Date: 13 May 2022
Swissmedic, Swiss Agency for Therapeutic Products

Swiss Public Assessment Report

Minjuvi

International non-proprietary name: tafasitamab

Pharmaceutical form: powder for concentrate for solution for infusion

Dosage strength(s): 200 mg

Route(s) of administration: intravenous

Marketing Authorisation Holder: Incyte Biosciences International

Marketing Authorisation No.: 68083

Decision and Decision date: temporary authorisation in accordance with Art. 9a TPA approved on 22.03.2022

Note:

Assessment Report as adopted by Swissmedic with all information of a commercially confidential nature deleted.

The SwissPAR is a “final” document, which provides information relating to a submission at a particular point in time and will not be updated after publication.

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Table of contents

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1 Terms, Definitions, Abbreviations

ADCC	Antibody-dependent cellular cytotoxicity
ADCP	Antibody-dependent cellular phagocytosis
ASCT	Autologous stem cell transplant
CART-cell	Chimeric antigen receptor T-cell
CHMP	Committee for Medicinal Products for Human Use, a committee of EMA
CHO cells	Chinese hamster ovary cells
CI	Confidence interval
CR	Complete response
DLBCL	Diffuse large B-cell lymphoma
ECOG	Eastern Cooperative Oncology Group
EMA	European Medicines Agency
FDA	U.S. Food and Drug Administration
ICH	International Council for Harmonisation
IRC	Independent review committee
IPI	International prognostic index
LoQ	List of Questions
MAH	Marketing Authorisation Holder
MRHD	Maximum recommended human dose
MTD	Maximum tolerated dose
NHL	Non-Hodgkin lymphoma
ORR	Objective response rate
OS	Overall survival
PD	Pharmacodynamics
PFS	Progression-free survival
PK	Pharmacokinetics
R-CHOP	Combination therapy consisting of rituximab, cyclophosphamide, doxorubicin, vincristine and prednisone
RMP	Risk Management Plan
R/R	Relapsed or refractory
SwissPAR	Swiss Public Assessment Report
TPA	Federal Act of 15 December 2000 on Medicinal Products and Medical Devices (SR 812.21)
TTP	Time to progression

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2 Background Information on the Procedure

2.1 Applicant's Request(s)

New Active Substance status
The applicant requested the status of a new active entity for the active substance tafasitamab of the medicinal product mentioned above.

Orphan drug status
The applicant requested Orphan Drug Status in accordance with Article 4 a^{decies} no. 2 of the TPA.
The Orphan Status was granted on 31 August 2020.

Temporary authorisation for human medicinal products
The applicant requested a temporary authorisation in accordance with Art. 9a TPA.

Project Orbis
The applicant requested a marketing authorisation procedure within the framework of Project Orbis. Project Orbis is a programme coordinated by the US FDA to review and approve promising cancer treatments. It provides a framework for concurrent submission and review of oncology products among international partners. It currently involves the regulatory authorities of: Australia (TGA), Brazil (ANVISA), Israel (MOH), Canada (HC), Singapore (HSA), Switzerland (Swissmedic), and the United Kingdom (MHRA).

2.2 Indication and Dosage

2.2.1 Requested 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, or who refuse, an autologous stem cell transplant (ASCT).

2.2.2 Approved 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) after at least one prior line of systemic therapy including an anti-CD20 antibody, who are not eligible for autologous stem cell transplant (ASCT).

2.2.3 Requested Dosage

Summary of the applied standard dosage:

Table 1 Proposed Dose Regimen and Administration Schedule

Drug	Dose	Route	Treatment Schedule	Duration
Tafasitamab	12.0 mg/kg	IV Infusion	Cycle 1: Days 1, 4, 8, 15, and 22 Cycles 2 and 3: Days 1, 8, 15, and 22 Cycle 4 onwards: Days 1 and 15	Until disease progression
Lenalidomide	Starting dose: 25 mg	Oral Capsule	Cycles 1 to 12 (once per day): Days 1-21 Treatment with lenalidomide may be modified or discontinued based on clinical and/or laboratory findings	12 cycles

Each cycle has 28 days
IV = intravenous

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Premedication:
30 min - 2 hours before the Minjuvi infusion a premedication consisting of an antipyretic (e.g. paracetamol), H1 antagonist (e.g. diphenhydramine), H2 antagonist (e.g. cimetidine) or glucocorticosteroids (e.g. methylprednisolone) is compulsory for the first 3 infusions, after which it is optional for patients who have not suffered from infusion-related reactions.

2.2.4 Approved Dosage

(see appendix)

2.3 Regulatory History (Milestones)

Application	01 December 2020
Formal control completed	17 December 2020
List of Questions (LoQ)	15 April 2021
Answers to LoQ	14 July 2021
First Predecision (rejection)	4 October 2021
Answers to first Predecision	19 October 2021
Second Predecision (approval)	15 December 2021
Answers to second Predecision	10 February 2022
Final Decision	22 March 2022
Decision	approval (temporary authorisation in accordance with Art. 9a TPA)

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3 Medical Context

Diffuse large B cell lymphomas (DLBCL) represent approximately one third of all non-Hodgkin lymphomas (NHL) and consist of a group of aggressive mature B-cell malignancies. For nearly two decades, the standard first-line chemotherapy has been 6 to 8 cycles of immuno-chemotherapy with the anti-CD20 antibody rituximab in combination with cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP). Approximately half of patients will relapse, and their prognosis is dismal. Patients who are young and fit enough to receive salvage chemotherapy and respond to it may then receive high-dose chemotherapy followed by autologous haematopoietic stem cell transplantation (ASCT). Patients not eligible for ASCT due to age or comorbidities, or patients having relapsed after ASCT, have no standard treatment option and will receive palliative treatment with a median overall survival time of 6 to 9 months. Therefore, these patients present an unmet medical need.

