MINJUVI® (tafasitamab) Pharmacy Manual

This document is a guide for pharmacists on the storage, preparation and administration of MINJUVI (tafasitamab) in line with the MINJUVI Swissmedic Professional Information (see www.swissmedicinfo.ch)

Proprietorship statement

Key contact details

Incyte's medical information	E-mail: globalmedinfo@incyte.com or eumedinfo@incyte.com For product complaints, or to report adverse events, please contact eumedinfo@incyte.com Tel: (Please dial + or 00) 800 00027423 Local telephone numbers are available from https://www.incyteglobalmedicalinformation.com/contact-us.aspx

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Scope of this document

This document provides the required information and instructions for the handling of MINJUVI by the pharmacy. This manual is provided for the use of pharmacists only and is not intended for the public.

Abbreviations and definitions of terms

°C	Degrees Celsius
°F	Degrees Fahrenheit
DLBCL	Diffuse large B-cell lymphoma
IV	Intravenous
IRR	Infusion-related reaction
mAb	Monoclonal antibody
SmPC	Summary of Product Characteristics
WFI	Water for injection

Further abbreviations listed below according figures and tables.

1. Product overview

Overview	Contents
Pharmaceutical form	White to slightly yellowish lyophilised powder Supplied in single-use 20 mL glass vials containing 200 mg of tafasitamab Genotoxicity, carcinogenicity or reproductive studies have not been performed. May be harmful if swallowed, in contact with skin or inhaled
Excipients	Each vial contains 414.6 mg excipients: • Sodium citrate dihydrate (31.6 mg) • Citric acid monohydrate (3.7 mg) • Trehalose dihydrate (378.3 mg) • Polysorbate 20 (1.0 mg)
Storage conditions	MINJUVI should be stored unopened in its original packaging to protect from light. The carton has the following dimensions: 60 × 75 × 35 mm The shelf life of unopened vials is 4 years Store unopened vials at 2–8 °C (36–46 °F) Chemical and physical in-use stability of the reconstituted solution (prior to dilution) has been demonstrated for up to 24 hours at 2–25 °C (36–77 °F) Chemical and physical in-use stability of the diluted solution (for infusion) has been demonstrated for a maximum of 36 hours at 2–8 °C (36–46 °F) followed by up to 24 hours at up to 25 °C (77 °F)
Reconstitution and dilution	Use appropriate aseptic technique for reconstitution and dilution under ambient light Reconstitute with 5.0 mL WFI, resulting in a concentration of 40 mg/mL and final density of 1.043 g/mL To ensure that 5.0 mL, corresponding to 200 mg, can be extracted from the vials after reconstitution, an overfill of 0.4 mL is applied The reconstituted solution is diluted for infusion in a 0.9% sodium chloride infusion bag (250 mL standard)

Required administration equipment	Administered by IV infusion No light protection or filter units are needed The Phaseal closed-system transfer device may be used upon a satisfactory risk assessment; MINJUVI has not been tested in other closed systems Compatible with infusion containers made of glass, polypropylene, polyvinylchloride, polyethylene, polyethylene terephthalate and polyolefin Compatible with infusion sets made of polyurethane or polyvinylchloride Compatible with 0.2 µm in-line filters made of polyethersulfone or positively charged polyethersulfone or 15 µm mesh filter made of nylon

IV, intravenous; WFI, water for injection.

2. Indication

MINJUVI is indicated in combination with lenalidomide followed by MINJUVI monotherapy for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) after at least one prior line of systemic therapy including an anti-CD20 antibody, who are not eligible for autologous stem cell transplant (ASCT).[1]

