ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

▼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 adverse reactions. See section 4.8 for how to report adverse reactions.

1. NAME OF THE MEDICINAL PRODUCT

MINJUVI 200 mg powder for concentrate for solution for infusion

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One vial of powder contains 200 mg of tafasitamab.

After reconstitution each mL of solution contains 40 mg of tafasitamab.

Tafasitamab is a humanised CD19-specific monoclonal antibody of the immunoglobulin G (IgG) subclass produced in mammalian (Chinese hamster ovary) cells by recombinant DNA technology.

Excipient with known effect
Each vial of MINJUVI contains 7.4 mg of sodium. For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Powder for concentrate for solution for infusion (powder for concentrate).
White to slightly yellowish lyophilised powder.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

MINJUVI is indicated in combination with lenalidomide followed by MINJUVI monotherapy for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) who are not eligible for autologous stem cell transplant (ASCT).

4.2 Posology and method of administration

MINJUVI must be administered by a healthcare professional experienced in treatment of cancer patients.

Recommended premedication
A premedication to reduce the risk of infusion-related reactions should be administered 30 minutes to 2 hours prior to tafasitamab infusion. For patients not experiencing infusion-related reactions during the first 3 infusions, premedication is optional for subsequent infusions.
The premedication may include antipyretics (e.g. paracetamol), histamine H1 receptor blockers (e.g. diphenhydramine), histamine H2 receptor blockers (e.g. cimetidine), or glucocorticosteroids (e.g. methylprednisolone).

Treatment of infusion-related reactions
If an infusion-related reaction occurs (Grade 2 and higher), the infusion should be interrupted. In addition, appropriate medical treatment of symptoms should be initiated. After signs and symptoms are resolved or reduced to Grade 1, MINJUVI infusion can be resumed at a reduced infusion speed (see Table 1).

If a patient has experienced a Grade 1 to 3 infusion-related reaction, premedication should be administered before subsequent tafasitamab infusions.

Posology
The recommended dose of MINJUVI is 12 mg per kg body weight administered as an intravenous infusion according to the following schedule:

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

Each cycle has 28 days.

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

Treatment with lenalidomide should be stopped after a maximum of twelve cycles of combination therapy. Patients should continue to receive MINJUVI infusions as single agent on day 1 and 15 of each 28-day cycle, until disease progression or unacceptable toxicity.

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

Table 1: Dose modifications in case of adverse reactions

Adverse reaction	**Severity**	**Dosage modification**
Infusion-related reactions	Grade 2 (moderate)	• 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 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.

Adverse reaction	Severity	Dosage modification
	Grade 4 (life-threatening)	• Stop the infusion immediately and permanently discontinue MINJUVI.
Myelosuppression	Platelet count of less than 50,000/µL	• Withhold MINJUVI and lenalidomide and monitor complete blood count weekly until platelet count is 50,000/µL or higher. • Resume MINJUVI at the same dose and lenalidomide at a reduced dose if platelets return to ≥ 50,000/µL. Refer to the lenalidomide SmPC 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 less than 500/µL	• Withhold MINJUVI and lenalidomide and monitor complete blood count weekly until neutrophil count is 1,000/µL or higher. • Resume MINJUVI at the same dose and lenalidomide at a reduced dose if neutrophils return to ≥ 1000/µL. Refer to the lenalidomide SmPC for dosage modifications.

Special populations

Paediatric population
The safety and efficacy of MINJUVI in children under 18 years have not been established.
No data are available.

Elderly
No dose adjustment is needed for elderly patients (≥ 65 years).

Renal impairment
No dose adjustment is needed for patients with mild or moderate renal impairment (see section 5.2). There are no data in patients with severe renal impairment for dosing recommendations.

Hepatic impairment
No dose adjustment is needed for patients with mild hepatic impairment (see section 5.2). There are no data in patients with moderate or severe hepatic impairment for dosing recommendations.

Method of administration
MINJUVI is for intravenous use 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, the rate should be increased to complete the first infusion within a 2.5-hour period.
- All subsequent infusions should be administered within a 1.5 to 2-hour period.
- In case of adverse reactions, consider the recommended dose modifications provided in Table 1.
- MINJUVI must not be co-administered with other medicinal products through the same infusion line.
- MINJUVI must not be administered as an intravenous push or bolus.

For instructions on reconstitution and dilution of the medicinal product before administration, see section 6.6.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Traceability
In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

Infusion-related reactions
Infusion-related reactions may occur and have been reported more frequently during the first infusion (see section 4.8). Patients should be monitored closely throughout the infusion. Patients should be advised 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. A premedication should be administered to patients prior to starting tafasitamab infusion. Based on the severity of the infusion-related reaction, tafasitamab infusion should be interrupted or discontinued and appropriate medical management should be instituted (see section 4.2).