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4 Quality Aspects

4.1 Drug Substance

Tafasitamab, the active substance of Minjuvi, is an Fc-enhanced monoclonal antibody that targets the CD19 antigen expressed on the surface of pre-B and mature B lymphocytes. CD19 is broadly and homogeneously expressed across different B-cell malignancies, including diffuse large B-cell lymphoma. CD19 amplifies B-cell receptor signalling and tumour cell proliferation. Upon binding to CD19, tafasitamab mediates B-cell lysis through 1) engagement of immune effector cells, like NK cells and phagocytes, and 2) direct induction of cell death (apoptosis).
Two amino acid modifications were introduced into the Fc-domain of tafasitamab, leading to increased affinity to Fcγ receptors. The strongest increase was observed for Fcγ receptor IIIa. This results in more potent immune effector cell mechanisms, including enhanced antibody-dependent cellular cytotoxicity (ADCC) and antibody-dependent cellular phagocytosis (ADCP).
The drug substance tafasitamab is expressed in a eukaryotic recombinant Chinese hamster ovary (CHO) cell line. Tafasitamab is secreted as a disulfide-linked glycosylated tetramer consisting of two identical 451 amino acid heavy chains (HCs) and two identical 219 amino acid kappa light chains (LCs). The HC bears an N-linked glycosylation site at position N301.
The predicted average molecular weight of tafasitamab corresponding to the molecular formula without the attached glycan and excluding the C-terminal lysines is 147,170 Da and, with the G0F glycan structure attached, 150,060 daltons.
Tafasitamab is produced in a bioreactor. The cell culture supernatant is harvested by centrifugation, and the antibody is purified by several chromatographic and filtration steps, including virus inactivation and virus removal steps, formulation, filtration, and splitting. The manufacturing process has been validated with four full-scale drug substance batches. The characterisation of the drug substance and its impurities was performed using state of the art methods.
The specifications include e.g. tests for identity, heterogeneity, purity, and assays for potencies. All the analytical methods are described, and non-compendial methods have been validated in accordance with ICH guidelines.
Batch information and analytical release data from tafasitamab drug substance batches that were used for clinical supply, stability studies, process performance qualification or intended for market supply were provided.
The drug substance is stored at – 40°C. No significant changes were observed within the proposed storage conditions as well as under accelerated conditions. A shelf life of 36 months has been accepted.

4.2 Drug Product

Minjuvi is a lyophilised powder for reconstitution and intravenous infusion. Tafasitamab drug product is a white to slightly yellowish lyophilisate for reconstitution with water for injection. The container closure system consists of a type I glass vial closed with a butyl rubber stopper and an aluminium seal.
After reconstitution, tafasitamab is presented at a concentration of 40 mg/mL in a citrate-buffered, isotonic solution at pH 6.0. The surfactant polysorbate 20 and the osmolyte trehalose are used to obtain the required colloidal stability and osmolality. All excipients comply with current compendial standards.
The manufacturing process for the finished drug product consists of sterile filtration, filling and partial stoppering, lyophilisation including complete stoppering, crimping, vial coding, visual inspection, and secondary packaging and labelling. Process validation studies were executed at commercial scale using three validations batches.
The specifications for the drug product were set based on compendial requirements, experience from clinical trials, and commercial process capability. They include relevant tests for appearance and descriptions, general tests, identity, heterogeneity, purity, and potency. All non-compendial methods are validated in accordance with ICH guidelines.

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Batch analysis data from a total of 34 batches were provided. All batch release data comply with the corresponding specifications.
The container closure system for tafasitamab drug product consists of a type I borosilicate glass vial, closed with a coated rubber stopper and secured with an aluminium flip-off cap. All components coming into contact with the finished product comply with current compendial standards.
The drug product is stored at 2 – 8°C protected from light. No significant changes were observed within the proposed storage conditions. A shelf life of 36 months has been accepted.
The manufacturing processes for the drug substance and drug product incorporate adequate control measures to prevent contamination and maintain control with regard to viral and non-viral contaminants.

4.3 Quality Conclusions

The manufacturing processes (drug substance and drug product) are well described and demonstrate a consistent quality of drug substance and drug product. The shelf-life for the drug substance and drug product is supported by data from recommended storage conditions, as well as accelerated and stress studies. Safety aspects with regard to viral and non-viral contaminants were satisfactorily addressed.The risk for adventitious agents is minimised.

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5 Nonclinical Aspects

For Minjuvi (new active substance tafasitamab), the Division Nonclinical Assessment conducted an abridged evaluation based on assessment reports from FDA and EMA/CHMP.
Overall, the submitted nonclinical documentation is considered appropriate to support the approval of Minjuvi in the proposed indication. The pharmaco-toxicological profile was sufficiently characterised. The B-cell depletion and related microscopic changes observed in tafasitamab-treated monkeys at all doses are considered to be due to the intended pharmacological action.
In line with ICH guidelines S6 (R1) and S9, studies on genotoxicity and carcinogenicity were not conducted. The pivotal 13-week toxicity study in sexually mature cynomolgus monkeys included parameters on fertility. As agreed by FDA and EMA, no studies were conducted to evaluate the reproductive and developmental toxicity of tafasitamab. This is considered acceptable based on the proposed indication and intended patient population. The combination product lenalidomide is a teratogen and causes embryofetal lethality, and hence is contraindicated in pregnant women and women of child-bearing potential who are not using contraception. Due to the mechanism of action, tafasitamab may cause effects on the immune system of fetuses and newborns (B-cell depletion), which is addressed in the information for healthcare professionals.
Since tafasitamab is a protein it is not expected to pose a risk to the environment.

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6 Clinical and Clinical Pharmacology Aspects

6.1 Clinical Pharmacology

The evaluation of the clinical pharmacology data in this application has been carried out in reliance on previous regulatory decisions by FDA and EMA. The available assessment report and respective product information from FDA and EMA were used as a basis for the clinical pharmacology evaluation. For details concerning clinical pharmacology, see Chapter 8 of this report.

6.2 Dose Finding and Dose Recommendation

One phase 1 dose escalation study (XmAB5574-01) has been performed in 27 patients with relapsed or refractory (R/R) chronic lymphocytic leukaemia (CLL) or small lymphocytic lymphoma (SLL). This was the first-in-human trial with tafasitamab, which was administered intravenously (IV) as monotherapy at doses ranging from 0.3 to 12 mg/kg for up to seven 28-day cycles.

A total of 27 male and female subjects 40 to 84 years old were enrolled in six cohorts of tafasitamab: 0.3 mg/kg (n=1), 1 mg/kg (n=1), 3 mg/kg (n=3), 6 mg/kg (n=3), 9 mg/kg (n=3) and 12 mg/kg (n=16).

Tafasitamab was administered in Cycle 1 on Days 1, 4, 8, 15, and 22, and in Cycle 2 on Days 1, 8, 15, and 22, with a total of 9 doses of tafasitamab over two 28-day cycles of therapy. In the optional extended therapy phase for subjects in the 12 mg/kg cohort, 8 subjects could receive an additional 4 administrations as a single infusion every 28 days (Day 1 of Cycles 4, 5, 6, and 7) for an additional 20 weeks at the same dose level. The primary objectives were to identify the maximum tolerated dose (MTD) and/or recommended dose(s) of tafasitamab for further clinical studies; to characterise the safety and tolerability profile of IV dosing of tafasitamab; and to characterise the PK, PD, and immunogenicity of IV dosing of tafasitamab.

