swissmedic

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Swissmedic, Swiss Agency for Therapeutic Products

Swiss Public Assessment Report

Extension of therapeutic indication

Minjuvi

International non-proprietary name:	tafasitamab
Pharmaceutical form:	powder for solution for infusion
Dosage strength(s):	200 mg
Route(s) of administration:	intravenous use
Marketing authorisation holder:	Incyte Biosciences International
Marketing authorisation no.:	68083
Decision and decision date:	extension of therapeutic indication approved on 19 December 2025

Note:

This assessment report is as adopted by Swissmedic with all information of a commercially confidential nature deleted.

SwissPARs are final documents that provide information on submissions at a particular point in time. They are not updated after publication.

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1 Terms, Definitions, Abbreviations

ADA	Anti-drug antibody
AE	Adverse event
AESI	Adverse event of special interest
$AUC_{0\text{-}56d}$	Area under the plasma concentration-time curve for the 56-day dosing interval
CI	Confidence interval
FDG	Fluorodeoxyglucose
FL	Follicular lymphoma
GELF	Groupe d'Etude des Lymphome Folliculaires
HR	Hazard ratio
IRR	Infusion-related reaction
LEN	Lenalidomide
LoQ	List of Questions
MAH	Marketing Authorisation Holder
NHL	Non-Hodgkin's lymphoma
ORR	Overall response rate
OS	Overall survival
PD	Pharmacodynamics
PET-CR	Positron emission tomography complete remission
PFS	Progression-free survival
PK	Pharmacokinetics
PopPK	Population pharmacokinetics
R2	Rituximab + Revlimid (lenalidomide)
R-CHOP	Rituximab, cyclophospamide, doxorubicin, vincristine, and prednisone
RMP	Risk management plan
rrFL	Relapsed/refractory follicular lymphoma
SAE	Serious adverse event
SwissPAR	Swiss Public Assessment Report
TEAE	Treatment-emergent adverse event
TPA	Federal Act of 15 December 2000 on Medicinal Products and Medical Devices (SR 812.21)
TPO	Ordinance of 21 September 2018 on Therapeutic Products (SR 812.212.21)

2 Background information on the procedure

2.1 Applicant's request(s) and information regarding procedure

Extension(s) of the therapeutic indication(s)
The applicant requested the addition of a new therapeutic indication or modification of an approved one in accordance with Article 23 TPO.

Orphan drug status
The applicant requested orphan drug status in accordance with Article 4 paragraph 1 letter a^{decies} no. 2 TPA.
Orphan drug status was granted on 13 May 2025.

2.2 Indication and dosage

2.2.1 Requested indication

MINJUVI, in combination with lenalidomide and rituximab, is indicated for the treatment of adult patients with relapsed or refractory follicular lymphoma (FL) after at least one line of systemic therapy.

2.2.2 Approved indication

MINJUVI is indicated in combination with lenalidomide and rituximab for the treatment of adult patients with relapsed or refractory follicular lymphoma (FL), after at least one prior line of systemic therapy (see Section "Properties/Effects").
MINJUVI is not indicated for the treatment of marginal zone lymphoma.

2.2.3 Requested dosage

Summary of the requested standard dosage:
Cycles of 28 days
Tafasitamab:
Cycles 1-3: 12 mg/kg on days 1, 8, 15, and 22
Cycles 4-12: 12 mg/kg on days 1 and 15

Rituximab:
Cycle 1: 375 mg/m^2 on days 1, 8, 15, and 22
Cycles 2-5: 375 mg/m^2 on day 1

Lenalidomide: 20 mg on days 1-21 of each cycle

2.2.4 Approved dosage

(see appendix)

2.3 Regulatory history (milestones)

Application	13 June 2025
Formal control completed	25 June 2025
Preliminary decision	20 October 2025
Response to preliminary decision	18 November 2025
Final decision	19 December 2025
Decision	approval

3 Medical context

Follicular lymphoma (FL) is the most common indolent non-Hodgkin's lymphoma (NHL). It accounts for approximately 10-20% of all NHL cases. Although usually responsive to initial therapy, FL is considered an incurable disease, and patients typically relapse over time.
For patients who require second-line therapy, treatment varies and may include anti-CD20 antibodies as monotherapy or in combination with chemotherapy or immunotherapy. Targeted therapies are also approved for the treatment of FL in a refractory or recurrent setting (rrFL). While the anti-CD20 era therapies have shifted median survival towards 20 years, patients with rrFL after ≥2 prior lines of therapy are a particularly poor prognostic group, with overall survival (OS) reaching 5 years.

