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 and 1.0 mg of polysorbate 20. 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).

MINJUVI is indicated in combination with lenalidomide and rituximab for the treatment of adult patients with relapsed or refractory follicular lymphoma (FL) (Grade 1-3a) after at least one line of systemic therapy.

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), and/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.

Combination with lenalidomide
As MINJUVI is indicated in combination with lenalidomide, please refer to the lenalidomide Summary of Product Characteristics (SmPC) for the recommendations on prophylactic antithrombotic medicines.

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

Recommended dose for the treatment of adult patients with relapsed or refractory FL after at least one line of systemic therapy
The recommended dose of MINJUVI is 12 mg per kg body weight administered as an intravenous infusion according to the following schedule:
- 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.

Each cycle has 28 days.

The recommended starting dose of rituximab is 375 mg/m^2 administered as an intravenous infusion according to the following schedule:
- Cycle 1: on days 1, 8, 15 and 22.
- Cycles 2 to 5: on day 1 of each cycle.

Each cycle has 28 days. Please refer to the SmPC of rituximab intravenous formulations for information on its method of administration and premedication and prophylactic medications.

In addition, patients should self-administer lenalidomide capsules at the recommended starting dose of 20 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 SmPC.

MINJUVI in combination with lenalidomide plus rituximab is given for up to twelve cycles for MINJUVI and lenalidomide, and five cycles for rituximab. Treatment with rituximab should be stopped after five cycles of combination therapy. Patients should continue to receive MINJUVI infusions in combination with oral lenalidomide up to cycle twelve. Treatment with tafasitamab plus lenalidomide should be stopped after a maximum of twelve cycles.

Dose modifications
Table 1 provides dose modifications for MINJUVI 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.

Adverse reaction	Severity	Dosage modification
	Grade 3 (severe)	• Interrupt MINJUVI infusion immediately and manage signs and symptoms. • Once signs and symptoms resolve or reduce to Grade 1, resume MINJUVI infusion at no more than 25% of the rate at which the reaction occurred. If the patient does not experience further reaction within 1 hour and vital signs are stable, the infusion rate may be increased every 30 minutes as tolerated to a maximum of 50% of the rate at which the reaction occurred. • If after rechallenge the reaction returns, stop the infusion immediately.
	Grade 4 (life-threatening)	• Stop the infusion immediately and permanently discontinue MINJUVI.
Myelosuppression	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. Tumour lysis syndrome has been reported during treatment with tafasitamab. 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.

CD19-negative or CD20-negative disease
There are no data available on patients with CD19-negative or CD20-negative FL treated with tafasitamab in combination with lenalidomide and rituximab, and it is possible that patients with CD19-negative or CD20-negative FL may have less benefit compared to patients with CD19-positive and CD20-positive FL. The potential risks and benefits associated with treatment of patients with CD19-negative or CD20-negative FL with tafasitamab in combination with lenalidomide and rituximab should be considered.

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.
This medicinal product contains 5.0 mg of polysorbate 20 per 5 vials. Polysorbate 20 may cause allergic reactions.

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

Patients with relapsed or refractory DLBCL

The safety of tafasitamab in patients with DLBCL was evaluated in the open-label, multicentre, single-arm phase 2 study L-MIND in 81 patients with relapsed or refractory DLBCL. Patients received tafasitamab 12 mg/kg intravenously in

combination with lenalidomide for a maximum of 12 cycles, followed by tafasitamab monotherapy until disease progression or unacceptable toxicity.
The median duration of exposure to tafasitamab was 7.7 months.
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%).

Patients with relapsed or refractory FL after at least one line of systemic therapy
The safety of tafasitamab in patients with FL was evaluated in the randomised, double-blind, placebo-controlled multicenter phase 3 study inMIND in 652 patients, including 546 participants with relapsed or refractory (R/R) follicular lymphoma and 106 participants with R/R marginal zone lymphoma. Patients received tafasitamab 12 mg/kg (n = 327) or placebo (n = 325) intravenously in combination with rituximab 375 mg/m^2 intravenously (for a maximum of 5 cycles) and lenalidomide 20 mg orally (for a maximum of 12 cycles). Tafasitamab treatment was stopped after 12 cycles. Among patients who received tafasitamab, 83% were exposed for 6 months or longer. The median duration of exposure to tafasitamab was 322 days.