Myelosuppression
Treatment with tafasitamab can cause serious and/or severe myelosuppression including neutropenia, thrombocytopenia and anaemia (see section 4.8). Complete blood counts should be monitored throughout treatment and prior to administration of each treatment cycle. Based on the severity of the adverse reaction, tafasitamab infusion should be withheld (see Table 1). Refer to the lenalidomide SmPC for dosage modifications.

Neutropenia
Neutropenia, including febrile neutropenia, has been reported during treatment with tafasitamab. Administration of granulocyte colony-stimulating factors (G-CSF) should be considered, in particular in patients with Grade 3 or 4 neutropenia. Any symptoms or signs of developing infection should be anticipated, evaluated and treated.

Thrombocytopenia
Thrombocytopenia has been reported during treatment with tafasitamab. Withholding of concomitant medicinal products that may increase bleeding risk (e.g. platelet inhibitors, anticoagulants) should be considered. Patients should be advised to report signs or symptoms of bruising or bleeding immediately.

Infections
Fatal and serious infections, including opportunistic infections, occurred in patients during treatment with tafasitamab. Tafasitamab should be administered 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.
Patients should be advised to contact their healthcare professionals if fever or other evidence of potential infection, such as chills, cough or pain on urination, develops.

Progressive Multifocal Leukoencephalopathy
Progressive multifocal leukoencephalopathy (PML) has been reported during combination therapy with tafasitamab. Patients should be monitored for new or worsening neurological symptoms or signs that may be suggestive of PML. The symptoms of PML are nonspecific and can vary depending on the affected region of the brain. These include altered mental status, memory loss, speech impairment, motor deficits (hemiparesis or monoparesis), limb ataxia, gait ataxia, and visual symptoms such as hemianopia and diplopia. If PML is suspected, further dosing of tafasitamab must be immediately suspended. Referral to a neurologist should be considered. Appropriate diagnostic measures may

include MRI scan, cerebrospinal fluid testing for JC viral DNA and repeat neurological assessments. If PML is confirmed, tafasitamab must be permanently discontinued.

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

Immunisations
The safety of immunisation with live vaccines following tafasitamab therapy has not been investigated and vaccination with live vaccines is not recommended concurrently with tafasitamab therapy.

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

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed.

4.6 Fertility, pregnancy and lactation

Treatment with tafasitamab in combination with lenalidomide should not be initiated in female patients unless pregnancy has been excluded. Please also refer to the SmPC of lenalidomide.

Women of childbearing potential/Contraception in females
Women of childbearing potential should be advised to use effective contraception during and for at least 3 months after end of treatment with tafasitamab.

Pregnancy
Reproductive and developmental toxicity studies have not been conducted with tafasitamab.

There are no data on the use of tafasitamab in pregnant women. However, IgG is known to cross the placenta and tafasitamab may cause foetal B-cell depletion based on the pharmacological properties (see section 5.1). 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 (see section 4.4).

Tafasitamab is not recommended during pregnancy and in women of childbearing potential not using contraception.

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.

Breast-feeding
It is not known whether tafasitamab is excreted in human milk. However, maternal IgG is known to be excreted in human milk. There are no data on the use of tafasitamab in breast-feeding women and a risk for breast-feeding children cannot be excluded. Women should be advised not to breast-feed during and for at least 3 months after the last dose of tafasitamab.

Fertility
No specific studies have been conducted to evaluate potential effects of tafasitamab on fertility. No adverse effects on male and female reproductive organs were observed in a repeat-dose toxicity study in animals (see section 5.3).

4.7 Effects on ability to drive and use machines

MINJUVI has no or negligible influence on the ability to drive and use machines. However, fatigue has been reported in patients taking tafasitamab and this should be taken into account when driving or using machines.

4.8 Undesirable effects

Summary of the safety profile

The most common adverse reactions are: 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%).

Tabulated list of adverse reactions

Adverse reactions reported in clinical trials are listed by MedDRA System Organ Class and by frequency. The frequencies of adverse reactions is based on the pivotal phase 2 trial MOR208C203 (L-MIND) with 81 patients. Patients were exposed to tafasitamab for a median of 7.7 months. The adverse reaction frequencies from clinical trials 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.