4 Nonclinical aspects

The applicant did not submit any new nonclinical studies to support the requested new indication, which is considered acceptable. The new indication is unlikely to result in any significant risk to the environment. From the nonclinical point of view, there are no objections to the approval of the new indication applied for.

5 Clinical aspects

5.1 Pharmacokinetics (PK)

The clinical pharmacology profile of tafasitamab has been characterised previously in a variety of studies in combination with lenalidomide (LEN). In the current application, its clinical pharmacology has been further updated to incorporate data from patients with FL receiving tafasitamab in combination with lenalidomide and rituximab, based on the Phase III INCMOR0208-301 (inMIND) study. The updated population pharmacokinetic (popPK) analysis remains generally consistent with the original submission. The comedication rituximab was not retained as a covariate.
A total of 3,905 serum samples from 652 participants were analysed for anti-drug antibodies (ADA). The incidence of treatment-emergent ADA was low and comparable between arms (0.9% tafasitamab vs. 1.8% placebo), and no neutralising antibodies were detected, indicating a minimal immunogenicity risk. Given the very limited number of ADA-positive patients, any potential impact on PK, efficacy, or safety could not be determined.

5.2 Pharmacodynamics

Exposure-response analysis indicated a flat relationship for efficacy endpoints (overall response rate (ORR) and progression-free survival (PFS)) with tafasitamab + LEN + rituximab +cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP), consistent with findings for tafasitamab + LEN in the original submission. No significant association was observed between overall survival and $AUC_{0\text{-}56d}$; however, this analysis remains inconclusive due to the limited number of events (n=13).

Safety endpoints occurring in ≥10% of patients included treatment-emergent adverse events (TEAE) leading to dose modification, Grade ≥3 TEAEs, Grade ≥3 neutropenia, serious adverse events (SAE), and Grade ≥3 infections. Median onset ranged from 7 to 18 weeks after treatment initiation. No higher exposure was observed in patients with these events; in fact, exposure was generally lower, significantly so for TEAEs leading to dose modification, likely due to dose reductions implemented to allow treatment continuation.

5.3 Dose finding and dose recommendation

No specific dose-finding study was performed for this indication.

5.4 Efficacy

The applicant submitted 1 pivotal Phase III, double-blind, placebo-controlled, randomised trial (INCMOR 0208-301) to support the proposed indication.

This study was conducted to evaluate the efficacy and safety of tafasitamab in combination with rituximab and lenalidomide (R2) versus placebo in combination with R2 in adult patients with relapsed/refractory FL. Included patients had to have histologically confirmed Grade 1, 2, or 3a follicular lymphoma and documented expression of CD19+ and CD20+ on lymphoma cells and had to have relapsed or refractory disease after at least 1 prior line of systemic therapy, including an anti-CD20 therapy or chemo-immunotherapy. In addition, Groupe d'Etude des Lymphome Folliculaires (GELF) criteria were recommended as guidance to the investigators, to identify the FL patients who needed treatment. For details regarding the included patient population, please refer to the attached Information for healthcare professionals.

Included patients received tafasitamab plus R2 or placebo plus R2 for up to 12 cycles of 28 days each. Tafasitamab 12 mg/kg was intravenously administered on days 1, 8, 15, and 22 of cycles 1 to 3 and on days 1 and 15 of cycles 4 to 12. Dosing of lenalidomide was 20 mg orally once daily on days 1 to 21 of cycles 1 to 12, and rituximab 375 mg/m² intravenously on days 1, 8, 15, and 22 of cycle 1 and on day 1 of cycles 2 to 5. For details regarding dosing, please refer to the attached Information for healthcare professionals.