The dose-response study showed no benefit at the 3 mg/kg dose or below, although only two patients were treated at lower doses. Objective responses were seen in the 6, 9, and 12 mg/kg cohorts. Due to the acceptable safety profile of the highest administered dose, 12 mg/kg, this cohort was expanded to a total of 16 patients. In the 12 mg/kg cohort, tafasitamab showed preliminary antitumour efficacy with an objective response rate (ORR) of 37.5%. The best response was partial response (PR), and no patients experienced a complete response (CR) in any of the dose cohorts. The longest time to progression (TTP) and progression-free survival (PFS) were seen in the 12 mg/kg cohort. The 12 mg/kg dose level was considered the optimal dose and was used in subsequent studies. Overall, the selected dose is acceptable. However, no dose finding was performed for the combination with lenalidomide.

6.3 Efficacy

The L-MIND trial enrolled R/R diffuse large B cell lymphoma (DLBCL) patients who were not eligible for autologous stem cell transplantation (ASCT) or who refused ASCT. Patients received lenalidomide at the maximum authorised dose of 25 mg per day during the first 21 days of a 28-day cycle in addition to tafasitamab at 12 mg/kg body weight administered weekly during the first 3 cycles with an additional loading dose on day 4 of cycle 1. Starting with cycle 4, tafasitamab was administered every 2 weeks on days 1 and 15 of each cycle. Lenalidomide was administered for a maximum of 12 cycles. After 12 cycles, tafasitamab was continued as monotherapy in patients without disease progression. No dose-finding study was performed for the combination of the two agents. The rationale to combine lenalidomide with tafasitamab was lenalidomide's antiproliferative activity in addition to its activating effect on natural killer cells. In addition, preclinical data suggest a synergistic effect with tafasitamab. For DLBCL, lenalidomide as single agent is proposed only in relapsed/refractory patients with germinal centre B cell type of origin disease, and then possibly in combination with rituximab. Both agents, tafasitamab and lenalidomide, were chosen at their maximum tolerated doses. It remains unclear whether a lower dose of either agent could provide the same benefit.

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The L-MIND trial enrolled 81 patients, of whom 80 received the combination treatment. One patient never received lenalidomide because an adverse event of kidney injury was discovered after administration of the first dose of tafasitamab, and lenalidomide was therefore never started.

The objective response rate (ORR) assessed by an independent review committee (IRC) was 56.8% (46/81), with 39.5% (32/81) complete responses (CR). Duration of response was 43.9 months with approximately 29 months of follow-up. Median progression-free survival (PFS) was 11.6 months and median overall survival (OS) was 31.6 months.

While these findings are encouraging in a disease with an expected median OS of 6-9 months with current treatments, there are several uncertainties. This was a single-arm study and selection bias is a possibility. Only a minority of patients (23.5%) had presented an early disease relapse within < 12 months of first-line therapy, with 75% relapsing > 12 months after the first-line treatment. Of the 81 enrolled patients, only 71 had centrally confirmed DLBCL, the remaining patients had various low grade NHL. Patients who were eligible for ASCT but who refused this treatment option were also enrolled and may have a different prognosis from patients who are ineligible for ASCT.

Time to event endpoints are difficult to interpret in a single-arm study. The applicant submitted a matched cohort study of patients treated with lenalidomide monotherapy, which is not a recommended treatment for R/R DLBCL. This cohort study was based on medical records, and several biases were observed, such as worse ECOG performance status and higher international prognostic index (IPI) scores in the lenalidomide monotherapy cohort compared to patients from the L-MIND study. In addition, a retrospective matching cohort study cannot make up for the absence of randomisation, because there could be many other unrecognised confounders.

PFS censoring rules in the L-MIND study were addressed with a sensitivity analysis for patients having an event after a missed assessment, and for patients starting new anti-cancer therapy, counting it as an event since this indicates a possible clinical progression. This analysis was consistent with the primary analysis although, as expected, median PFS was shorter in the sensitivity analysis (8.4 months versus 11.6 months in the primary analysis).

Finally, there is also uncertainty as to whether anti-CD19 CART-cell therapy may lose efficacy if administered after treatment with tafasitamab. Two patients who discontinued the L-MIND study received CART-cell therapy as subsequent treatment. While one patient did not respond and died shortly afterwards, the other patient showed a response that was ongoing at the time of data cut-off. The uncertainty about the efficacy of anti-CD19 CART-cell therapy after tafasitamab is reflected in the product information in the section “Warnings and precautions”.

6.4 Safety

The most common adverse events (20%) observed in patients treated with tafasitamab are neutropenia, fatigue, anaemia, diarrhoea, thrombocytopenia, cough, pyrexia, peripheral oedema, respiratory tract infection, and decreased appetite. Most of the observed adverse events are known adverse drug reactions of lenalidomide. However, in the absence of a randomised trial, it is impossible to disentangle possible cumulative toxicity of the two substances. In particular, there were cases of QTc prolongation and syncope. Since the applicant was not able to demonstrate the absence of a possible causality with tafasitamab, a warning and precaution has been included in the product information. Currently, the presented safety database comprises 708 patients who either received the combination of tafasitamab with lenalidomide (80), tafasitamab monotherapy (142), or tafasitamab in combination with other anti-neoplastic agents.

6.5 Final Clinical and Clinical Pharmacology Benefit Risk Assessment

Promising efficacy is shown for tafasitamab in combination with lenalidomide in patients with R/R DLBCL regarding objective response rate (56.8%) as well as duration of response (43.9 months, 95% CI: 26.1, NR). However, given the single-arm study design as well as the small number of patients

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(only 71 patients had centrally confirmed DLBCL), time to event results such as progression-free survival as well as overall survival are difficult to interpret. The submitted safety data currently relate to 708 patients receiving tafasitamab as monotherapy (142) or in combination with other anti-neoplastic agents. However, only 80 patients received the combination of tafasitamab and lenalidomide. Rare, but potentially serious and/or severe, adverse reactions may have been missed. Currently, the presented data are insufficient for a definitive risk-benefit assessment and therefore cannot support a regular marketing authorisation. However, a temporary marketing authorisation is justified given the medical need, the manageable toxicity profile and the efficacy regarding response rate and durability of response. A randomised phase 3 trial is ongoing in relapsed/refractory DLBCL patients not eligible for ASCT, comparing tafasitamab plus bendamustine versus rituximab plus bendamustine (NCT02763319).