3. Mechanism of action[2]

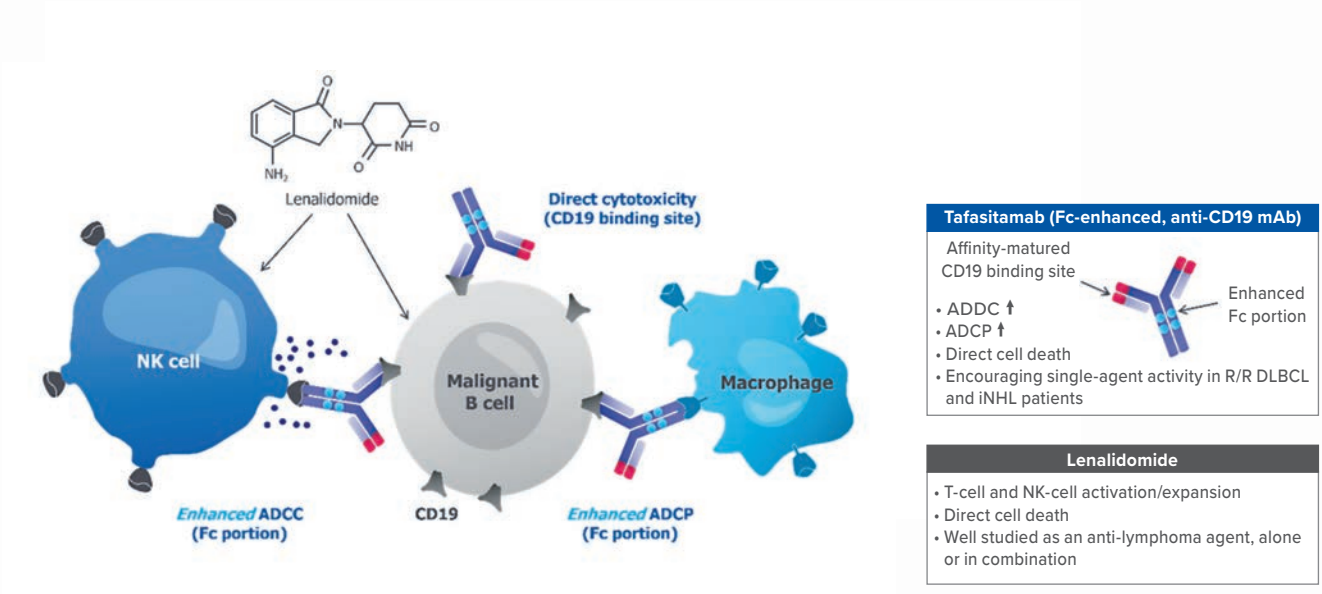
Tafasitamab is an Fc-enhanced monoclonal antibody that targets the CD19 antigen expressed on the surface of pre-B and mature B lymphocytes (Figure 1).

Upon binding to CD19, tafasitamab mediates B-cell lysis through:

- Engagement of immune effector cells like natural killer cells, 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.

Figure 1. Tafasitamab and lenalidomide mechanism of action[2-6]



Adapted from Horton et al 2008.[2]

ADCC, antibody-dependent cellular cytotoxicity; ADCP, antibody-dependent cellular phagocytosis; DLBCL, diffuse large B-cell lymphoma; Fc, crystallisable fragment; iNHL, indolent non-Hodgkin lymphoma; mAb, monoclonal antibody; NK, natural killer; R/R, relapsed/refractory.

4. Description of the product

MINJUVI is a lyophilised powder for reconstitution and intravenous (IV) infusion. It is a colourless-to-slightly-yellow lyophilisate for reconstitution with 5 mL water for injection (WFI), supplied in single-use 20 R glass vials with a butyl rubber stopper and an aluminium seal (Figure 2).

Figure 2. MINJUVI 200 mg vial and carton

5. Composition

The qualitative and quantitative composition of the product and a vial containing reconstituted drug product is described in Table 1 below.

Table 1. Composition of the MINJUVI drug product

Components*	Concentration in reconstituted DP, mmol/L	Concentration in reconstituted DP, mg/ml	Nominal amount, mg/vial	Function
Tafasitamab MW: 150 kDa	0.267	40.00	200.0	Active ingredient
Sodium citrate dihydrate MW: 294.10 g/mol	21.5	6.32	31.6	Buffer component
Citric acid monohydrate MW: 210.14 g/mol	3.5	0.74	3.7	Buffer component
Trehalose dihydrate MW: 378.34 g/mol	200	75.67	378.3	Osmolyte, cake former
Polysorbate 20	–	0.20	1.0	Stabiliser, surfactant
WFI	–	–	Removed during lyophilisation	Solvent

*Nitrogen gas is used for backfilling (aeration of lyophilisation chamber).
DP, drug product; MW, molecular weight; WFI, water for injection.

6. Dosage

The number of vials needed will depend on the patient's body weight (Table 2).

- Determine the dose of MINJUVI in mg by multiplying the patient weight in kg by 12.
- Then calculate the number of MINJUVI vials needed (each vial contains 200 mg tafasitamab).