The primary endpoint in the INCMOR 0208-301 study was PFS as assessed by the investigator according to the Lugano 2014 criteria. PFS by investigator assessment in the overall population (FL and marginal zone lymphoma patients), PET-CR rate (defined as the proportion of participants who achieved a CR as per Lugano classification (Cheson et al 2014), with a PET-negative result among the participants with a positive PET scan at baseline (Deauville score of 4 or 5)) by investigator assessment in the FL fluorodeoxyglucose- (FDG) avid set, and overall survival were key secondary endpoints which were included in the hierarchy testing.
A total of 548 patients with FL were randomised, including 273 patients in the tafasitamab + R2 group and 275 patients in the placebo + R2 group. Baseline characteristics were balanced between the arms. The median age was 64 years, and the majority of patients were male (54.6%), and White (79.9%). The majority (54.7%) of participants had received 1 prior line of systemic anticancer therapy. All participants in the FL population had received prior systemic anti-CD20–containing lines of therapy; most participants had received 1 (61.3%) or 2 (24.8%) prior lines of anti–CD20–containing therapies. More than half of the patients had relapsed disease (56.9), followed by refractory disease (38.1%). Please refer to the attached Information for healthcare professionals for details regarding demographics and baseline characteristics.

The results of INCMOR 0208-301 primary analysis were submitted with a data cut-off date of February 2024.

A total of 206 PFS events were observed in the FL population: 75 events (27.5%) in the tafasitamab arm and 131 events (47.6%) in the placebo arm. There was a statistically significant difference in PFS between the tafasitamab + R2 and the placebo groups, with a hazard ratio (HR) of 0.43 (95% CI: 0.32, 0.58) and a p-value of < 0.0001. The estimated median PFS was 22.37 months (95% CI: 19.2, NE) in the tafasitamab + R2 group and 13.9 months (95% CI: 11.5; 16.39) in the placebo group.

The first and second key secondary endpoints PFS by investigator assessment in the overall population, and PET-CR rate by investigator assessment in the FL FDG-avid set, were also statistically significant.

As at the data cut-off date, 15 patients (5.5%) in the tafasitamab +R2 group and 23 patients (8.4%) in the placebo group had OS events. The estimated HR was 0.587 (95% CI: 0.306, 1.128). The predefined boundary for the nonbinding interim futility analysis for the key secondary endpoint, OS in the FL population (HR > 1.24), was not reached.

5.5 Safety

In the pivotal study INCMOR 0208-301, the most frequent TEAEs reported in more than 10% of patients in the experimental arm were nausea, pruritus, infusion-related reaction, anaemia, thrombocytopenia, asthenia, pneumonia, and back pain.

Overall, 71.2% of patients in the FL population who were treated with tafasitamab + R2 had at least 1 Grade 3 or 4 TEAE. The most frequent Grade 3-4 TEAEs reported in more than 5% of patients were neutropenia, pneumonia, thrombocytopenia, COVID-19, and neutrophil count decreased.

Overall, 36.1% of patients in the FL population who were treated with tafasitamab + R2 had at least 1 serious adverse event (SAE). The most frequent SAEs reported in more than 2% of patients were pneumonia, COVID-19, COVID-19 pneumonia, acute kidney injury, and febrile neutropenia.

In total, 15 FL patients (5.5%) in the tafasitamab+R2 group died during the study. Six of these patients died due to adverse events.
The most frequent adverse events of special interests (AESIs) in the FL population in the tafasitamab+R2 group were infusion-related reactions (IRRs) and second primary malignancies, which occurred with a higher frequency in the tafasitamab+R2 group compared with the placebo+R2 group. Even though the rate of second malignancy is low, longer follow-up is required to better characterise the long-term risk of malignancies in patients treated with tafasitamab. This risk was adequately described in the Information for healthcare professionals.

For further details regarding safety, please refer to the attached Information for healthcare professionals.

5.6 Final clinical benefit-risk assessment

Follicular lymphoma is an incurable disease with a high unmet medical need, particularly in patients with relapsed or refractory disease after ≥2 prior lines of therapy.
The INCMOR 0208-301 study met its predefined primary endpoint with a statistically and clinically significant improvement in PFS. Overall survival data are still immature; however, a separation of the OS Kaplan-Meier curves in favour of the experimental treatment has been observed, with no detriment. Follow-up for OS data is ongoing, and an additional OS analysis is expected to occur at the end of the study. These data will be requested as a post-authorisation requirement.
The toxicity of the triplet combination is manageable. Relevant risks are adequately described in the Information for healthcare professionals.
The overall benefit-risk assessment of tafasitamab + R2 in rrFL was considered positive.