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7 Risk Management Plan Summary

The RMP summaries contain information on the medicinal products' safety profiles and explain the measures that are taken in order to further investigate and monitor the risks as well as to prevent or minimise them.
The RMP summaries are published separately on the Swissmedic website. Marketing Authorisation Holders are responsible for the accuracy and correctness of the content of the published RMP summaries. As the RMPs are international documents, their summaries might differ from the content in the information for healthcare professionals / product information approved and published in Switzerland, e.g. by mentioning risks occurring in populations or indications not included in the Swiss authorisations.

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8 Appendix

Approved Information for Healthcare Professionals

Please be aware that the following version of the information for healthcare professionals relating to Minjuvi was approved with the submission described in the SwissPAR. This information for healthcare professionals may have been updated since the SwissPAR was published.

Please note that the reference document, which is valid and relevant for the effective and safe use of medicinal products in Switzerland, is the information for healthcare professionals currently authorised by Swissmedic (see www.swissmedicinfo.ch).

Note:
The following information for healthcare professionals has been translated by the MAH. The Authorisation Holder is responsible for the correct translation of the text. Only the information for healthcare professionals approved in one of the official Swiss languages is binding and legally valid.

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▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected new or serious adverse reactions. See the "Undesirable effects" section for advice on the reporting of adverse reactions.

MINJUVI 200 mg powder for concentrate for solution for infusion

MINJUVI is authorised for a limited period of time (see section *"Properties/Effects"*).

Composition

Active substances

Tafasitamab (produced in Chinese hamster ovary cells by recombinant DNA technology.)

Excipients

Sodium citrate dihydrate, Citric acid monohydrate, Trehalose dihydrate, Polysorbate 20
One vial of MINJUVI contains 7.4 mg of sodium.

Pharmaceutical form and active substance quantity per unit

Powder for concentrate for solution for infusion (intravenous use).
White to slightly yellowish lyophilised powder.
Each vial contains 200 mg of tafasitamab.
After reconstitution, each mL contains 40 mg of tafasitamab.

Indications/Uses

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) after at least one prior line of systemic therapy including an anti-CD20 antibody, who are not eligible for autologous stem cell transplant (ASCT).

Dosage/Administration

MINJUVI must be administered by a healthcare professional experienced in treatment of cancer patients.
Pre-medication
Administer pre-medication to reduce the risk of infusion-related reactions 30 minutes to 2 hours prior to MINJUVI infusion. For patients not experiencing infusion-related reactions during the first 3 infusions, pre-medication is optional for subsequent infusions.
The pre-medication may include antipyretics (e.g. paracetamol), histamine H1 receptor blockers (e.g. diphenhydramine), histamine H2 receptor blockers (e.g. cimetidine), glucocorticosteroids (e.g. methylprednisolone).

Treatment of infusion-related reactions

If an infusion-related reaction occurs (Grade 2 and higher), interrupt the infusion. In addition, initiate appropriate medical treatment of symptoms through administration of an antihistamine and/or paracetamol or methylprednisolone (or equivalent) and, if necessary, further medicinal products (e.g. epinephrine, bronchodilator). After signs and symptoms are resolved or reduced to Grade 1, MINJUVI infusion can be resumed at a reduced infusion rate. In case of Grade 4 reaction, the infusion should be stopped immediately and treatement with MINJUVI should be permanently discontinued (see Table 1).

If a patient has had a Grade 1 to 3 infusion-related reaction, pre-medication should be administered before subsequent MINJUVI infusions.

Usual dosage

The recommended dose is 12 mg of MINJUVI per kg body weight administered as an intravenous infusion according to the following schedule. Each cycle has 28 days.

- Cycle 1: Administer the infusion on cycle days 1, 4, 8, 15 and 22.
- Cycles 2 and 3: Administer the infusion on days 1, 8, 15 and 22 of each cycle.
- Cycle 4 until disease progression: Administer the infusion on days 1 and 15 of each cycle.

In addition, patients should self-administer lenalidomide capsules at the recommended starting dose of 25 mg daily on days 1 to 21 of each 28-day cycle. The starting dose and subsequent dosing may be adjusted according to the lenalidomide professional information.

To ensure traceability of biotechnological medicinal products, it is recommended that the tradename and batch number should be documented for each treatment.

Duration of treatment

MINJUVI in combination with lenalidomide is given for up to twelve 28-day cycles.

After a maximum of twelve cycles of combination therapy, stop treatment with lenalidomide and continue MINJUVI infusions as single agent on days 1 and 15 of each 28-day cycle, until disease progression or unacceptable toxicity.

Dose adjustment following undesirable effects/interactions

Table 1 provides dose modifications in case of adverse reactions. For dose modifications regarding lenalidomide, please also refer to the lenalidomide professional information.

Table 1: Dose modifications in case of adverse reactions

Adverse Reaction	Severity	Dosage Modification
Infusion-related reactions *[see Warnings and precautions]*	Grade 2 (moderate)	• Interrupt MINJUVI infusion immediately and manage signs and symptoms. • Once signs and symptoms resolve or reduce to Grade 1, resume MINJUVI

Adverse Reaction	Severity	Dosage Modification
		infusion at no more than 50% of the rate at which the reaction occurred. If the patient does not experience further reaction within 1 hour and vital signs are stable, the infusion rate may be increased every 30 minutes as tolerated to the rate at which the reaction occurred.
	Grade 3 (severe)	• Interrupt MINJUVI infusion immediately and manage signs and symptoms. • Once signs and symptoms resolve or reduce to Grade 1, resume MINJUVI infusion at no more than 25% of the rate at which the reaction occurred. If the patient does not experience further reaction within 1 hour and vital signs are stable, the infusion rate may be increased every 30 minutes as tolerated to a maximum of 50% of the rate at which the reaction occurred. • If after rechallenge the reaction returns, stop the infusion immediately.
	Grade 4 (life-threatening)	• Stop the infusion immediately and permanently discontinue MINJUVI.
Myelosuppression *[see Warnings and precautions]*	Platelet count of less than 50,000/µL	• Withhold MINJUVI and lenalidomide and monitor complete blood count (CBC) weekly until platelet count is 50,000/µL or higher. • Resume MINJUVI at the same dose and lenalidomide at a reduced dose. Refer to lenalidomide professional information for dosage modifications.
	Neutrophil count of less than 1,000/µL for at least 7 days OR Neutrophil count of less than 1,000/µL with an increase of body temperature to 38°C or higher OR Neutrophil count of less than 500/µL	• Withhold MINJUVI and lenalidomide and monitor CBC weekly until neutrophil count is 1,000/µL or higher. • Resume MINJUVI at the same dose and lenalidomide at a reduced dose. Refer to lenalidomide professional information for dosage modifications.