Table 2. Calculation of the number of vials needed for each 2-month treatment

Patient body weight range	Number of vials per admin	Number of vials in Cycle 1 (5 admin)	Number of vials in Cycle 2 (4 admin)	First order Total number of vials for first 2 months of treatment	Second order Total number of vials (Cycle 3 = 4 admin; Cycle 4 = 2 admin)	Third order onwards Total number of vials (2 admin per cycle)
51–66 kg	4	20	16	36	24	16
67–83 kg	5	25	20	45	30	20
84–100 kg	6	30	24	54	36	24

Admin, administration(s).

7. Storage, reconstitution and dilution

7.1. Storage

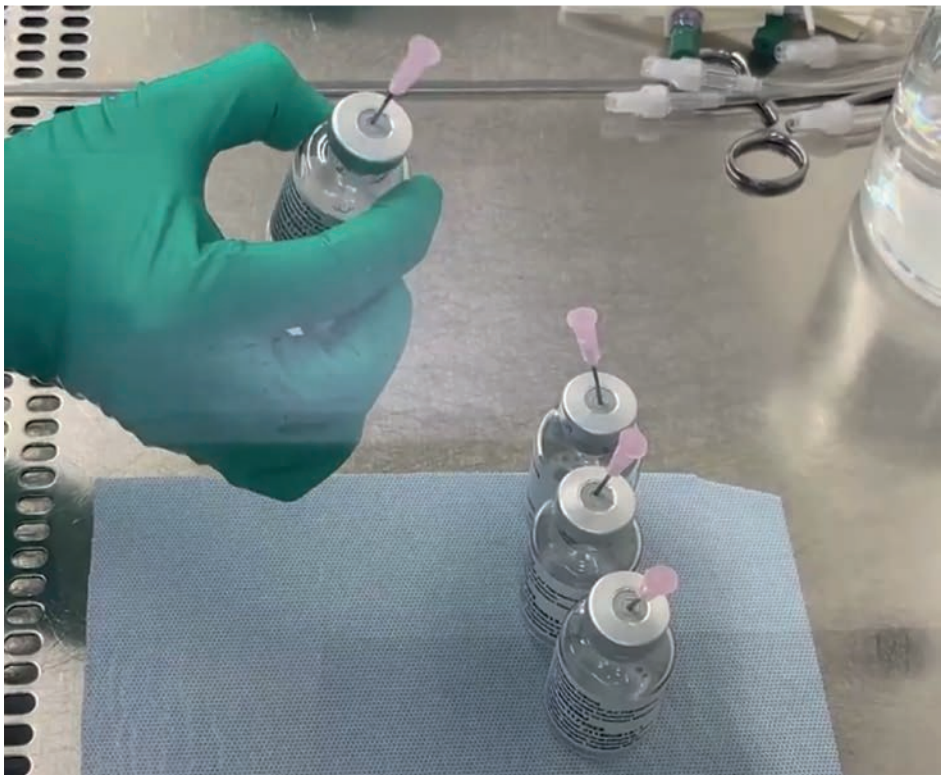
Unopened vials of MINJUVI must be stored at 2–8 °C (36–46 °F). The vials should not be exposed to direct sunlight. Do not use this medicine after the expiry date ("EXP") stated on the packaging.

For information on the storage of reconstituted solution (prior to dilution) or diluted solution (for infusion), please see sections 7.2 or 7.3, respectively.

7.2. Reconstitution

For each preparation of MINJUVI, the vials should be taken from the refrigerator just before preparation. MINJUVI must be reconstituted and diluted inside a laminar flow hood using appropriate aseptic technique (Figure 3).