In the inMIND study, the most common adverse reactions were infections (68%), including viral infections (41%) and bacterial infections (27%); neutropenia (57%), rash (36.4%), asthenia (34.9%), pyrexia (19%), thrombocytopenia (17%), anaemia (17%), infusion related reaction (15.9%), pruritus (15.6%) 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%), acute kidney injury (2.8%) and pyrexia (1.8%).
Permanent discontinuation of tafasitamab due to an adverse reaction occurred in 11.6% of patients. The most common adverse reactions leading to permanent discontinuation of tafasitamab were viral infections (2.4%), including COVID-19 (1.5%) and COVID-19 pneumonia (1.2%), infusion-related reaction (0.9%) and pyrexia (0.9%).
The frequency of tafasitamab dose modification or interruption due to adverse reactions was 74.9%. The most common adverse reactions leading to tafasitamab dose modification and interruption were neutropenia (38.8%) and viral infections (23.9%) including COVID-19 (21.1%) and COVID-19 pneumonia (3.7%).

Tabulated list of adverse reactions
Adverse reactions reported for tafasitamab in clinical trials are listed by MedDRA System Organ Class and by frequency.

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 combination with lenalidomide 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

System organ class	Frequency	Adverse reactions
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.

Table 3: Adverse reactions in patients with relapsed or refractory FL who received tafasitamab in combination with rituximab and lenalidomide in INCMOR 0208-301 (inMIND)

System organ class / Adverse reaction	All grades frequency	Grade 3-4[a] frequency
Infections and infestations		
Viral infections[b]	Very common	Very common
Bacterial infections[c]	Very common	Common
Pneumonia	Very common	Common
Bronchitis	Common	-
Sepsis	Common	Uncommon
Blood and lymphatic system disorders		
Neutropenia[d]	Very common	Very common
Thrombocytopenia[e]	Very common	Common
Anaemia[f]	Very common	Common
Febrile neutropenia	Common	Common
Leukopenia	Common	Uncommon
Metabolism and nutrition disorders		
Tumour lysis syndrome	Uncommon	Uncommon

System organ class / Adverse reaction	All grades frequency	Grade 3-4[a] frequency
Nervous system disorders		
Headache	Very common	Uncommon
Gastrointestinal disorders		
Diarrhoea	Very common	Uncommon
Constipation	Very common	Uncommon
Abdominal pain[g]	Very common	-
Skin and subcutaneous tissue disorders		
Rash[h]	Very common	Common
Pruritus	Very common	Uncommon
General disorders and administration site conditions		
Asthenia[i]	Very common	Common
Pyrexia	Very common	Common
Chills	Common	-
Investigations		
ALT increased	Common	Uncommon
AST increased	Common	Uncommon
Injury, poisoning, and procedural complications		
Infusionrelated reaction	Very common	Uncommon

[a] The severity of adverse drug reactions was assessed based on the CTCAE, defining grade 1 = mild, grade 2 = moderate, grade 3 = severe, grade 4=life threatening, and 5=death.

[b] Includes viral infection, COVID-19, COVID-19 pneumonia, coronavirus infection, coronavirus test positive, cytomegalovirus chorioretinitis, cytomegalovirus infection reactivation, gastroenteritis rotavirus, genital herpes, Hepatitis B, herpes ophthalmic, herpes simplex, herpes simplex reactivation, herpes virus infection, herpes zoster, herpes zoster reactivation, influenza, laryngitis viral, nasal herpes, norovirus infection, oral herpes, parainfluenzae virus infection, pneumonia viral, progressive multifocal leukoencephalopathy, respiratory syncytial virus infection, respirovirus test positive, rhinovirus infection, skin papilloma, varicella zoster pneumonia, varicella zoster virus infection, and viral upper respiratory tract infection.