6 Risk management plan summary

The RMP summaries contain information on the medicinal products′ safety profiles and explain the measures that are taken 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. It is the responsibility of the marketing authorisation holder to ensure that the content of the published RMP summaries is accurate and correct. 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 that occur in populations or indications not included in the Swiss authorisations.

7 Appendix

Approved Information for healthcare professionals

Please be aware that the following version of the Information for healthcare professionals for 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 valid and relevant reference document 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. It is the responsibility of the authorisation holder to ensure the translation is correct. The only binding and legally valid text is the Information for healthcare professionals approved in one of the official Swiss languages.

▼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

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 and 1.0 mg of polysorbate 20.

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).
MINJUVI is indicated in combination with lenalidomide and rituximab for the treatment of adult patients with relapsed or refractory follicular lymphoma (FL), after at least one prior line of systemic therapy (see Section “Properties/Effects”).
MINJUVI is not indicated for the treatment of marginal zone lymphoma.

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 treatment 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

Recommended dose for the treatment of adult patients with relapsed or refractory DLBCL

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 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.

Recommended dose for the treatment of adult patients with relapsed or refractory FL after at least one line of systemic therapy

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 to 3: infusion on day 1, 8, 15 and 22 of each cycle.
- Cycles 4 to 12: infusion on day 1 and 15 of each cycle.

Administer MINJUVI in combination with lenalidomide 20 mg (days 1-21 in Cycles 1 to 12) and rituximab 375 mg/m^2 (Cycles 1 to 5) (See section Properties/Effects). Refer to the rituximab professional information and lenalidomide professional information for the respective dosage recommendations, including lenamidomide dosage recommendations for patients with renal insufficiency.

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

For the treatment of adult patients with relapsed or refractory DLBCL MINJUVI is given in combination with lenalidomide 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.
For the treatment of adult patients with relapsed or refractory FL Minjuvi is given in combination with lenalidomide plus rituximab for up to twelve cycles for MINJUVI and lenalidomide, and five cycles for rituximab.

Dose adjustment following undesirable effects/interactions

Table 1 provides dose modifications for MINJUVI 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 treat signs and symptoms. • Once signs and symptoms resolve or reduce to Grade 1, resume MINJUVI 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 reach the rate at which the reaction occurred.
	Grade 3 (severe)	• Interrupt MINJUVI infusion immediately and treat 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.

Adverse Reaction	Severity	Dosage Modification
	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 if platelet count gets back to a value ≥ 50,000/μL. 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 if Neutrophil count gets back to a value ≥ 1,000/μL. 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%). Among the 274 patients with FL treated with tafasitamab in the inMIND study, 50% were ≥ 65 years of age and 20% were ≥ 75 years of age.

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 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.

Progressive multifocal leukoencephalopathy

Cases of Progressive multifocal leukoencephalopathy (PML) have been reported during combination therapy including tafasitamab. Patients should be monitored for new or worsening of neurological symptoms or signs suggestive of PML. If PML is suspected, treatment with MINJUVI should be immediately suspended. Referral to a neurologist should be considered. Appropriate diagnostic measures may include MRI, cerebrospinal fluid testing for JC virus DNA, and repeat neurological examinations. If PML is confirmed, treatment with MINJUVI should be permanently discontinued.

Tumour Lysis Syndrome

Patients with high tumour burden and rapidly proliferative tumour may be at increased risk of tumour lysis syndrome (TLS). Tumour lysis syndrome during treatment with MINJUVI has been reported. 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.

Second primary malignancies

Cases of second primary malignancies (SPM), including squamous cell carcinoma and squamous cell carcinoma of the skin, have been reported in the phase 3 study inMIND, in patients with follicular lymphoma and marginal zone lymphoma receiving tafasitamab in combination with lenalidomide and rituximab. In that study, SPM incidence was 3.4% in the tafasitamab arm.
Second primary malignancies are a potential long-term complication of lymphoma and someof the agents used in the treatment of lymphomas. Patients should be monitored for the development of

secondary malignancies. In patients who develop SPM, the benefits and risks of continuing treatment with MINJUVI should be carefully considered.