Patients with hepatic disorders

The effect of hepatic impairment was not formally tested in dedicated clinical trials; however no clinically meaningful differences in the pharmacokinetics of tafasitamab were observed for mild

hepatic impairment (total bilirubin ≤ upper limit of normal (ULN) and aspartate aminotransferase (AST) > ULN, or total bilirubin 1 to 1.5 times ULN and any AST). The effect of moderate to severe hepatic impairment (total bilirubin > 1.5 times ULN and any AST) is unknown.

Patients with renal disorders

The effect of renal impairment was not formally tested in dedicated clinical trials; however, no clinically meaningful differences in the pharmacokinetics of tafasitamab were observed for mild to moderate renal impairment (creatinine clearance (CrCL) ≥ 30 and < 90 mL/min estimated by the Cockcroft-Gault equation). The effect of severe renal impairment to end-stage renal disease (CrCL < 30 mL/min) is unknown.

Elderly patients

No dose adjustment is needed for elderly patients (≥ 65 years). Among 81 patients treated in the L-MIND study, 56 (69%) patients were > 65 years of age. Patients > 65 years of age had a numerically higher incidence of serious treatment emergent adverse events (TEAEs) (55%) than patients ≤ 65 years (44%).

Children and adolescents

The safety and efficacy of tafasitamab in children under 18 years have not been studied. No data are available.

Mode of administration

MINJUVI is for infusion after reconstitution and dilution.

- For the first infusion of cycle 1, the intravenous infusion rate should be 70 mL/h for the first 30 minutes. Afterwards, increase the rate to complete the first infusion within a 2.5-hour period.
- All subsequent infusions should be administered over a period of 1.5 to 2 hours.
- Do not co-administer other medicines through the same infusion line.

Do not administer MINJUVI as an intravenous push or bolus.

For instructions on reconstitution and dilution of the medicinal product before administration, see Instructions for reconstitution and dilution.

Contraindications

Hypersensitivity to tafasitamab or any of the excipients listed under Composition.

Warnings and precautions

Infusion-related reactions

Infusion-related reactions may occur and have been reported more frequently during the first infusion; see section Undesirable Effects. Patients should be monitored closely throughout the infusion. Advise patients to contact their healthcare professionals if they experience signs and symptoms of infusion-related reactions including fever, chills, rash or breathing problems within 24 hours of infusion.

Premedicate patients prior to starting MINJUVI infusion (see section Dosage/Administration). Monitor patients frequently during infusion. Based on the severity of the infusion-related reaction, interrupt or discontinue treatment with MINJUVI (see section Dosage/Administration). Initiate appropriate medical management.

Myelosuppression

Treatment with MINJUVI can cause serious and/or severe myelosuppression including neutropenia, thrombocytopenia and anaemia (see section Undesirable Effects). Monitor complete blood counts throughout treatment and prior to administration of each treatment cycle. Withhold MINJUVI based on the severity of the adverse reaction (see Table 1).
Refer to the lenalidomide professional information for dosage modifications.

Neutropenia

Neutropenia, including febrile neutropenia, has been reported during treatment with MINJUVI. Administration of granulocyte colony-stimulating factors (G-CSF) may be considered. Anticipate, evaluate and treat any symptoms or signs of developing infection.

Thrombocytopenia

Thrombocytopenia has been reported during treatment with MINJUVI. Consider withholding concomitant medications that may increase bleeding risk (e.g. platelet inhibitors, anticoagulants). Advise patients to report any signs or symptoms of bruising or bleeding immediately.

Infections

Fatal and serious infections, including opportunistic infections, occurred in patients during treatment with MINJUVI. Administer MINJUVI to patients with an active infection only if the infection is treated appropriately and well controlled. Patients with a history of recurring or chronic infections may be at increased risk of infection and should be monitored appropriately.
Advise patients to contact their healthcare professionals if fever or other signs of potential infection such as chills, cough or pain on urination develop.

Tumour Lysis Syndrome

Patients with high tumour burden and rapidly proliferative tumour may be at increased risk of tumour lysis syndrome (TLS). In patients with relapsed or refractory DLBCL, tumour lysis syndrome during treatment with MINJUVI has been observed. Appropriate measures/prophylaxis in accordance with local guidelines should be taken prior to treatment with MINJUVI. Patients should be monitored closely for TLS during treatment with MINJUVI.

Immunisations

The safety of immunisation with live vaccines following MINJUVI therapy has not been investigated. Vaccination with live vaccines is not recommended concomitantly with MINJUVI therapy.

QTc prolongation

Cases of QT prolongation have been reported during treatment with tafasitamab.

Syncope

Cases of syncope have been reported during treatment with tafasitamab.

CAR-T Cells

To date only limited data are available to indicate whether treatment with anti-CD19 CAR-T cells is safe and effective after prior treatment with tafasitamab.

Excipient

This medicinal product contains 37.0 mg sodium per 5 vials (the dose for a patient weighing 83 kg), equivalent to 1.85% of the WHO recommended maximum daily intake of 2 g sodium for an adult.

Interactions

No interaction studies have been performed for tafasitamab. No clinically meaningful differences in tafasitamab pharmacokinetics were observed when used concomitantly with lenalidomide.

Pregnancy, lactation

Women of childbearing potential

Treatment with tafasitamab in combination with lenalidomide should not be initiated in female patients unless pregnancy has been excluded. Please also refer to the professional information for lenalodomide.
Based on tafasitamab mechanism of action, immunotoxicity cannot be excluded in the newborn, in particular the possibility of B cell depletion. Advise females of reproductive potential to use effective contraception during treatment with tafasitamab and for at least 3 months after end of treatment.

Pregnancy

Tafasitamab is administered in combination with lenalidomide for up to 12 cycles. Lenalidomide can cause embryo-foetal harm and is contraindicated for use in pregnancy and in women of childbearing potential unless all of the conditions of the lenalidomide pregnancy prevention programme are met. There are no data on the use of tafasitamab in pregnant women. No animal reproductive and developmental toxicity studies have been conducted with tafasitamab. However, IgG is known to cross the placenta and tafasitamab may cause foetal B-cell depletion based on its mechanism of action. In case of exposure during pregnancy, newborns should be monitored for B-cell depletion and vaccinations with live virus vaccines should be postponed until the infant’s B-cell count has recovered. MINJUVI should not be used during pregnancy unless the clinical condition of the woman requires treatment with tafasitamab.