[c] Includes bacterial infection, abdominal infection, abscess, appendicitis, asymptomatic bacteriuria, atypical pneumonia, bacteraemia, bacterial sepsis, breast abscess, bronchopulmonary aspergillosis, campylobacter gastroenteritis, campylobacter infection, carbuncle, catheter site infection, cellulitis, cholecystitis, chronic sinusitis, clostridium difficile colitis, clostridium difficile infection, corynebacterium infection, device related infection, diverticulitis, ear infection, ear lobe infection, empyema, enterobacter bacteraemia, erysipelas, erythrasma, escherichia infection, escherichia sepsis, eye infection, folliculitis, furuncle, hemophilus bacteraemia, hemophilus infection, helicobacter gastritis, helicobacter infection, infected cyst, infected dermal cyst, lower respiratory tract infection, moraxella infection, mycobacterium chelonae infection, myopericarditis, myringitis, otitis externa, otitis media, perineal infection, periodontitis, peritonitis bacterial, pneumocystis jirovecii pneumonia, pneumonia moraxella, pneumonia pneumococcal, pneumonia streptococcal, postoperative wound infection, proctitis, prostatitis, pseudomonal sepsis, pseudomonal skin infection, pseudomonas infection, pulmonary sepsis, pulpitis dental, pyelonephritis, salmonellosis, septic shock, sinusitis, skin infection, soft tissue infection, staphylococcal bacteraemia, staphylococcal infection, tooth abscess, tooth infection, urinary tract infection, urosepsis, vaginal infection, and wound infection.

[d] Includes neutropenia and neutrophil count decreased.

[e] Includes thrombocytopenia and platelet count decreased.

[f] Includes anaemia and haematocrit decreased.

[g] Includes abdominal pain, abdominal discomfort, abdominal pain lower, abdominal pain upper, and gastrointestinal pain.

[h] Includes rash, rash erythematous, rash maculo-papular, rash papular, rash pruritic, rash pustular, rash vesicular, and urticaria.

[i] Includes asthenia, malaise, and fatigue.

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 led to interruption of tafasitamab in 41% and to tafasitamab discontinuation in 1.2%.
In the inMIND study, 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) and 63.1% of patients treated with lenalidomide and rituximab (placebo 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%.
Myelosuppression was managed by reduction or interruption of lenalidomide, interruption of tafasitamab and/or rituximab. In addition, severe neutropenia was managed by the administration of GCSF (see sections 4.2 and 4.4).

Neutropenia/febrile neutropenia
In the L-MIND study, 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).
In the inMIND study, incidence of neutropenia was 56.9% in the tafasitamab group (tafasitamab, lenalidomide and rituximab) and 54.2% in the placebo group (lenalidomide and rituximab). Incidence of Grade 3 or 4 neutropenia was 46.8% in the tafasitamab group and 45.5% in the placebo group. Incidence of Grade 3 or Grade 4 febrile neutropenia was 4.3% in the tafasitamab group and 3.4% in the placebo group. Median duration of any adverse reaction of neutropenia was 11 days (range 1 – 433 days). Median duration of febrile neutropenia was 5 days (range 1 – 57 days); median time to onset to first occurrence of neutropenia was 57 days (range 1 – 338 days); median time to onset to first occurrence of febrile neutropenia was 77 days (range 3 – 304 days).

Thrombocytopenia
In the L-MIND study, 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).
In the inMIND study, incidence of thrombocytopenia was 17.1% in the tafasitamab group (tafasitamab, lenalidomide and rituximab) and 20.6% in the placebo group (lenalidomide and rituximab). Incidence of Grade 3 or Grade 4 thrombocytopenia was 6.4% in the tafasitamab group and 9.8% in the placebo group. Median duration of thrombocytopenia was 16 days (range 2 – 434 days); median time to onset to first occurrence of thrombocytopenia was 33 days (range 1 – 324 days).

Anaemia
In the L-MIND study, 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).
In the inMIND study, incidence of anaemia was 17.1% in the tafasitamab group (tafasitamab, lenalidomide and rituximab) and 14.5% in the placebo group (lenalidomide and rituximab). Incidence of Grade 3 or 4 anaemia was 6.4% in the tafasitamab group and 6.5% in the placebo group. Median duration of any adverse reaction of anaemia was 23 days (range 1 – 432 days); median time to onset to first occurrence of anaemia was 49 days (range 1 – 274 days).

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).
Infection led to dose interruption of tafasitamab in 27% and tafasitamab discontinuation in 4.9%.
In the inMIND study, infections occurred in 52.3% of patients in the tafasitamab group (tafasitamab, lenalidomide and rituximab) and in 45.2% of patients in the placebo group (lenalidomide and rituximab). Viral infections occurred in 41.3% of patients in the tafasitamab group and 32% in the placebo group. Bacterial infections occurred in 27.2% of patients in the tafasitamab group and 25.2% in the placebo group. Incidence of Grade 3 or 4 viral infections was 11.6% in the tafasitamab group and 4.6% in the placebo group. Incidence of Grade 3 or 4 bacterial infections was 7.6% in the tafasitamab group and 7.7% in the placebo 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 4.4.