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); and not known (cannot be estimated from the available data). Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

Table 2: Adverse reactions in patients with relapsed or refractory DLBCL who received tafasitamab in the clinical trial MOR208C203 (L-MIND)

System organ class	Frequency	Adverse reactions
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)
	Common	Sepsis (including neutropenic sepsis)
Neoplasms benign, malignant and unspecified (incl. cysts and polyps)	Common	Basal cell carcinoma
Blood and lymphatic system disorders	Very common	Febrile neutropenia[+], neutropenia[+], thrombocytopenia[+], anaemia, leukopenia[+]
	Common	Lymphopenia
Immune system disorders	Common	Hypogammaglobulinaemia
Metabolism and nutrition disorders	Very common	Hypokalaemia, decreased appetite
	Common	Hypocalcaemia, hypomagnesaemia
Nervous system disorders	Common	Headache, paraesthesia, dysgeusia
Respiratory, thoracic and mediastinal disorders	Very common	Dyspnoea, cough
	Common	Exacerbation of chronic obstructive pulmonary disease, nasal congestion
Gastrointestinal disorders	Very common	Diarrhoea, constipation, vomiting, nausea, abdominal pain
Hepatobiliary disorders	Common	Hyperbilirubinaemia, transaminases increased (includes ALT and/or AST increased), Gamma-glutamyltransferase increased
Skin and subcutaneous tissue disorders	Very common	Rash (includes different types of rash, e.g. rash, rash maculopapular, rash pruritic, rash erythematous)
	Common	Pruritus, alopecia, erythema, hyperhidrosis
Musculoskeletal and connective tissue disorders	Very common	Back pain, muscle spasms
	Common	Arthralgia, pain in extremity, musculoskeletal pain
Renal and urinary disorders	Common	Blood creatinine increased
General disorders and administration site conditions	Very common	Asthenia[++] , oedema peripheral, pyrexia
	Common	Mucosal inflammation
Investigations	Common	Weight decreased, C-reactive protein increased
Injury, poisoning and procedural complications	Common	Infusion related reaction

+Further information on this adverse reaction is provided in the text below.

[++] Asthenia includes asthenia, fatigue and malaise.

Compared with the incidences on combination therapy with lenalidomide, the incidences of non-haematological adverse reactions on tafasitamab monotherapy decreased by at least 10% for decreased appetite, asthenia, hypokalaemia, constipation, nausea, muscle spasms, dyspnoea and C-reactive protein increased.

Description of selected adverse reactions

Myelosuppression

Treatment with tafasitamab can cause serious or severe myelosuppression including neutropenia, thrombocytopenia and anaemia (see sections 4.2 and 4.4).

In the L-MIND study, myelosuppression (i.e. neutropenia, febrile neutropenia, thrombocytopenia, leukopenia, lymphopenia or anaemia) occurred in 65.4% of patients treated with tafasitamab. Myelosuppression was managed by reduction or interruption of lenalidomide, interruption of tafasitamab and/or administration of G-CSF (see sections 4.2 and 4.4). Myelosuppression led to interruption of tafasitamab in 41% and to tafasitamab discontinuation in 1.2%.

Neutropenia/febrile neutropenia
Incidence of neutropenia was 51%. Incidence of Grade 3 or 4 neutropenia was 49% and of Grade 3 or 4 febrile neutropenia was 12%. Median duration of any adverse reaction of neutropenia was 8 days (range 1 – 222 days); median time to onset to first occurrence of neutropenia was 49 days (range 1 – 994 days).

Thrombocytopenia
Incidence of thrombocytopenia was 31%. Incidence of Grade 3 or 4 thrombocytopenia was 17%. Median duration of any adverse reaction thrombocytopenia was 11 days (range 1 – 470 days); median time to onset to first occurrence of thrombocytopenia was 71 days (range 1 – 358 days).

Anaemia
Incidence of anaemia was 36%. Incidence of Grade 3 or 4 anaemia was 7%. Median duration of any adverse reaction of anaemia was 15 days (range 1 – 535 days); median time to onset to first occurrence of anaemia was 49 days (range 1 – 1129 days).

When patients in the L-MIND study were switched from tafasitamab and lenalidomide in the combination therapy phase to tafasitamab alone in the extended monotherapy phase, the incidences of haematological events decreased by at least 20% for neutropenia, thrombocytopenia and anaemia; no incidences of febrile neutropenia were reported with tafasitamab monotherapy (see sections 4.2 and 4.4).