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.

Excipients

This medicinal product contains 7.4 mg sodium per vial, equivalent to 0.4% of the WHO recommended maximum daily intake of 2 g sodium for an adult.
This medicinal product also contains 1.0 mg of polysorbate 20 per vial. Polysorbate 20 may cause allergic reactions.

Interactions

No drug 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 lenalidomide.
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 1000 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 693 patients with B-cell malignancies who received at least 1 dose of tafasitamab, 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, as well as 327 participants with R/R FL or MZL from the pivotal study INCMOR 0208-301 (inMIND) in which tafasitamab was used in combination with lenalidomide and rituximab. Serious adverse events occurred in 45.7% of patients with B-cell malignancies who received tafasitamab. The most frequent serious adverse events (occurring in ≥3% of patients with B-cell malignancies) included pneumonia (8.4%), COVID-19 (4.9%), febrile neutropenia (4.0%) and COVID-

19 pneumonia (3.3%)Fatal adverse events occurred in 6.8% of patients with B-cell malignancies who received tafasitamab, the most frequent of which were infections and infestations (3.9%).
Permanent discontinuation of tafasitamab due to an adverse event occurred in 16% of patients. The most frequent adverse events which resulted in permanent discontinuation of tafasitamab were infections and infestations (6.6%), general disorders and administration site conditions (1.9%), blood and lymphatic system disorders (1.6%) and respiratory, thoracic and mediastinal disorders (1.0%).

Summary of the safety profile in Diffuse large-B Cell lymphoma

The most common adverse reactions were: infections (73%), neutropenia (51%), asthenia (40%), anaemia (36%), diarrhoea (36%), thrombocytopenia (31%), cough (26%), oedema peripheral (24%), pyrexia (24%), decreased appetite (22%).
The most common serious adverse reactions were infection (26%) including pneumonia (7%), and febrile neutropenia (6%).
Permanent discontinuation of tafasitamab due to an adverse reaction occurred in 15% of patients. The most common adverse reactions leading to permanent discontinuation of tafasitamab were infections and infestations (5%), nervous system disorders (2.5%), and respiratory, thoracic and mediastinal disorders (2.5%).
The frequency of dose modification or interruption due to adverse reactions was 65%. The most common adverse reactions leading to tafasitamab treatment interruption were blood and lymphatic system disorders (41%).

Summary of the safety profile in Follicular lymphoma

In the inMIND study the most common adverse reactions were infections (68%), including viral infections (41%) and bacterial infections (27%); neutropenia (57%), diarrhoea (37.6%), rash (36.4%), asthenia (34.9%), constipation (27.5%), pyrexia (19%), thrombocytopenia (17%), anaemia (17%), infusion related reaction (15.9%), pruritus (15.6%), abdominal pain(11.9%), pneumonia (11.6%) and headache (10.4%).
The most common serious adverse reactions were infections (26%), including viral infections (13%), and bacterial infections (6%); febrile neutropenia (2.8%), and pyrexia (1.8%).
Permanent discontinuation of tafasitamab due to an adverse reaction occurred in 7.3% of patients. The most common adverse reactions leading to permanent discontinuation of tafasitamab were viral infections (2.4%), infusion-related reaction (0.9%), and pyrexia (0.9%).
The frequency of tafasitamab dose modification or interruption due to adverse reactions was 67.9%. The most common adverse reactions leading to tafasitamab dose modification and interruption were neutropenia (38.8%) and viral infections (23.9%).