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.
In study inMIND, infusion-related reactions occurred in 15.9% of patients in the tafasitamab group (tafasitamab, lenalidomide and rituximab) and 15.1% in the placebo group (lenalidomide and rituximab). Grade 3 infusion-related reactions occurred in 6.1% of patients in the tafasitamab group. 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, hypertension and rash (see sections 4.2 and 4.4).

Immunogenicity
In 245 patients treated with tafasitamab in the initial clinical studies, 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.
Anti-drug antibodies (ADAs) were tested in 327 patients with relapsed or refractory follicular lymphoma or relapsed or refractory marginal zone lymphoma who received tafasitamab in study inMIND. The incidence of tafasitamab treatment-emergent ADAs was 0.9% (3/327) using a bridging enzyme-linked immunosorbent assay.
No neutralizing antibodies were detected. There was no apparent clinically meaningful effect of ADAs on the pharmacokinetics, pharmacodynamics, safety, or effectiveness of tafasitamab over the median treatment duration of 322.5 days.

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%).
Among the 274 patients with FL treated with tafasitamab in study inMIND, 50% were ≥ 65 years of age and 20% were ≥ 75 years of age. No clinically meaningful differences in safety or effectiveness were observed between these patients and younger patients but greater sensitivity of some older individuals cannot be ruled out.

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 Yellow Card Scheme: Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

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

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 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-cells 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 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 4.

Table 4: 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.

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 randomised, double-blind, placebo-controlled phase 3 study (inMIND; INCMOR 0028-301).
Eligible patients were adults aged 18 years and above with histologically confirmed grade 1-3a follicular lymphoma (WHO 2016) whose disease relapsed or became refractory after at least 1 prior line of systemic therapy, including an anti-CD20 therapy. In addition, GELF criteria were recommended as guidance to the investigators, to identify the FL patients that were in need of treatment. As per inclusion criteria, all patients included in the study were required to have documented CD20+ and CD19+ expression based on local or central pathology review. The study excluded patients with CNS involvement 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 (R^2) or placebo plus R^2 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 study inMIND, 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 (range 0 to 34 years). Most participants (56.8%) had Ann Arbor Stage IV disease at study entry. Approximately half of participants had high-risk disease as per FLIPI score, and most participants met at least one GELF criterion for high tumour burden. Most participants had ECOG performance status of 0 (66.4%) and 37.8% of participants had a bulky disease (> 7cm).
The majority (54.7%) of participants had received 1 prior systemic anticancer line of therapy; the median number of prior therapies was 1 (range: 1 to 10), 209 patients (38.1%) were refractory to their last prior therapy. All participants in the FL Population had received prior anti-CD20 therapy; most participants had received 1 (61.3%) or 2 (24.8%) prior anti–CD20 therapies. Two participants, both in the placebo arm, received prior anti-CD 19 containing therapy. Prior treatments included R-CHOP (23.9% of participants), R-CHOP +R-maintenance (27.9% of participants), R-bendamustine (21.7% of participants), rituximab monotherapy (17.2% of participants), R-bendamustine +R-maintenance (12.2% of participants), R-CVP (6.8% of participants), and R-CVP +R-maintenance (5.8% of participants). Twenty-eight (5.1%) participants had received prior ASCT.
One third (34.3%) of participants were anti-CD20 refractory, and 31.6% had progression of disease within 24 months of initial diagnosis (POD24).
A total of 546 participants (99.6%) with R/R FL were treated, including 273 participants (100.0%) in the tafasitamab+R2 group and 273 participants (99.3%) in the placebo+R2 group.
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. 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 and Figure 1.

