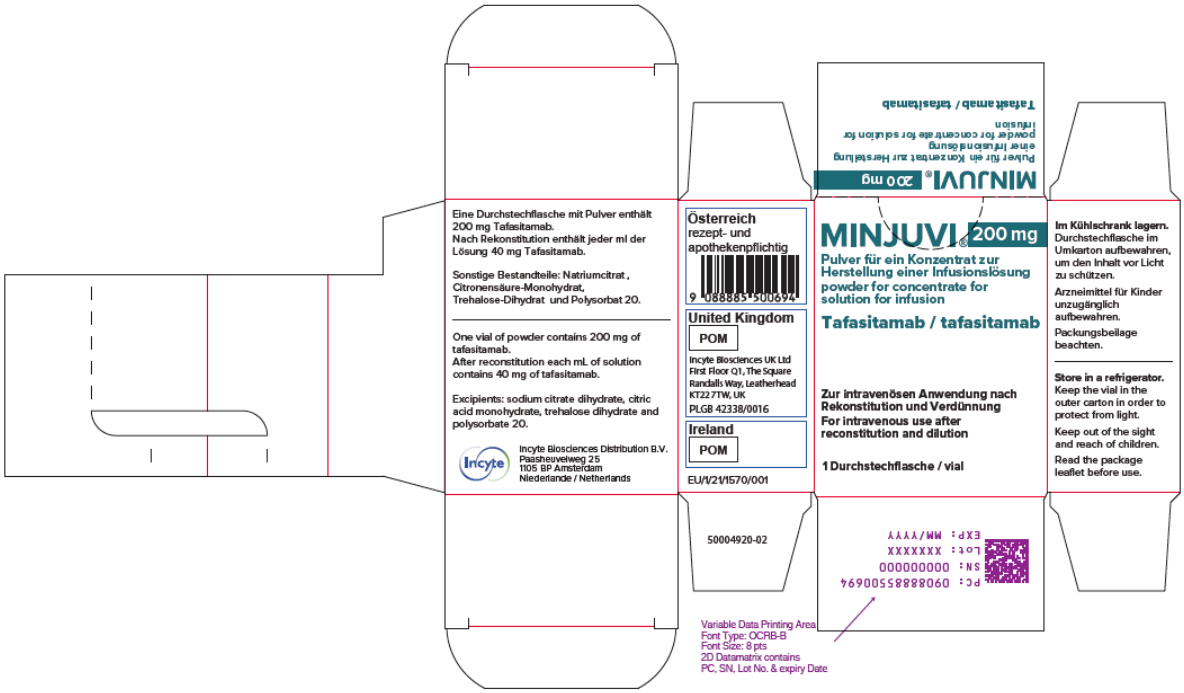
Description	Due date
In order to provide further evidence of the efficacy and safety of tafasitamab in DLBCL, the MAH will provide the results of an open-label single-arm phase 2 study of tafasitamab plus lenalidomide in patients with relapsed or refractory diffuse large B-cell lymphoma	December 2026
In order to provide further evidence of the safety of tafasitamab in DLBCL, the MAH will provide the results of a phase 3, multicentre, randomized, double-blind, placebo-controlled trial comparing the efficacy and safety of tafasitamab plus lenalidomide in addition to R-CHOP versus R-CHOP in previously untreated, high-intermediate and high-risk patients with newly-diagnosed diffuse large B-cell lymphoma (DLBCL)	December 2025

In order to provide further evidence of the safety of tafasitamab in DLBCL, the MAH will provide the results of a phase 2/3, randomised, multicentre study of tafasitamab with bendamustine versus rituximab with bendamustine in patients with relapsed or refractory Diffuse Large B-Cell Lymphoma (R-R DLBCL) who are not eligible for high-dose chemotherapy (HDC) and autologous stem-cell transplantation (ASCT)	December 2025

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 is available on the MHRA website.

Representative copies of the labels at the time of UK licensing are provided below.



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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**

Annex 1

Summary of fulfilment of the criteria for orphan drug designation

Product:	Minjuvi 200 mg powder for concentrate for solution for infusion
Active substance:	Tafasitamab
Orphan Designation Number:	PLGB 42338/0016/OD1

Background:
This application was evaluated for fulfilment of orphan designation criteria by the Commission on Human Medicines (CHM) and the orphan designation criteria were considered fulfilled.

Evaluation:
Orphan condition
The orphan condition proposed was diffuse large B-cell lymphoma (DLBCL). This is acceptable and in line with the guidance on what constitutes a valid condition.

Non-Hodgkin lymphoma (NHL) is the most common hematologic malignancy and about 30% of NHLs are diffuse large B-cell lymphomas (DLBCL). The underlying cause is not known though the condition is associated with gene mutations.

Orphan indication
The orphan indication for Minjuvi 200 mg powder for concentrate for solution for infusion is 'in combination with lenalidomide followed by Minjuvi monotherapy for the treatment of adult patients with relapsed or refractory diffuse large B cell lymphoma who are not eligible for autologous stem cell transplant'.

Life threatening/debilitating condition
DLBCL is a life-threatening condition.

Prevalence of the Condition in Great Britain (GB)
Suitable evidence has been provided that demonstrates that, at the time of orphan designation, the condition affects less than 5 in 10,000 people in GB. This does not exceed the upper limit of prevalence for orphan designation, which is 5 in 10,000 people in GB.

Existing methods of treatment
Guidelines from the European Society for Medical Oncology (ESMO) include chimeric antigen receptor (CAR)-T cell therapies requiring administration in accredited centres as an existing method of treatment for diffuse large B-cell lymphoma (DLBCL). It is noted that CAR-T cell therapies require time to be manufactured which will lead to delay in treatment of the patient.

The Applicant has considered all existing treatment methods.

Justification of significant benefit
Methods for the treatment of the orphan condition already exist in GB. Suitable justification has been provided that Minjuvi 200 mg powder for concentrate for solution for infusion provide a significant benefit to those affected by the condition as specified in the orphan indication.

Significant benefit has been demonstrated with the product as demonstrated by the submitted clinical studies. Tafasitamab has a different mode of action compared to other products and so offers an alternative compared to existing methods.

Conclusion on acceptability of orphan designation
Minjuvi 200 mg powder for concentrate for solution for infusion fulfils the criteria for an orphan drug designation.

All medicines that gain an orphan drug designation from the UK Licensing Authority are listed on its publicly available Orphan Register until the end of the market exclusivity period. The authorised orphan indication defines the scope of orphan market exclusivity.

Decision: Grant