Adverse reactions observed and their frequencies calculated from the pooled safety population of patients with B-cell malignancies 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[+](46.6%), including viral infections[a] (31.6%), bacterial infections[b] (27.4%), pneumonia (12.1%) or other opportunistic infections with fatal outcomes (e.g. bronchopulmonary aspergillosis, bronchitis, and urinary tract infection)

Common: Sepsis

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

Uncommon: Basal cell carcinoma

Blood and lymphatic system disorders

Very common: Neutropenia[c] (57.3%)[+], anaemia[e] (26.6%)[+], thrombocytopenia[d] (25.7%)[+] and leukopenia (12.6%)

Common: Febrile neutropenia[+] and lymphopenia

Immune system disorders

Common: Hypogammaglobulinaemia, C-reactive protein increased

Metabolism and nutrition disorders

Very common: Hypokalaemia (12.4%), decreased appetite (15.0%)

Common: Hypomagnesaemia, weight decreased, hypocalcaemia

Uncommon: Tumor Lysis Syndrome

Nervous system disorders

Very common: Headache (11.4%)

Common: Paraesthesia, dysgeusia

Frequency unknown: Progressive multifocal leukoencephalopathy

Respiratory, thoracic and mediastinal disorders

Very common: Cough (19.0%), dyspnoea (10.0%)

Common: Nasal congestion, and exacerbation of chronic obstructive pulmonary disease

Gastrointestinal disorders

Very common: Diarrhoea (34.2%), nausea (24.0%), constipation (25.3%), and vomiting (11.8%), abdominal pain[f] (15.6%)

Hepatobiliary disorders

Common: Transaminases (ALT or AST) increased, gamma-glutamyltransferase increased, and hyperbilirubinaemia

Skin and subcutaneous tissue disorders

Very common: Rash (15.0%)[g], pruritus (10.1%)

Common: , alopecia, hyperhidrosis, and erythema

Musculoskeletal and connective tissue disorders

Very common: Muscle spasms (11.1%), back pain (10.8%)

Common: , 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[h] (38.0%), peripheral oedema (11.1%), and pyrexia (19.8%)

Common: Chills, mucosal inflammation

Injury, poisoning and procedural complications

Very common: Infusion related reaction (11.5%)[+]

+ Further information on this ADR is provided in the text below.
[a]Includes MedDRA terms for viral infection medical concept.
[b]Includes MedDRA terms for bacterial infection medical concept.
[c]Includes neutropenia and neutrophil count decreased.
dIncludes thrombocytopenia and platelet count decreased.
[e]Includes anaemia and haematocrit decreased.
[f]Includes abdominal pain, abdominal discomfort, abdominal pain lower, abdominal pain upper, and gastrointestinal pain.
[g]Includes rash, rash erythematous, rash maculo-papular, rash papular, rash pruritic, rash pustular, rash vesicular, and urticaria.
[h]Includes asthenia, malaise, and fatigue.

Description of specific adverse reactions and additional information

Selected undesirables effects are described for the pivotal studies MOR208C203 (L-MIND) and INCMOR0208-301 (inMIND).

Myelosuppression

Treatment with tafasitamab can cause serious or severe myelosuppression including neutropenia, thrombocytopenia and anaemia (see “Warnings and precautions”). In study MOR208C203 (L-MIND), 49.4% of patients treated with tafasitamab and lenalidomide experienced neutropenia. Grade 3 or

higher blood and lymphatic system disorders adverse reactions occurred in 55.6% of patients, including neutropenia (48.1%), thrombocytopenia (16%), febrile neutropenia (12.3%), leukopenia (9.9%) and anaemia (7.4%). Grade 4 blood and lymphatic system disorders adverse reactions occurred in 30.9% 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 were at least 20 percentage points lower for neutropenia, anaemia and thrombocytopenia; no cases of febrile neutropenia were reported with tafasitamab monotherapy.
In study INCMOR0208-301, myelosuppression (i.e. neutropenia, febrile neutropenia, thrombocytopenia, leukopenia, lymphopenia or anaemia) occurred in 63.3% of patients treated with tafasitamab, lenalidomide, and rituximab (tafasitamab group. Grade 4 haematological adverse reactions included neutropenia, thrombocytopenia, and febrile neutropenia. Myelosuppression led to interruption of tafasitamab in 42.8% and to tafasitamab discontinuation in 1.5%.