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

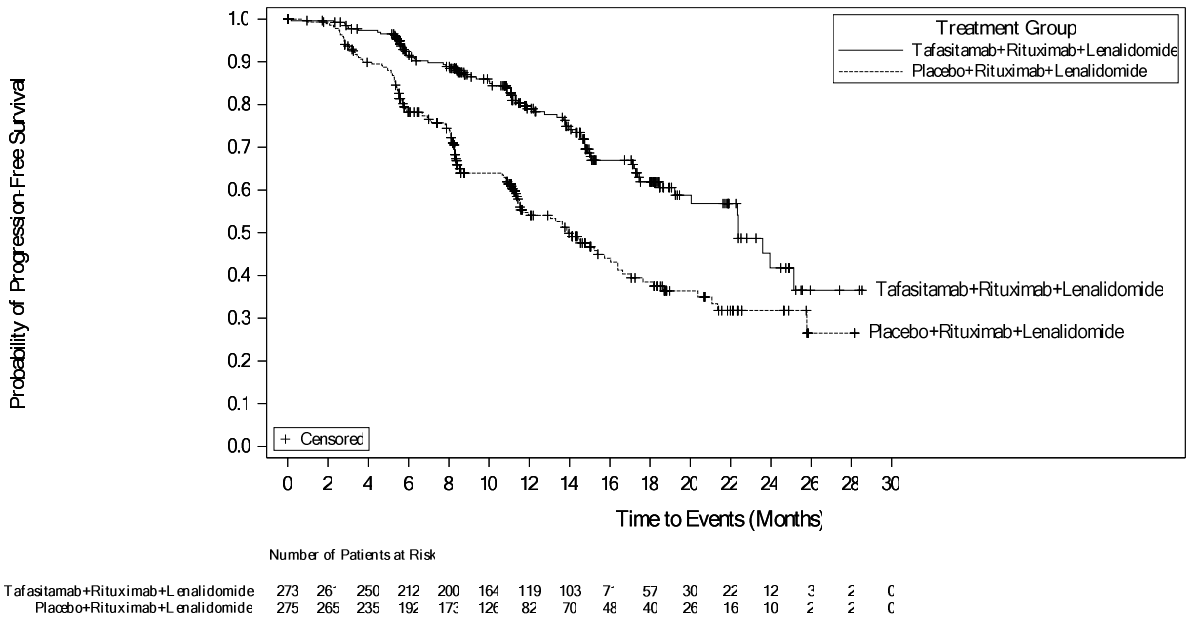
[c] Two-sided 95% CIs based on Brookmeyer and Crowley method.

[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 FDG-avid FL population who achieved a complete metabolic response at any time after the start of treatment as per Lugano classification among the patients with a positive PET scan at baseline. 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.

Figure 1: Kaplan-Meier Curve for Progression-Free Survival by Investigator Assessment in inMIND



At the interim analysis, the key secondary endpoint of OS was immature, and median OS was not reached in either treatment group (stratified hazard ratio of 0.587 (95% CI: 0.306, 1.128); p-value 0.1061).

Elderly
In the ITT set of L-MIND study, 36 of 81 patients were ≤ 70 years and 45 of 81 patients were > 70 years.
Among the 273 patients with R/R follicular lymphoma treated with tafasitamab in inMIND study, 178 were ≤ 70 years and 95 were > 70 years.
No overall differences in efficacy were observed for patients ≤ 70 years versus patients > 70 years of age.

Paediatric population
The Medicines and Healthcare products Regulatory Agency has waived the obligation to submit the results of studies with MINJUVI in all subsets of the paediatric population in mature B-cell neoplasms (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 Medicines and Healthcare products Regulatory 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
Tafasitamab average serum trough concentrations (± standard deviation) were 178.4 (± 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 163.2 (± 74.3) µg/mL. Mean maximum tafasitamab serum concentrations were 488.4 (± 126.6) µg/mL.

Distribution
The total volume of distribution at steady state for tafasitamab was 7.11 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 0.44 L/day and terminal elimination half-life was 13.4 days. Following long-term observations, tafasitamab clearance was found to decrease over time to 0.29 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 severe renal impairment (creatinine clearance (CrCL) ≥ 15 and < 90 mL/min estimated by the Cockcroft-Gault equation). The effect of end-stage renal disease (CrCL < 15 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 to moderate hepatic impairment (total bilirubin ≤ upper limit of normal (ULN) and aspartate aminotransferase (AST) > ULN, or total bilirubin 1 to 3 times ULN and any AST). The effect of moderate to severe hepatic impairment (total bilirubin > 3 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
6 years

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

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

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KT22 7TW, UK

8 MARKETING AUTHORISATION NUMBER(S)

PLGB 42338/0016

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

19/08/2025

10 DATE OF REVISION OF THE TEXT

21/04/2026