Infections
In the L-MIND study, infections occurred in 73% of patients. Incidence of Grade 3 or 4 infections was 28%. The most frequently reported Grade 3 or higher infections were pneumonia (7%), respiratory tract infections (4.9%), urinary tract infections (4.9%) and sepsis (4.9%). Infection was fatal in < 1% of patients (pneumonia) within 30 days of last treatment.
Median time to first onset of Grade 3 or 4 infection was 62.5 days (4 – 1014 days). Median duration of any infection was 11 days (1 – 392 days).
Recommendations for management of infections are provided in section 4.4.
Infection led to dose interruption of tafasitamab in 27% and tafasitamab discontinuation in 4.9%.

Infusion-related reactions
In the L-MIND study, infusion-related reactions occurred in 6% of patients. All infusion related reactions were Grade 1 and resolved on the day of occurrence. Eighty percent of these reactions occurred during cycle 1 or 2. Symptoms included chills, flushing, dyspnoea and hypertension (see sections 4.2 and 4.4).

Immunogenicity
In 245 patients treated with tafasitamab, no treatment-emergent or treatment-boosted anti-tafasitamab antibodies were observed. Pre-existing anti-tafasitamab antibodies were detected in 17/245 patients (6.9%) with no impact on pharmacokinetics, efficacy or safety of tafasitamab.

Special populations

Elderly
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%).

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

4.9 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.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antineoplastic agents, monoclonal antibodies, ATC code: L01FX12.

Mechanism of action
Tafasitamab is an Fc-enhanced monoclonal antibody that targets the CD19 antigen expressed on the surface of pre-B and mature B lymphocytes.

Upon binding to CD19, tafasitamab mediates B-cell lysis through:
- engagement of immune effector cells like natural killer cells, γδ T cells and phagocytes
- direct induction of cell death (apoptosis)

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

Pharmacodynamic effects
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 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 plus lenalidomide followed by tafasitamab monotherapy was studied in the 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 or who had refused ASCT. One of the prior systemic therapies had to include a CD20 targeted therapy. 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. Patients with a known history of "double/triple-hit" genetics DLBCL were also excluded at study entry.

For the first three cycles, patients received 12 mg/kg tafasitamab via infusion on day 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. Premedication 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 L-MIND study. The median age was 72 years (range 41 to 86 years), 89% were white and 54% were males. Out of 81 patients, 74 (91.4%) had ECOG performance score of 0 or 1 and 7 (8.6%) had ECOG score of 2. The median number of prior therapies was two (range: 1 to 4), with 40 patients (49.4%) receiving one prior therapy and 35 patients (43.2%) receiving 2 prior lines of treatment. Five patients (6.2%) had 3 prior lines of therapies and 1 (1.2%) had 4 prior lines of treatment. All patients had received a prior anti-CD20-containing therapy. Eight

patients had a diagnosis of DLBCL transformed from low-grade lymphoma. Fifteen patients (18.5%) had primary refractory disease, 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 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 treatment was 9.2 months (range: 0.23, 54.67 months). Thirty-two (39.5%) patients completed 12 cycles of tafasitamab. Thirty (37.0%) patients completed 12 cycles of lenalidomide.

The primary efficacy endpoint was best objective response rate (ORR), defined as the proportion of complete and partial responders, as assessed by an independent review committee (IRC). Other efficacy endpoints included duration of response (DoR), progression-free survival (PFS) and overall survival (OS). The efficacy results are summarised in Table 3.

Table 3: 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]*)	
	30-NOV-2019 cut-off (24 months analysis)	**30-OCT-2020 cut-off** (35 months analysis)
Primary endpoint		
Best objective response rate (per IRC)		
Overall response rate, n (%) (95% CI)	46 (56.8) [45.3, 67.8]	46 (56.8) [45.3, 67.8]
Complete response rate, n (%) (95% CI)	32 (39.5) [28.8, 51.0]	32 (39.5) [28.8, 51.0]
Partial response rate, n (%) (95% CI)	14 (17.3) [9.8, 27.3]	14 (17.3) [9.8, 27.3]
Secondary endpoint		
Overall duration of response (complete + partial response) [a]		
Median, months (95% CI)	34.6 [26.1, NR]	43.9 [26.1, NR]

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

Overall survival (OS) was a secondary endpoint in the study. After a median follow up time of 42.7 months (95% CI: 38.0; 47.2), the median OS was 31.6 months (95% CI: 18.3; not reached). Amongst 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.

Elderly
In the ITT set, 36 of 81 patients were ≤ 70 years and 45 of 81 patients were > 70 years. No overall differences in efficacy were observed for patients ≤ 70 years versus patients > 70 years of age.

Paediatric population
The European Medicines Agency has waived the obligation to submit the results of studies with MINJUVI in all subsets of the paediatric population in diffuse large B-cell lymphoma (see section 4.2 for information on paediatric use).