Lactation

It is not known whether tafasitamab is excreted in human milk. However, maternal IgG is known to be excreted in human milk. Because of the potential for adverse reactions in nursing infants from tafasitamab, advise women not to breastfeed during treatment with tafasitamab until at least 3 months after the last dose.

Fertility

No specific studies have been conducted to evaluate potential effects of tafasitamab on fertility. However, no adverse effects on male and female reproductive organs were observed in a repeat-dose toxicity study in animals.

Effects on ability to drive and use machines

MINJUVI has negligible influence on the ability to drive and use machines.

Undesirable effects

Summary of the safety profile

More than 500 patients have been exposed to MINJUVI in the clinical development programme, either as monotherapy or in combination with other treatments. The adverse drug reactions described in this section were identified during treatment of 239 patients with non-Hodgkin lymphoma (NHL), including 81 patients with non-transplant eligible relapsed or refractory DLBCL from the pivotal study MOR208C203 (L-MIND), in which tafasitamab was used in combination with lenalidomide.

Serious adverse events occurred in 39% of patients with NHL who received tafasitamab. The most frequent serious adverse events (occurring in ≥3% of patients with NHL) included febrile neutropenia (6.7%) and pneumonia (4.2%). Fatal adverse events occurred in 3.3% of patients with NHL who received tafasitamab, the most frequent of which were infections and infestations (2.1%).

Permanent discontinuation of tafasitamab due to an adverse event occurred in 11% of patients. The most frequent adverse events which resulted in permanent discontinuation of tafasitamab were infections and infestations (3.8%), blood and lymphatic system disorders (1.3%), and respiratory, thoracic and mediastinal disorders (1.3%).

Adverse reactions observed and their frequencies derived from the pooled safety population of patients with NHL who received tafasitamab are listed below. The adverse reaction frequencies are based on all-cause adverse event frequencies, where a proportion of the events for an adverse reaction may have other causes than the medicinal product, such as the disease, other medicines or unrelated causes.

Adverse reactions are listed by MedDRA System Organ Class and by frequency. Frequencies are defined as follows: very common (≥ 1/10); common (≥ 1/100 to < 1/10); uncommon (≥ 1/1,000 to

< 1/100); rare (≥ 1/10,000 to < 1/1,000); very rare (< 1/10,000), not known (cannot be estimated from the available data).

Within each frequency grouping, adverse reactions are presented in order of decreasing frequency.

Infections and infestations

Very common: Bacterial, viral and fungal infections[+], including opportunistic infections with fatal outcomes (e.g. bronchopulmonary aspergillosis, bronchitis, pneumonia and urinary tract infection) [51%]

Common: Sepsis[++]

Neoplasms benign, malignant and unspecified (incl. cysts and polyps)

Uncommon: Basal cell carcinoma

Blood and lymphatic system disorders

Very common: Neutropenia (39%)[+], anaemia (29%)[+], thrombocytopenia (19%)[+], and leukopenia (11%)[+]

Common: Febrile neutropenia[+] and lymphopenia

Immune system disorders

Common: Hypogammaglobulinaemia, C-reactive protein increased

Metabolism and nutrition disorders

Very common: Hypokalaemia (15%), decreased appetite (10%)

Common: Hypomagnesaemia, weight decreased, hypocalcaemia

Nervous system disorders

Very common: Headache (10%)

Common: Paraesthesia, dysgeusia

Respiratory, thoracic and mediastinal disorders

Very common: Cough (15%)

Common: Dyspnoea, nasal congestion, and exacerbation of chronic obstructive pulmonary disease

Gastrointestinal disorders

Very common: Diarrhoea (23%), nausea (17%), constipation (15%), and vomiting (12%)

Common: Abdominal pain

Hepatobiliary disorders

Common: Transaminases increased[+++], gamma-glutamyltransferase increased, and hyperbilirubinaemia

Skin and subcutaneous tissue disorders

Very common:	Rash (11%)[++++]
Common:	Pruritus, alopecia, hyperhidrosis, and erythema

Musculoskeletal and connective tissue disorders

Very common:	Back pain (13%)
Common:	Muscle spasms, pain in extremities, and arthralgia
Uncommon:	Musculoskeletal pain

Renal and urinary disorders

Common:	Blood creatinine increased

General disorders and administration site conditions

Very common:	Asthenia (includes malaise) (19%), fatigue (15%), peripheral oedema (14%), and pyrexia (14%)
Common:	Mucosal inflammation

Injury, poisoning and procedural complications

Very common:	Infusion related reaction (13%)[+]

+ Further information on this ADR is provided in the text below.
++ Sepsis includes sepsis, device related sepsis, Escherichia sepsis, klebsiella sepsis, neutropenic sepsis, streptococcal sepsis, and urosepsis
+++ Transminases increased includes transaminases increased, ALT increased, and AST increased
++++ Rash includes rash, rash erythematous, rash maculo-papular, rash papular, rash pruritic, and rash pustular

Description of specific adverse reactions and additional information

Selected undesirables effects are described for the pivotal study MOR208C203 (L-MIND).

Myelosuppression

Treatment with tafasitamab can cause serious or severe myelosuppression including neutropenia, thrombocytopenia and anaemia (see “Warnings and precautions”). In study MOR208C203, 49% of patients treated with tafasitamab and lenalidomide experienced neutropenia. Grade 3 or higher blood and lymphatic system disorders adverse reactions occurred in 53% of patients, including neutropenia (47%), thrombocytopenia (16%), febrile neutropenia (12%), leukopenia (9.9%) and anaemia (7.4%). Grade 4 blood and lymphatic system disorders adverse reactions occurred in 31% of patients including neutropenia (including agranulocytosis), thrombocytopenia, febrile neutropenia and leukopenia.

When patients in study MOR208C203 were switched from tafasitamab and lenalidomide in the combination therapy phase to tafasitamab alone in the extended monotherapy phase, the incidences of blood and lymphatic system disorders events decreased by at least 20% for neutropenia, anaemia and thrombocytopenia; no incidences of febrile neutropenia were reported with tafasitamab monotherapy.

Infections

Bacterial, fungal, and new or reactivation of viral infections can occur during and following tafasitamab therapy (see “Warnings and Precautions”). In study MOR208C203, 73% of patients treated with tafasitamab and lenalidomide experienced an infection. Grade 3 or higher infections occurred in 30% of patients treated with tafasitamab and lenalidomide. The most frequently reported Grade 3 or higher infections were pneumonia (9.9%), sepsis (including klebsiella sepsis, neutropenic sepsis, and streptococcal sepsis) (4.9%); and lower respiratory tract infection, upper respiratory tract infection, and urinary tract infection (2.5% each). Infection-related death was reported in 1.2% of patients within 30 days of last treatment.