Infections
Bacterial, fungal, and new or reactivation of viral infections can occur during and following tafasitamab therapy (see “Warnings and Precautions”). In study MOR208C203 (L-MIND), 72.8% of patients treated with tafasitamab and lenalidomide experienced an infection. Grade 3 or higher infections occurred in 35.8% 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 2.5% of patients within 30 days of last treatment.
In study INCMOR0208-301, infections occurred in 52.3% of patients in the tafasitamab group (tafasitamab, lenalidomide and rituximab). Viral infections occurred in 41.3% of patients in the tafasitamab group. Bacterial infections occurred in 27.2% of patients in the tafasitamab group. Incidence of Grade 3 or 4 viral infections was 11.6% in the tafasitamab group. Incidence of Grade 3 or 4 bacterial infections was 7.6% in the tafasitamab group. Infections were fatal in 3 patients in the tafasitamab group (two cases of COVID-19 and one of sepsis).
Median time to first onset of any infection ≥ Grade 3 was 10 days (2 – 311 days).
Recommendations for management of infections are provided in section Warnings and Precautions.

Infusion-related reactions
In the MOR208C203 (L-MIND) 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. In study INCMOR 0208-301, infusion-related reactions occurred in 15.9% of patients in the tafasitamab group (tafasitamab, lenalidomide and rituximab). In the tafasitamab group infusion-related reactions occurred in 15.3% of patients during cycle 1, in 1.3% of patients during cycle 2 and in 0.3% of patients during cycle 3. 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.
Following tafasitamab treatment, anti-tafasitamab antibodies developed in 0.9% (3/327) of patients with FL in Study inMIND. Because of the low occurrence of ADA, the effect of these antibodies on the pharmacokinetics, pharmacodynamics, safety, and effectiveness of tasfasitamab products is unknown.

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

Tafasitamab induced a rapid reduction in peripheral blood B cell counts. In patients with relapsed or refractory DLBCL, 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.
In patients with relapsed or refractory follicular lymphoma, circulating B-cell decreased to undetectable levels by Day 8 following administration of the recommended dosage of tafasitamab in patients who had detectable B cells at treatment initiation. The depletion was sustained while patients remained on 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

Relapsed or refractory DLBCL
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 anti-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 78.45 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, data cut-off date 14 November 2022

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)	33 (40.7) (29.9 ; 52.2)
Partial response rate, n (%) (95% CI)	13 (16.0) (8.8, 25.9)[a]
Key Secondary Endpoints	
Overall duration of response (complete + partial response) [a]	
Median, months (95% CI)	NR (33.8, 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 (two patients a CR, five patients a PR) and one patient had a stable disease as the best response to tafasitamab + lenalidomide treatment.

Relapsed or refractory FL after at least one line of systemic therapy

The efficacy of tafasitamab in combination with lenalidomide and rituximab in patients with relapsed or refractory follicular lymphoma was evaluated in a randomized, double-blind, placebo-controlled phase 3 study (inMIND; INCMOR 0208-301).

Eligible patients were adults aged 18 years and above with histologically-confirmed grade 1-3a follicular lymphoma whose disease relapsed or became refractory after at least 1 prior line of systemic therapy, including an anti-CD20 therapy. The study excluded patients with CNS involvement of lymphoma, or prior allogeneic HSCT.

A total of 548 patients with R/R follicular lymphoma were randomized in a 1:1 ratio to receive tafasitamab plus lenalidomide and rituximab or placebo plus lenalidomide and rituximab for up to twelve 28-day cycles. Randomization was stratified by progression of disease within 24 months after initial diagnosis (POD24) (yes vs no), refractoriness to prior CD20-directed antibody therapy (yes vs no), and the number of prior lines of therapy (< 2 vs ≥ 2).

Dosing in each treatment arm was as follows:

- Tafasitamab 12 mg/kg intravenously (Days 1, 8, 15, and 22 of Cycles 1 to 3 and on Days 1 and 15 of Cycles 4 to 12) and lenalidomide 20 mg orally once daily (Days 1 to 21 of Cycles 1 to 12) with rituximab 375 mg/m² intravenously (Days 1, 8, 15, and 22 of Cycle 1 and on Day 1 of Cycles 2 to 5).

Placebo intravenously (Days 1, 8, 15, and 22 of Cycles 1 to 3 and on Days 1 and 15 of Cycles 4 to 12) and lenalidomide 20 mg orally once daily (Days 1 to 21 of Cycles 1 to 12) with rituximab 375 mg/m² intravenously (Days 1, 8, 15, and 22 of Cycle 1 and on Day 1 of Cycles 2 to 5).