This medicinal product has been authorised under a so-called 'conditional approval' scheme. This means that further evidence on this medicinal product is awaited.
The European Medicines Agency will review new information on this medicinal product at least every year and this SmPC will be updated as necessary.

5.2 Pharmacokinetic properties

The absorption, distribution, biotransformation and elimination were documented based on a population pharmacokinetic analysis.

Absorption
Based on an analysis of tafasitamab in combination with lenalidomide, tafasitamab average serum trough concentrations (± standard deviation) were 179 (± 53) µg/mL during weekly (plus an additional dose on day 4 of cycle 1) intravenous administrations of 12 mg/kg. 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.

Biotransformation
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.

Special populations
Age, body weight, sex, tumour size, disease type, B-cell or absolute lymphocyte counts, anti-drug antibodies, lactate dehydrogenase and serum albumin levels had no relevant effect on the pharmacokinetics of tafasitamab. The influence of race and ethnicity on the pharmacokinetics of tafasitamab is unknown.

Renal impairment
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.

Hepatic impairment
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.

5.3 Preclinical safety data

Preclinical data reveal no special hazards for humans.

Repeat dose toxicology studies
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.

Mutagenicity/carcinogenicity
As tafasitamab is a monoclonal antibody, genotoxicity and carcinogenicity studies have not been conducted, since such tests are not relevant for this molecule in the proposed indication.

Reproductive toxicity
Reproductive and developmental toxicity studies as well as specific studies to evaluate the effects on fertility have not been conducted with tafasitamab. However, no adverse effects on reproductive organs in males and females and no effects on menstrual cycle length in females were observed in the 13-week repeat-dose toxicity study in cynomolgus monkeys.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium citrate dihydrate
Citric acid monohydrate
Trehalose dihydrate
Polysorbate 20

6.2 Incompatibilities

This medicinal product must not be mixed with other medicinal products except those mentioned in section 6.6.
No incompatibilities have been observed with standard infusion materials.

6.3 Shelf life

Unopened vial
5 years

Reconstituted solution (prior to dilution)
Chemical and physical in-use stability has been demonstrated for up to 30 days at 2 °C – 8 °C or up to 24 hours at 25 °C.
From a microbiological point of view, the reconstituted solution should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user and would normally not be longer than 24 hours at 2 – 8 °C, unless reconstitution has taken place in controlled and validated aseptic conditions. Do not freeze or shake.

Diluted solution (for infusion)
Chemical and physical in-use stability has been demonstrated for a maximum of 14 days at 2 °C – 8 °C followed by up to 24 hours at up to 25 °C.
From a microbiological point of view, the diluted solution should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2 – 8 °C, unless dilution has taken place in controlled and validated aseptic conditions. Do not freeze or shake.

6.4 Special precautions for storage

Store in a refrigerator (2 °C – 8 °C).
Keep the vial in the outer carton in order to protect from light.

For storage conditions after reconstitution and dilution of the medicinal product, see section 6.3.

6.5 Nature and contents of container

Clear type I glass vial with a butyl rubber stopper, aluminium seal and a plastic flip-off cap containing 200 mg tafasitamab. Pack size of one vial.

6.6 Special precautions for disposal and other 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 by the patient weight (kg). Then calculate the number of tafasitamab vials needed (each vial contains 200 mg tafasitamab) (see section 4.2).
- Using a sterile syringe, gently add 5.0 mL sterile water for injections into each MINJUVI vial. Direct the stream toward the walls of each vial and not directly on 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 to 8 mg/mL of tafasitamab.
- Gently mix the intravenous 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.

7. MARKETING AUTHORISATION HOLDER

Incyte Biosciences Distribution B.V.
Paasheuvelweg 25
1105 BP Amsterdam
Netherlands

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/21/1570/001

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 26 August 2021
Date of latest renewal: 17 September 2025

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency https://www.ema.europa.eu.

ANNEX II

A. MANUFACTURERS OF THE BIOLOGICAL ACTIVE SUBSTANCE AND MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

E. SPECIFIC OBLIGATION TO COMPLETE POST-AUTHORISATION MEASURES FOR THE CONDITIONAL MARKETING AUTHORISATION

A. MANUFACTURERS OF THE BIOLOGICAL ACTIVE SUBSTANCE AND MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturers of the biological active substance
Boehringer Ingelheim Pharma GmbH & Co KG
Birkendorfer Str. 65
88397 Biberach a.d.R.
Germany

Incyte Biosciences Technical Operations S.a.r.l.
Avenue Des Sciences 12,
Yverdon Les Bains, 1400,
Switzerland

Name and address of the manufacturer responsible for batch release
Incyte Biosciences Distribution B.V.
Paasheuvelweg 25
1105 BP Amsterdam
Netherlands

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to restricted medical prescription (see Annex I: Summary of Product Characteristics, section 4.2).