Infusion-related reactions

In the MOR208C203 study, 6.2% of patients experienced an infusion-related reaction. Eighty percent of these reactions occurred during cycle 1 or 2; all were Grade 1 and resolved on the day of occurrence. Symptoms included chills, flushing, dyspnoea and hypertension (see Warnings and Precautions).

Immunogenicity

The immunogenicity of tafasitamab has not been fully characterised so far.

The detection of antibody formation is highly dependent on the sensitivity and specificity of the assays. Additionally, the observed incidence of antibody (including neutralising antibody) positivity in an assay may be influenced by several factors, including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies against tafasitamab with the incidence of antibodies in other studies or to other medicinal products may be misleading.

Reporting suspected adverse reactions after authorisation of the medicinal product is very important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions online via the ElViS portal (Electronic Vigilance System). You can obtain information about this at www.swissmedic.ch.

Overdose

In the case of an overdose, patients should be carefully observed for signs or symptoms of adverse reactions and supportive care should be administered, as appropriate.

Properties/Effects

ATC code

L01FX12

Mechanism of action

Tafasitamab is an Fc-modified monoclonal antibody that targets the CD19 antigen expressed on the surface of pre-B cells 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
- direct induction of cell death (apoptosis)

The Fc modification results in enhanced antibody-dependent cellular cytotoxicity and antibody-dependent cellular phagocytosis.
Tafasitamab in combination with lenalidomide resulted in increased cytotoxicity in vitro, greater than the effects of either agent alone.

Pharmacodynamics

In patients with relapsed or refractory DLBCL, tafasitamab led to a reduction in peripheral blood B-cell counts. The reduction relative to baseline B-cell count reached 97% after eight days of treatment in the MOR208C203 (L-MIND) study. The maximum B-cell reduction at approximately 100% (median) was reached within 16 weeks of treatment.
Although the depletion of B-cells in the peripheral blood is a measurable pharmacodynamic effect, it is not directly correlated with the depletion of B-cells in solid organs or in malignant deposits.

Clinical efficacy

Tafasitamab in combination with lenalidomide followed by tafasitamab monotherapy was studied in the MOR208C203 (L-MIND) study, an open-label multicentre single-arm study. This study was conducted in adult patients with relapsed or refractory DLBCL after 1 to 3 prior systemic DLBCL therapies, who at the time of the trial were not candidates for high dose chemotherapy followed by ASCT. One of the prior systemic therapies had to include a CD20 targeted therapy. Patients with a known history of “double/triple-hit” genetics DLBCL were excluded at study entry. In addition, the study excluded patients with severe hepatic impairment (total serum bilirubin > 3 mg/dL) and patients with renal impairment (CrCL< 60 mL/min), as well as patients with history or evidence of clinically significant cardiovascular, CNS and/or other systemic disease.
Lenalidomide increases the risk of thrombotic events in patients who are at high risk of thrombosis; therefore the study also excluded patients with history of, or at high risk for a thromboembolic event who were not willing/able to take venous thromboembolic event prophylaxis during the entire treatment period.
For the first three cycles, patients received 12 mg/kg tafasitamab via infusion on days 1, 8, 15 and 22 of each 28-day cycle, plus a loading dose on day 4 of cycle 1. Thereafter, tafasitamab was administered on days 1 and 15 of each cycle until disease progression. Pre-medication, including

antipyretics, histamine H1 and H2 receptor blockers and glucocorticosteroids, was given 30 to 120 minutes prior to the first three tafasitamab infusions.
Patients self-administered 25 mg lenalidomide daily on days 1 to 21 of each 28-day cycle, up to 12 cycles.
A total of 81 patients were enrolled in the study. The median age was 72 years (range 41 to 86 years), 89% were white and 54% were males. The median number of prior therapies was two (range 1 to 4) with 40 patients (49.4%) having received one prior therapy and 35 patients (43.2%) having received two prior therapies. Five patients (6.2%) had received 3 prior therapies and 1 patient (1.2%) had received 4 prior therapies. All patients had received a prior CD20-containing therapy. Eight patients had a DLBCL diagnosis transformed from a low-grade lymphoma. Fifteen patients (18.5%) had a primary refractory disease (i.e. showing a response of less than a partial reponse to first-line treatment or disease recurrence/progression within < 6 months from the completion of first-line therapy), 36 (44.4%) were refractory to their last prior therapy and 34 (42.0%) were refractory to rituximab. Nine patients (11.1%) had received prior ASCT. The primary reasons for patients (full analysis set) not being candidates for ASCT included age (45.7%), refractory to salvage chemotherapy (23.5%), comorbidities (13.6%) and refusal of high dose chemotherapy/ASCT (16.0%). One patient received tafasitamab, but not lenalidomide. The remaining 80 patients received at least one dose of tafasitamab and lenalidomide. All patients enrolled in the L-MIND study had a diagnosis of DLBCL based on local pathology. However, as per central pathology review, 10 patients could not be classified as DLBCL.The median duration of exposure to tafasitamab and lenalidomide was 9.2 months (range 0.23 to 54.67 months). Thirty-two (39.5%) patients completed 12 cycles of tafasitamab treatment. Thirty (37.0%) patients completed 12 cycles of lenalidomide treatment.
Efficacy evaluation was based on best objective response rate (ORR), defined as the proportion of complete and partial responders and duration of response (DoR), as assessed by an independent review committee, based upon International Working Group 2007 response assessment criteria. Other efficacy endpoints were progression-free survival (PFS) and overall survival (OS).
Key efficacy results are summarised in Table 3.

Table 3: Key efficacy results in patients with relapsed or refractory diffuse large B-cell lymphoma in the MOR208C203 (L-MIND) study

Efficacy parameter	**Tafasitamab + lenalidomide** (N = 81 [ITT]*)
Primary Endpoint	
Best objective response rate (per independent review committee)	
Overall response rate, n (%) (95% CI)	46 (56.8) (45.3, 67.8) [a]
Complete response rate, n (%) (95% CI)	32 (39,5) (28,8 ; 51,0)
Partial response rate, n (%) (95% CI)	14 (17,3) (9,8, 27,3)[a]
Key Secondary Endpoints	
Overall duration of response (complete + partial response) [a]	
Median, months (95% CI)	43.9 (26.1, NR)
Progression-free survival [a]	
Median, months (95% CI)	11.6 (5.7 – 45.7)
Overall survival [a]	
Median, months (95% CI)	31.6 (18.3, NR)

ITT=intention to treat; NR = not reached
*One patient received only tafasitamab
CI: Binomal exact confidence interval using Clopper Pearson method
a Kaplan Meier estimates

Among the eight patients who had a DLBCL transformed from a prior indolent lymphoma, seven patients had an objective response (three patients a CR, four patients a PR) and one patient had a stable disease as the best response to tafasitamab + lenalidomide treatment.