The baseline demographics and disease characteristics were generally well balanced between the two treatment groups. Among the 548 patients with R/R FL enrolled in the inMIND study, the median age was 64 years (range 31 to 88 years), 54.6% were male, and 79.9% were white. The median time since initial diagnosis was 5.3 years. More than half of participants (53.6%) had Grade 2 FL at study entry and 56.8% had Ann Arbor Stage IV disease. Approximately half of participants (52.4%) had high-risk disease as per FLIPI score, and most participants (82.8%) met at least one GELF criterion for high tumour burden.

The majority (54.7%) of participants had received 1 prior systemic anticancer line of therapy and the rest of the patients received 2 or more lines; the median number of prior therapies was 1 (range: 1 to 10), 209 patients (38.1%) were refractory to their last prior therapy, 34.3% were anti-CD20 mAb-refractory, and 31.6% had progression of disease within 24 months (POD24)..

The primary efficacy endpoint was investigator-assessed progression-free survival (PFS) in the FL population, defined as the time from randomization to first documented disease progression, or death from any cause, whichever occurs first. The key secondary endpoints included PET-CR rate by INV in the FDG-avid FL population, defined as a complete metabolic response at any time after start of treatment, as well as overall survival in the FL population. At the time of the main analysis, overall survival had not been reached in either of the two arms. The total number of deaths was 38 cases: 15 deaths (5.5%) in the tafasitamab group and 23 deaths (8.4%) in the placebo group. The median duration of PFS follow-up was 14.3 months (95% CI: 11.8, 15) in the tafasitamab group and 14.1 months (95% CI: 11.5, 15) in the placebo group.

The efficacy results are summarized in Table 5.

Table 5: Efficacy Results from Study INCMOR 0208-301 (inMIND)

Endpoint	**Tafasitamab with Lenalidomide plus Rituximab (N = 273)**	**Placebo with Lenalidomide plus Rituximab (N = 275)**
Progression-free survival[a, b]		
Patients with event, n (%)	75 (27.5)	131 (47.6)
Median PFS (months) (95% CI)[c]	22.4 (19.2, NE)	13.9 (11.5, 16.4)

Hazard ratio[d] (95% CI)	0.43 (0.32, 0.58)	
p-value	< 0.0001	
Participants with FDG-avid PET Scan at Baseline[a]	(N = 251)	(N = 254)
PET-CR rate (95% CI)[e, f]	49.4 (43.1, 55.8)	39.8 (33.7, 46.1)
Odds ratio (95% CI)	1.5 (1.04, 2.13)	
p-value	0.0286	

CI = confidence interval; NE = not evaluable.

[a] Investigator-assessed

[b] Per Cheson 2014 Response Criteria

[c] Two-sided 95% CIs based on Brookmeyer and Crowley method.

[d] Hazard ratio based on a stratified Cox proportional hazard model.

[e] The PET-CR rate was defined as the proportion of patients in the FL population who achieved a complete metabolic response at any time after the start of treatment as per Lugano classification. Patients with no postbaseline assessment by PET or who did not achieve a CMR were classified as non-CR responders.

[f] 95% CIs based on the Clopper-Pearson method.

Pharmacokinetics

Absorption

Tafasitamab average serum trough concentrations (± standard deviation) were 177 (± 66) µg/mL during weekly intravenous administrations of 12 mg/kg from cycle 1 to 3. During administration every 14 days from cycle 4 to 6, average trough serum concentrations were 166 (± 75) µg/mL. Mean maximum tafasitamab serum concentrations were 491 (± 128) µg/mL.

Distribution

The total volume of distribution at steady state for tafasitamab was 6.7 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 0.48 L/day and terminal elimination half-life was 11.3 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 or 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.
Once reconstituted, the preparation should not be stored. Chemical and physical in-use stability has been demonstrated for maximum 30 days at 2°C – 8°C or for maximum 24 hours at 25°C. For microbiological reasons, the ready-to-use preparation should be used immediately after opening. 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 reconstitution has taken place in controlled and validated aseptic conditions.
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 14 days at 2°C – 8°C, followed by up to 24 hours at maximum 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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October 2025