Figure 3. Pharmacist reconstitutes MINJUVI using aseptic technique

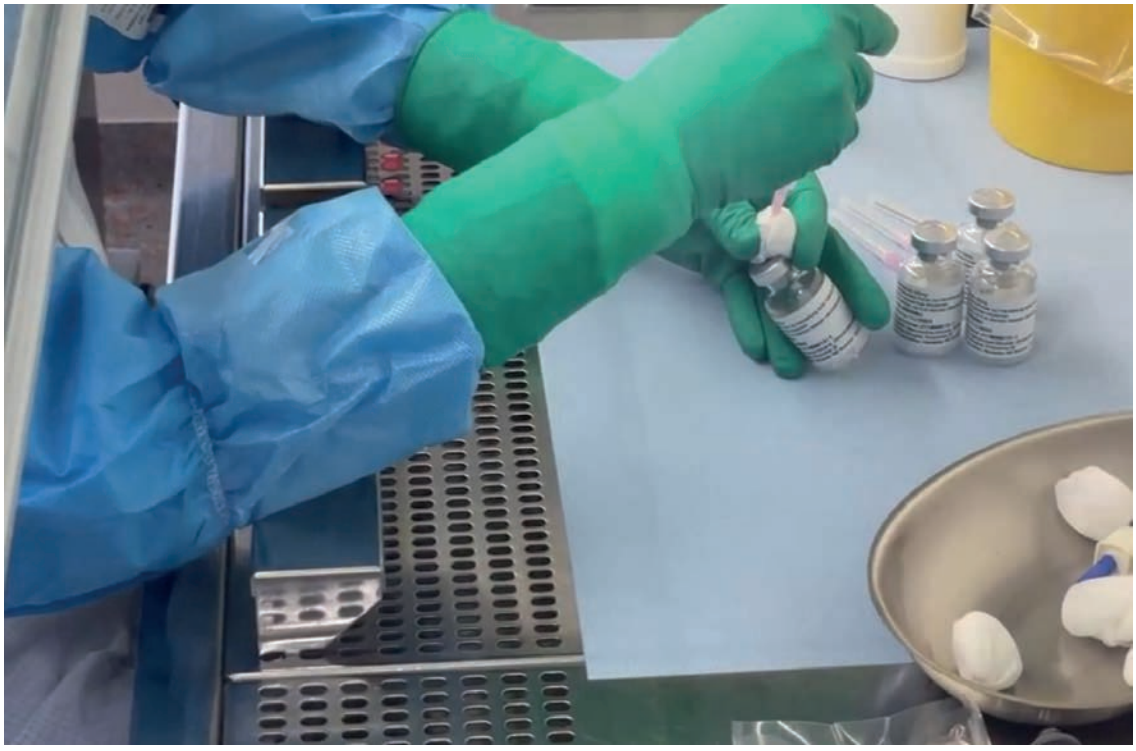


1. Determine the dose of MINJUVI based on patient weight by multiplying 12 mg by the patient weight (kg). Then calculate the number of MINJUVI vials needed (each vial contains 200 mg tafasitamab).
2. Using a sterile syringe, gently add 5.0 mL sterile WFI into each vial. Direct the stream toward the walls of each vial and not directly on the lyophilised powder (Figure 4).

3. Gently swirl the reconstituted vial(s) to aid the dissolution of the lyophilised powder (Figure 5). 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.
4. 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).
5. Use immediately for further dilution. Chemical and physical in-use stability of the reconstituted solution has been demonstrated for up to 24 hours at 2–25 °C (36–77 °F). Do not freeze or shake.

   From a microbiological point of view, unless the method of reconstitution precludes the risk of microbial contamination, the reconstituted solution should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user.

Figure 4. Pharmacist adds 5.0 mL sterile WFI along the walls of the vial



WFI, water for injection.

Figure 5. Pharmacist gently swirls the vial for up to 5 minutes to ensure dissolution of MINJUVI powder

7.2.1. Overfill

An overfill of 0.4 mL (target fill of 5.4 mL) equates to 216 mg tafasitamab in each vial. After reconstitution, and once the MINJUVI residue in the reconstitution vial and transfer syringe is compensated for, the amount of tafasitamab transferred into the infusion bag corresponds to 200 mg. Owing to machine accuracy, the actual filling volume can range between 5.2 and 5.6 mL, which equates to a range of 208–224 mg tafasitamab in each vial.

7.3. Dilution

For infusion, the reconstituted MINJUVI solution is diluted with sterile sodium chloride (0.9%) for injection (Figure 6).

Figure 6. Pharmacist dilutes the reconstituted MINJUVI with 0.9% sodium chloride

Please note that the standard dilution procedure requires dilution of MINJUVI with a 250 mL sodium chloride (0.9%) infusion bag. It is important to maintain a final concentration for infusion of between 2 and 8 mg/mL, and a total infusion time of no more than 2 hours (2.5 hours in case of the first infusion with Tafasitamab).