Temporary authorization

Due to incomplete clinical data at the time of review of the marketing authorization application, the medicinal product MINJUVI is authorized for a limited period of time (Art. 9a LPTh). The temporary authorization must be linked to the timely satisfaction of conditions. Once these conditions are met, the temporary authorization may be converted into ordinary authorization.

Pharmacokinetics

Absorption

Based on a population pharmacokinetic analysis of tafasitamab in combination with lenalidomide, tafasitamab average serum trough concentrations (± standard deviation) were 179 (± 53) µg/mL during weekly intravenous administrations of 12 mg/kg on days 1, 8, 15, and 22 of cycles 1-3 (plus an additional dose on day 4 of cycle 1). During administration every 14 days from cycle 4 onwards, average trough serum concentrations were 153 (± 68) µg/mL. Overall maximum tafasitamab serum concentrations were 483 (± 109) µg/mL.

Distribution

The total volume of distribution for tafasitamab was 9.3 L.

Metabolism

The exact pathway through which tafasitamab is metabolised has not been characterised. As a human IgG monoclonal antibody, tafasitamab is expected to be degraded into small peptides and amino acids via catabolic pathways in the same manner as endogenous IgG.

Elimination

The clearance of tafasitamab was 0.41 L/day and terminal elimination half-life was 16.9 days. Following long-term observations, tafasitamab clearance was found to decrease over time to 0.19 L/day after two years.

Kinetics in specific patient groups

Body weight (40 to 163 kg) has a significant effect on the pharmacokinetics of tafasitamab, with higher clearance and volume of distribution expected with higher body weight. No clinically meaningful differences in the pharmacokinetics of tafasitamab were observed based on age (16 to 90 years), sex, mild to moderate renal impairment (CrCL 30-89 mL/min estimated by the Cockcroft-Gault equation), and mild hepatic impairment (total bilirubin ≤ ULN and AST > ULN, or total bilirubin 1 to 1.5 times ULN and any AST). The effect of severe renal impairment to end-stage renal disease (CrCL < 30 mL/min), moderate to severe hepatic impairment (total bilirubin > 1.5 times ULN and any AST), and race/ethnicity on tafasitamab pharmacokinetics is unknown.

Preclinical data

Preclinical data reveal no special hazards for humans.

Tafasitamab has shown to be highly specific to the CD19 antigen on B cells. Toxicity studies following intravenous administration to cynomolgus monkeys have shown no other effect than the expected pharmacological depletion of B-cells in peripheral blood and in lymphoid tissues. These changes reversed after cessation of treatment.

Genotoxicity

No genotoxicity study has been conducted with tafasitamab.

Carcinogenicity

No carcinogenicity study has been been conducted with tafasitamab.

Reproductive toxicity

Reproductive and developmental toxicity studies as well as specific studies to evaluate the effects on fertility have not been conducted with tafasitamab.

In the 13-week repeat-dose general toxicity study in cynomolgus monkeys, no adverse effects on male and female reproductive organs were observed up to the highest dose tested, 100 mg/kg/week (approximately 8 times the human exposure based on AUC at the clinical dose of 12 mg/kg/week).

Other information

Incompatibilities

This medicinal product may be mixed only with those medicinal products listed under Instructions for handling.
No incompatibilities have been observed with standard infusion materials.

Shelf life

Do not use this medicine after the expiry date ("EXP") stated on the packaging.
Shelf life after opening

Reconstituted solution (prior to dilution)
The preparation does not contain a preservative.
From a microbiological point of view, the reconstituted tafasitamab solution should be used as soon as possible after reconstitution. If not used immediately, the reconstituted product may be stored prior to dilution for up to 24 hours at 2°C – 25°C.
Do not freeze or shake.
Diluted solution (solution for infusion)
Once diluted, the solution for infusion should not be stored. Chemical and physical in-use stability has been demonstrated for 36 hours at 2°C – 8°C, followed by up to 24 hours at 25°C. For microbiological reasons, the ready-to-use preparation should be used immediately after dilution. If this is not possible, in-use storage times and conditions are the responsibility of the user and should normally be no longer than 24 hours at 2 - 8°C, unless the dilution/reconstitution has taken place in controlled and validated aseptic conditions.
Do not freeze or shake.

Special precautions for storage

Store in the refrigerator (2 – 8°C).
Keep the vial in the outer carton in order to protect the contents from light.
Keep out of the reach of children.
Instructions for handling

MINJUVI is provided in sterile, preservative free single-use vials. MINJUVI should be reconstituted and diluted prior to intravenous infusion.
Use appropriate aseptic technique for reconstitution and dilution.

Instructions for reconstitution

- Determine the dose of tafasitamab based on patient weight by multiplying 12 mg with the patient weight (kg). Then calculate the number of tafasitamab vials needed (each vial contains 200 mg tafasitamab).
- Using a sterile syringe, gently add 5.0 mL sterile water for injection into each tafasitamab vial. Direct the stream towards the walls of each vial and not directly onto the lyophilised powder.
- Gently swirl the reconstituted vial(s) to aid the dissolution of the lyophilised powder. Do not shake or swirl vigorously. Do not remove the contents until all of the solids have been completely dissolved. The lyophilised powder should dissolve within 5 minutes.
- The reconstituted solution should appear as a colourless to slightly yellow solution. Before proceeding, ensure there is no particulate matter or discolouration by inspecting visually. If the solution is cloudy, discoloured or contains visible particles, discard the vial(s).

Instructions for dilution

- An infusion bag containing 250 mL sodium chloride 9 mg/mL (0.9%) solution for injection should be used.
- Calculate the total volume of the 40 mg/mL reconstituted tafasitamab solution needed. Withdraw a volume equal to this from the infusion bag and discard the withdrawn volume.
- Withdraw the total calculated volume (mL) of reconstituted tafasitamab solution from the vial(s) and slowly add to the sodium chloride 9 mg/mL (0.9%) infusion bag. Discard any unused portion of tafasitamab remaining in the vial.
- The final concentration of the diluted solution should be between 2 mg/mL and 8 mg/mL of tafasitamab.
- Gently mix the intravenous infusion bag by slowly inverting the bag. Do not shake.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

Authorisation number

68083

Packs

1 vial of 200 mg: 1 [A].

Marketing authorisation holder

Incyte Biosciences International Sàrl, 1110 Morges

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March 2022