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

- **Periodic safety update reports (PSURs)**

The requirements for submission of PSURs for this medicinal product are set out in Article 9 of Regulation (EC) No 507/2006 and, accordingly, the marketing authorisation holder (MAH) shall submit PSURs every 6 months.

The requirements for submission of PSURs for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

The marketing authorisation holder (MAH) shall submit the first PSUR for this product within 6 months following authorisation.

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

- **Risk management plan (RMP)**

The marketing authorisation holder (MAH) shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the marketing authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:
- At the request of the European Medicines Agency;

- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

E. SPECIFIC OBLIGATION TO COMPLETE POST-AUTHORISATION MEASURES FOR THE CONDITIONAL MARKETING AUTHORISATION

This being a conditional marketing authorisation and pursuant to Article 14-a of Regulation (EC) No 726/2004, the MAH shall complete, within the stated timeframe, the following measures:

Description	Due date
In order to confirm the efficacy and safety of Tafasitamab in combination with lenalidomide in diffuse Large B cell lymphoma in patients not eligible for ASCT, the MAH should conduct and submit the results of a single-arm study of Tafasitamab in combination with lenalidomide in the approved indication according to an agreed protocol.	December 2026
In order to confirm the efficacy and to re-confirm the safety profile of tafasitamab in combination with lenalidomide the applicant should submit the results of a phase 3, multicentre, randomized, double-blind, placebo-controlled trial comparing tafasitamab plus lenalidomide in addition to R-CHOP versus R-CHOP in previously untreated, high-intermediate and high-risk patients with newly-diagnosed diffuse large B-cell lymphoma (DLBCL).	December 2026

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON

1. NAME OF THE MEDICINAL PRODUCT

MINJUVI 200 mg powder for concentrate for solution for infusion
tafasitamab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One vial of powder contains 200 mg of tafasitamab.
After reconstitution each mL of solution contains 40 mg of tafasitamab.

3. LIST OF EXCIPIENTS

Excipients: sodium citrate dihydrate, citric acid monohydrate, trehalose dihydrate and polysorbate 20.
See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Powder for concentrate for solution for infusion
1 vial

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
For intravenous use after reconstitution and dilution

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator.
Keep the vial in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Incyte Biosciences Distribution B.V.
Paasheuvelweg 25
1105 BP Amsterdam
Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/21/1570/001

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted.

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

VIAL LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

MINJUVI 200 mg powder for concentrate
tafasitamab
IV use after reconstitution and dilution

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

6. OTHER

B. PACKAGE LEAFLET

Package leaflet: Information for the user

MINJUVI 200 mg powder for concentrate for solution for infusion
tafasitamab

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What MINJUVI is and what it is used for

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

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

What other medicines MINJUVI is given with
MINJUVI is used with another cancer medicine lenalidomide at the start of treatment, after which MINJUVI treatment is continued on its own.

2. What you need to know before you use MINJUVI

Do not use MINJUVI

- if you are allergic to tafasitamab or any of the other ingredients of this medicine (listed in section 6)

Warnings and precautions

Talk to your doctor or pharmacist before using MINJUVI if you have an infection or a history of recurring infections.

You might notice the following during treatment with MINJUVI:

- **Infusion-related reactions**
  Infusion-related reactions may occur most frequently during the first infusion. Your doctor will monitor you for infusion-related reactions during your infusion of MINJUVI. Inform your doctor immediately if you have reactions such as fever, chills, flushing, rash or breathing difficulties within 24 hours of infusion.
  Your doctor will give you treatment before each infusion to reduce the risk of infusion-related reactions. If you do not have reactions, your doctor may decide that you do not need these medicines with later infusions.
- **Reduced number of blood cells**
  Treatment with MINJUVI can severely reduce the number of some types of blood cells in your body, such as white blood cells called neutrophils, platelets and red blood cells. Tell your doctor immediately if you have fever of 38 °C or above, or any signs of bruising or bleeding, as these may be signs of such a reduction.
  Your doctor will check your blood cell counts throughout treatment and before starting each treatment cycle.
- **Infections**
  Serious infections, including infections that can cause death, can occur during and following MINJUVI treatment. Tell your doctor if you notice signs of an infection, such as fever of 38 °C or above, chills, cough or pain on urination.
- **Progressive multifocal leukoencephalopathy (PML)**
  PML is a very rare and life threatening infection in the brain. Tell your doctor straight away if you have symptoms such as memory loss, trouble speaking, difficulty walking, or problems with your eyesight or numbness or weakness in the face, arm, or leg.
  If you had any of these symptoms before or during treatment with MINJUVI, or you notice any changes, tell your doctor straight away as these may be signs of PML.
- **Tumour lysis syndrome**
  Some people may develop unusually high levels of some substances (such as potassium and uric acid) in the blood caused by the fast breakdown of cancer cells during treatment. This is called tumour lysis syndrome. Tell your doctor if you have symptoms such as nausea, vomiting, lack of appetite or fatigue, dark urine, decreased urine or side or back pain, muscle cramps, numbness, or heart palpitations. Your doctor may give you treatment before each infusion to reduce the risk of tumour lysis syndrome and perform blood tests to check you for tumour lysis syndrome.

Tell your doctor immediately if you notice any of these problems.

Children and adolescents

MINJUVI is not recommended in children and adolescents under 18 years, as there is no information about the use in this age group.

Other medicines and MINJUVI
Tell your doctor or pharmacist if you are using, have recently used or might use any other medicines.

The use of live vaccines during treatment with tafasitamab is not recommended.

Pregnancy and breast-feeding

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

- **Contraception**
  Use of effective contraception during treatment with MINJUVI and for at least 3 months after end of treatment is recommended for women of childbearing potential.

- **Pregnancy**
  Do not use MINJUVI during pregnancy and if you are of childbearing potential not using contraception. Pregnancy must be ruled out before treatment. Tell your doctor immediately if you become pregnant or think you may be pregnant during treatment with MINJUVI.

  MINJUVI is given with lenalidomide for up to 12 cycles. **Lenalidomide can harm the unborn baby and must not be used during pregnancy and in women of childbearing potential**, unless all of the conditions of the lenalidomide pregnancy prevention programme are met. Your doctor will provide you with more information and recommendations.

- **Breast-feeding**
  Do not breast-feed during treatment with MINJUVI until at least 3 months after the last dose. It is not known whether tafasitamab passes into breast milk.

Driving and using machines

MINJUVI has no or negligible influence on the ability to drive and use machines. However, fatigue has been reported in patients taking tafasitamab and this should be taken into account when driving or using machines.

MINJUVI contains sodium

This medicine contains 37.0 mg sodium (main component of cooking/table salt) in each dose of 5 vials (the dose of a patient weighing 83 kg). This is equivalent to 1.85% of the recommended maximum daily dietary intake of sodium for an adult.

3. How to use MINJUVI

A doctor experienced in treating cancer will supervise your treatment. MINJUVI will be given into one of your veins via infusion (drip). During and after the infusion, you will be checked regularly for infusion-related side effects.
MINJUVI will be given to you in cycles of 28 days. The dose you get is based on your weight and will be worked out by your doctor.

The recommended dose is 12 mg tafasitamab per kilogram body weight. This is given as an infusion into a vein according to the following schedule:
- Cycle 1: infusion on day 1, 4, 8, 15 and 22 of the cycle
- Cycles 2 and 3: infusion on day 1, 8, 15 and 22 of each cycle
- Cycle 4 and after: infusion on day 1 and 15 of each cycle

In addition, your doctor will prescribe you to take lenalidomide capsules for up to twelve cycles. The recommended starting dose of lenalidomide is 25 mg daily on days 1 to 21 of each cycle.
The doctor adjusts the starting dose and subsequent dosing if needed.

After a maximum of twelve cycles of combination therapy, treatment with lenalidomide is stopped. Treatment cycles with MINJUVI alone are then continued until the disease gets worse or you develop unacceptable side effects.

If you have been given more MINJUVI than you should

Because the medicine is given in hospital under a doctor’s supervision, this is unlikely. Tell your doctor if you think you may have been given too much MINJUVI.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Contact your doctor or nurse immediately if you notice any of the following serious side effects – you may need urgent medical treatment. These may be new symptoms or a change in your current symptoms.