Dilution **by volume** of reconstituted solution:

1. An infusion bag containing 250 mL sodium chloride 9 mg/mL (0.9%) solution for injection should be used.
2. Calculate the total volume of the 40 mg/mL reconstituted MINJUVI solution needed. Withdraw a volume equal to this from the infusion bag and discard the withdrawn volume.
3. Withdraw the total calculated volume (mL) of reconstituted MINJUVI solution from the vial(s) and slowly add to the sodium chloride 9 mg/mL (0.9%) infusion bag. Discard any unused portion of MINJUVI remaining in the vial.
4. The final concentration of the diluted solution should be between 2 mg/mL to 8 mg/mL of tafasitamab (Figure 6).
5. Gently mix the IV bag by slowly inverting it. Do not shake.

Dilution **by weight** of reconstituted solution:

1. Calculate the total volume (mL) of the 40 mg/mL reconstituted MINJUVI solution needed. Convert the total volume (mL) to the weight (g) using density (d) = 1.043 g/mL.
2. Withdraw the total calculated volume (mL) from Step 1 from a 250 mL sodium chloride (0.9%) infusion bag and discard it.

3. Withdraw the total calculated volume (mL) of the reconstituted solution from the vial(s) and measure the weight of the reconstituted solution.
4. Add the reconstituted solution with an amount equal to the calculated weight from Step 1 to the 250 mL sodium chloride infusion bag from Step 2 (Figure 7).

Figure 7. The diluted MINJUVI solution is ready to be transported to the nurse for immediate infusion to the patient

Storage of diluted solution (for infusion): Once diluted, the solution for infusion should not be stored. Chemical and physical in-use stability has been demonstrated for 36 hours at 2°C – 8°C, followed by up to 24 hours at 25°C. Do not freeze or shake.

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.

The Phaseal closed-system transfer device may be used upon a satisfactory risk assessment.

7.4. Further information on storage times of reconstitution and dilution

You can see the demonstrated chemical and physical in-use stability of the reconstituted solution (please see 7.2) additive to the chemical and physical in-use stability of the diluted solution (please see 7.3).

8. Administration

8.1. Premedication

Premedication to reduce the risk of infusion-related reactions (IRRs) should be administered 30 minutes to 2 hours prior to MINJUVI infusion. For patients not experiencing IRRs during the first 3 infusions, premedication is optional for subsequent infusions. If a patient experiences an IRR, administer premedication before each subsequent infusion.

8.2. Infusion

MINJUVI should be administered by a healthcare professional with experience in treating cancer patients, immediate access to emergency equipment and appropriate medical support to manage IRRs if necessary.

No incompatibilities have been observed for MINJUVI with standard infusion materials, including glass, polypropylene, polyvinylchloride, polyethylene, polyethylene terephthalate, polyolefin and infusion sets made of polyurethane or polyvinylchloride. Use materials designated as low protein binding where possible.

Cycle 1: Administer the first IV infusion at an infusion rate of 70 mL/hour for the first 30 minutes and subsequently increase to a rate of 125 mL/hour. The total infusion duration should ideally not exceed 2.5 hours.

All subsequent infusions: Administer at a constant rate of 125 mL/hour over a 1.5 to 2-hour period.

- In case of any IRRs, adjust the infusion rate or stop the infusion temporarily. Please see Appendix 1 for more information. The total infusion duration should ideally not exceed 2.5 hours.
- Do not administer other treatments through the same infusion line.
- After the infusion is completed, the infusion line should be flushed to administer the remaining MINJUVI through the line to the subject. This is done by connecting the infusion line to a new container of 0.9% sodium chloride and infusing at the same infusion rate.
- The infusion must not be administered as an IV push or bolus.