- serious infections, possible symptoms: fever, chills, sore throat, cough, shortness of breath, nausea, vomiting, diarrhoea. These could be particularly significant if you have been told you have a low level of white blood cells called neutrophils.
- pneumonia (lung infection)
- sepsis (infection within the bloodstream)

Other side effects
Tell your doctor or nurse if you notice any of the following side effects:
Very common (may affect more than 1 in 10 people)

- reduced number of blood cells
  - white blood cells, especially a type called neutrophils; possible symptoms: fever of 38 °C or above, or any symptoms of an infection
  - platelets; possible symptoms: unusual bruising or bleeding without or on only minor injury
  - red blood cells; possible symptoms: pale skin or lips, tiredness, shortness of breath
- bacterial, viral or fungal infections, such as respiratory tract infections, bronchitis, lung inflammation, urinary tract infections
- rash
- low blood potassium level in tests
- muscle cramps
- back pain
- swelling of arms and/or legs due to build-up of fluid
- weakness, tiredness, feeling generally unwell
- fever
- diarrhoea
- constipation
- abdominal pain
- nausea
- vomiting
- cough
- shortness of breath
- decreased appetite

Common (may affect up to 1 in 10 people)

- worsening of breathing difficulties caused by narrowed lung airways called chronic obstructive pulmonary disease (COPD)
- headache
- abnormal sensation of the skin, such as tingling, prickling, numbness
- itching
- redness of skin
- infusion-related reactions
  These reactions may occur during infusion of MINJUVI or within 24 hours after infusion. Possible symptoms are fever, chills, flushing or breathing difficulties.
- altered sense of taste
- hair loss
- abnormal sweating
- pain in arms and legs
- muscle and joint pain

- decreased weight
- nasal congestion
- inflammation of the membranes lining organs such as the mouth
- lack of certain white blood cells called lymphocytes in blood tests
- a problem with the immune system called hypogammaglobulinaemia
- in blood tests, low blood level of
  - calcium
  - magnesium
- in blood tests, increased blood level of
  - C-reactive protein, which could be the result of inflammation or infection
  - creatinine, a breakdown product from muscle tissue
  - liver enzymes: gamma-glutamyltransferase, transaminases
  - bilirubin, a yellow breakdown substance of the blood pigment
- a skin cancer called basal cell carcinoma

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store MINJUVI

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the vial label and carton after EXP. The expiry date refers to the last day of that month.

Store in a refrigerator (2 °C – 8 °C).
Keep the vial in the outer carton in order to protect from light.

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

6. Contents of the pack and other information

What MINJUVI contains

- The active substance is tafasitamab. One vial contains 200 mg of tafasitamab. After reconstitution each mL of solution contains 40 mg of tafasitamab.
- The other ingredients are sodium citrate dihydrate, citric acid monohydrate, trehalose dihydrate, polysorbate 20 (see section 2 “MINJUVI contains sodium”).

What MINJUVI looks like and contents of the pack

MINJUVI is a powder for concentrate for solution for infusion. It is a white to slightly yellowish lyophilised powder in a clear glass vial with a rubber stopper, aluminium seal and plastic flip-off cap. Each carton contains 1 vial.

Marketing Authorisation Holder and Manufacturer
Incyte Biosciences Distribution B.V.
Paasheuvelweg 25
1105 BP Amsterdam
Netherlands

This leaflet was last revised in MM/YYYY.

This medicine has been given 'conditional approval'. This means that there is more evidence to come about this medicine.
The European Medicines Agency will review new information on this medicine at least every year and this leaflet will be updated as necessary.

Other sources of information

Detailed information on this medicine is available on the European Medicines Agency website: https://www.ema.europa.eu.

This leaflet is available in all EU/EEA languages on the European Medicines Agency website.

The following information is intended for healthcare professionals only:

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 by 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 injections into each MINJUVI vial. Direct the stream toward the walls of each vial and not directly on 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 to 8 mg/mL of tafasitamab.
- Gently mix the intravenous bag by slowly inverting the bag. Do not shake.

Method of administration
- 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 within a 1.5 to 2-hour period.
- Do not co-administer other medicines through the same infusion line.
- Do not administer MINJUVI as an intravenous push or bolus.

Reconstituted solution (prior to dilution)
Chemical and physical in-use stability has been demonstrated for up to up to 30 days at 2 °C – 8 °C or 24 hours at 25 °C.

From a microbiological point of view, the reconstituted solution should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user and would normally not be longer than 24 hours at 2 – 8 °C, unless reconstitution has taken place in controlled and validated aseptic conditions. Do not freeze or shake.

Diluted solution (for infusion)
Chemical and physical in-use stability has been demonstrated for a maximum of 14 days at 2 °C – 8 °C followed by up to 24 hours at up to 25 °C.

From a microbiological point of view, the diluted solution should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2 to 8 °C, unless dilution has taken place in controlled and validated aseptic conditions. Do not freeze or shake.

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