8.3. Administration schedule

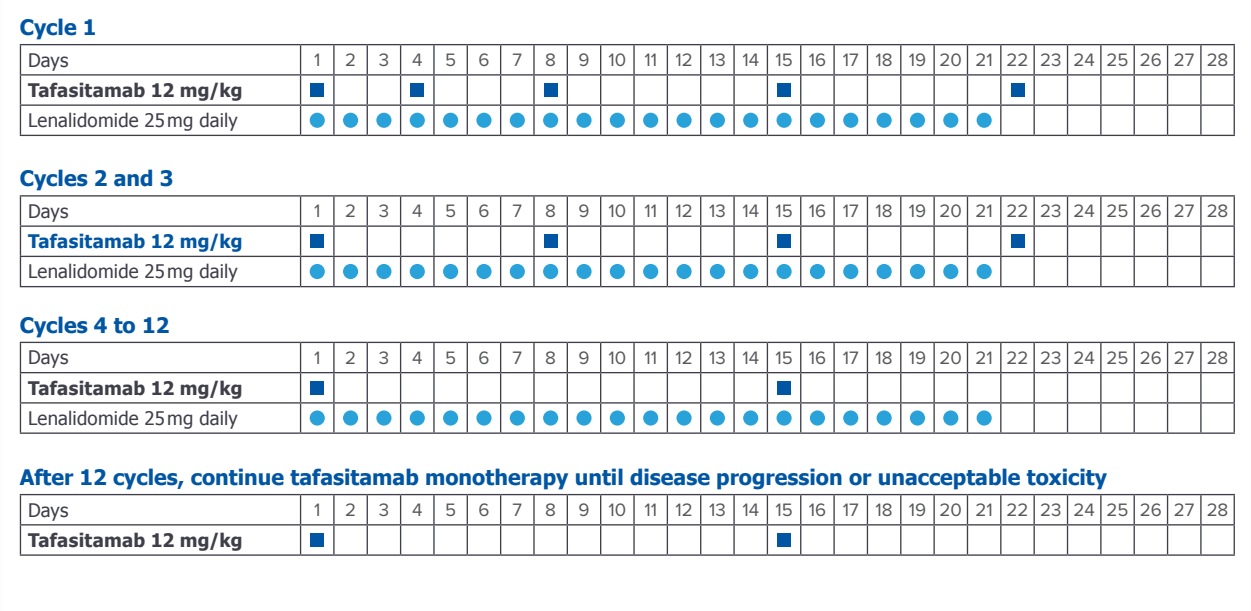
Administer MINJUVI only as an IV infusion; do not administer as an IV push or bolus. MINJUVI should only be administered by a healthcare professional possessing the training and the equipment to address and to manage potentially severe IRRs.

The recommended dose of tafasitamab is 12 mg/kg body weight, administered according to the following schedule (Figure 8):

- Cycle length: 28 days.
- Cycle 1: administer MINJUVI infusion on days 1, 4, 8, 15 and 22.
- Cycles 2–3: administer MINJUVI infusion on days 1, 8, 15 and 22 of each cycle.
- Cycle 4 until disease progression: administer MINJUVI infusion on days 1 and 15.

Treatment with Lenalidomide should be stopped after a maximum of 12 cycles of combination therapy. Patients should continue to receive MINJUVI infusions as single agent on days 1 and 15 of each 28-day cycle until disease progression or unacceptable toxicity.

Figure 8. MINJUVI and Lenalidomide administration schedule



Please see Appendix 1 for details of dose modifications in response to IRRs and myelosuppression.

Please refer to the full MINJUVI (tafasitamab) Swissmedic Professional Information for a detailed description of the product, warnings and precautions, as well as adverse reactions related to the use of MINJUVI, which may require premedication, reduction of the MINJUVI dose, delay or discontinuation of MINJUVI treatment.

Lenalidomide

Patients should self-administer Lenalidomide capsules at the recommended starting dose of 25 mg daily on days 1–21 of cycles 1–12. On days when both MINJUVI and Lenalidomide drugs are given, administer Lenalidomide prior to MINJUVI.

Lenalidomide dose adaptations are permitted as per the prescribing information. Refer to the Lenalidomide Professional Information for dosing guidelines and recommendations in response to myelosuppression.

9. References

1. MINJUVI (tafasitamab). Professional Information. See www.swissmedicinfo.ch

2. Horton HM, et al., Potent *In vitro* and *In vivo* Activity of an Fc-Engineered Anti-CD19 Monoclonal Antibody against Lymphoma and Leukemia. *Cancer Res.* 2008;68:8049–57.

3. Czuczman MS, et al., A Phase 2/3 Multicenter, Randomized, Open-Label Study to Compare the Efficacy and Safety of Lenalidomide Versus Investigator's Choice in Patients with Relapsed of Refractory Diffuse Large B-Cell Lymphoma. *Clin Cancer Res.* 2017;23:4127–37.

4. Jurczak W, et al., Phase IIa study of the CD19 antibody MOR208 in patients with relapsed or refractory B-cell non-Hodgkin's lymphoma *Ann Oncol.* 2018;29:1266–72.

5. Witzig TE, et al., A comprehensive review of lenalidomide therapy for B-Cell non-Hodgkin lymphoma. *Ann Oncol.* 2015;26:1667–77.

6. Woyach JA, et al., A phase 1 trial of the Fc-engineered CD19 antibody XmAb5574 (MOR00208) demonstrates safety and preliminary efficacy in relapsed CLL Prolonged lymphocytosis during ibrutinib therapy is associated with distinct molecular characteristics and does not indicate a suboptimal response to therapy *Blood.* 2014;124:3553–60.

All references are available upon request.

10. Appendices

Appendix 1. Management guidelines for IRRs and myelosuppression

Event	Appropriate action
Grade 2 (moderate) IRR	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) IRR	Interrupt infusion immediately and manage 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) IRR	Stop the infusion immediately and permanently discontinue MINJUVI therapy
Myelosuppression [*see Warnings and precautions*]	Platelet count of less than 50,000/µL • Withhold MINJUVI and lenalidomide and monitor complete blood count (CBC) weekly until platelet count is 50,000/µL or higher. • Resume MINJUVI at the same dose and lenalidomide at a reduced dose. Refer to lenalidomide professional information for dosage modifications.

Myelosuppression [*see Warnings and precautions*]	Neutrophil count of less than 1,000/µL for at least 7 days OR Neutrophil count of less than 1,000/µL with an increase of body temperature to 38°C or higher OR Neutrophil count of less than 500/µL • Withhold MINJUVI and lenalidomide and monitor CBC weekly until neutrophil count is 1,000/µL or higher. • Resume MINJUVI at the same dose and lenalidomide at a reduced dose. Refer to lenalidomide professional information for dosage modifications

IRR, infusion-related reaction.

▼ This medicinal product is subject to additional monitoring. For further information, see professional information MINJUVI on www.swissmedicinfo.ch.

MINJUVI (tafasitamab), 200 mg powder for concentrate for solution for infusion.

I: MINJUVI is indicated in combination with lenalidomide followed by MINJUVI monotherapy for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) after at least one line of systemic CD20-targeted antibody therapy who are not eligible for autologous stem cell transplantation (ASCT). **P:** MINJUVI must be administered by a healthcare professional experienced in treatment of cancer patients. The recommended dose is 12 mg of MINJUVI per kg body weight administered as an intravenous infusion. On cycles 1-3: Administer on days 1, 8, 15 and 22 with an additional dose on day 4 of cycle 1. From cycle 4 onwards: Administer on day 1 and 15 of each cycle. In addition, patients should self-administer lenalidomide capsules at the recommended starting dose of 25 mg daily on days 1 to 21 of each 28-day cycle for a maximum of 12 cycles. Dose adjustments due to adverse reactions are needed. **CI:** Hypersensitivity to tafasitamab or any of the excipients. **W/P:** Infusion-related reactions may occur. Patients should be monitored closely throughout infusion. Treatment can cause serious and/or severe myelosuppression. Monitor complete blood counts throughout treatment and prior to administration of each treatment cycle. Withhold MINJUVI based on the severity of the adverse reaction. Fatal and serious infections occurred. Monitor patients for symptoms and signs of progressive multifocal leukoencephalopathy (PML); suspend treatment in case of suspected PML. Administer MINJUVI to patients with an active infection only if the infection is treated appropriately and well controlled. Monitor patients closely for tumor lysis syndrome. QTc prolongation and syncopes have been observed during treatment with MINJUVI. MINJUVI can cause fetal harm. Women of childbearing potential should be advised not to become pregnant during treatment. **IA:** No interaction studies have been performed for tafasitamab. **UE:** The most common adverse reactions (≥ 20%) were infections, asthenia, neutropenia, anaemia, thrombocytopenia and diarrhea. The most common serious adverse reactions (≥ 3 %) were febrile neutropenia and pneumonia. For further information on UE, see www.swissmedicinfo.ch. **Dispensing cat.:** A. **Revision date:** May 2024. **Marketing authorisation holder:** Incyte Biosciences International Sàrl, CH-1110 Morges. MINJUVI and the "triangle" design are (registered) trademarks of Incyte. Refer to www.swissmedicinfo.ch for detailed information.