PRODUCT MONOGRAPH
INCLUDING PATIENT MEDICATION INFORMATION

[PR]MINJUVI™

Tafasitamab for injection
lyophilized powder for solution for infusion (200 mg single-use vial)
Professed Standard
Antineoplastic, monoclonal antibody
ATC code: L01FX12

Minjuvi, indicated in combination with lenalidomide for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) not otherwise specified, including DLBCL arising from low grade lymphoma, who are not eligible for autologous stem cell transplant (ASCT), has been issued marketing authorization with conditions, pending the results of trials to verify its clinical benefit. Patients should be advised of the nature of the authorization. For further information for Minjuvi, please refer to Health Canada's Notice of Compliance with conditions - drug products web site: https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/notice-compliance/conditions.html

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What is a Notice of Compliance with Conditions (NOC/c)?

An NOC/c is a form of market approval granted to a product on the basis of promising evidence of clinical effectiveness following review of the submission by Health Canada.

Products authorized under Health Canada's NOC/c policy are intended for the treatment, prevention or diagnosis of a serious, life-threatening or severely debilitating illness. They have demonstrated promising benefit, are of high quality and possess an acceptable safety profile based on a benefit/risk assessment. In addition, they either respond to a serious unmet medical need in Canada or have demonstrated a significant improvement in the benefit/risk profile over existing therapies. Health Canada has provided access to this product on the condition that sponsors carry out additional clinical trials to verify the anticipated benefit within an agreed upon time frame

TABLE OF CONTENTS

Minjuvi, indicated in combination with lenalidomide for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) not otherwise specified, including DLBCL arising from low grade lymphoma, who are not eligible for autologous stem cell transplant (ASCT), has been issued marketing authorization with conditions, pending the results of trials to verify its clinical benefit. Patients should be advised of the nature of the authorization. For further information for Minjuvi, please refer to Health Canada's Notice of Compliance with conditions - drug products website.

PART I: HEALTH PROFESSIONAL INFORMATION

1 INDICATIONS

Minjuvi (tafasitamab for injection) is indicated in combination with lenalidomide for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) not otherwise specified, including DLBCL arising from low grade lymphoma, who are not eligible for autologous stem cell transplant (ASCT).

Authorization was based on overall response rate, complete response rate and durability of response from a single-arm clinical study. An improvement in progression-free survival or overall survival has not been established (see Section 14 CLINICAL TRIALS).

1.1 Pediatrics

Pediatrics (< 18 years of age): No data are available to Health Canada; therefore, Health Canada has not authorized an indication for pediatric use.

1.2 Geriatrics

Geriatrics (≥ 65 years of age): Among 81 patients treated in the L-MIND study, 72% were 65 years and older. Patients 65 years of age and older had more serious treatment emergent adverse events (TEAEs) (57%) than younger patients (39%) (see Section 4.2 DOSAGE AND ADMINISTRATION, Recommended Dose and Dosage Adjustment, Dose Modifications for Special Populations, and Section 10.3 CLINICAL PHARMACOLOGY, Pharmacokinetics).

Evidence from clinical studies does not suggest that use in the geriatric population is associated with differences in effectiveness.

2 CONTRAINDICATIONS

Minjuvi (tafasitamab) is contraindicated in patients who are hypersensitive to this drug or to any ingredient in the formulation, including any non-medicinal ingredient, or component of the container. For a complete listing, (see Section 6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING).

3 SERIOUS WARNINGS AND PRECAUTIONS BOX

Serious Warnings and Precautions

- **Infection -** Clinically significant and/or life-threatening adverse events including fatal, life threatening, or serious infections, including opportunistic infections have been reported in patients treated with Minjuvi in combination with lenalidomide (see Section 7 WARNINGS AND PRECAUTIONS).
- **Myelosuppression** - Serious and severe myelosuppression, including neutropenia, febrile neutropenia, thrombocytopenia and anemia have been reported in patients treated with Minjuvi in combination with lenalidomide (see Section 7 WARNINGS AND PRECAUTIONS).
- **Progressive Multifocal Leukoencephalopathy -** PML can occur in patients receiving Minjuvi in combination with lenalidomide. Minjuvi treatment should be interrupted in case of PML suspicion, until the diagnosis can be clearly established. Discontinue Minjuvi therapy and consider discontinuation or reduction of lenalidomide therapy in patients who develop PML (see Section 7 WARNINGS AND PRECAUTIONS).
- **Hepatitis B Virus (HBV) Reactivation** – HBV reactivation has been observed in studies of Minjuvi in combination with lenalidomide. Patients should be screened for HBV infection before treatment initiation, and should be monitored during and after treatment with Minjuvi. In the event of HBV reactivation, Minjuvi should be discontinued (see Section 7 WARNINGS AND PRECAUTIONS).

4 DOSAGE AND ADMINISTRATION

4.1 Dosing Considerations

Minjuvi must be administered by a healthcare professional experienced in the treatment of cancer patients who has immediate access to emergency equipment and appropriate medical support to manage infusion-related reactions (IRRs) (see Section 7 WARNINGS AND PRECAUTIONS).

Minjuvi is administered by intravenous infusion only. DO NOT administer as an IV push or bolus dose.

Recommended Premedication

Administer premedication 30 minutes to 2 hours prior to Minjuvi infusion to reduce the risk of infusion-related reactions (see Section 7 WARNINGS AND PRECAUTIONS). Premedication may include antipyretics, histamine H1 receptor antagonists, histamine H2 receptor antagonists, and/or glucocorticosteroids. For patients who do not experience an infusion-related reaction during the first 3 infusions, premedication is optional for subsequent infusions.

Treatment of infusion-related reactions

If an infusion-related reaction occurs (grade 2 or higher), interrupt the infusion. In addition, initiate appropriate medical treatment of symptoms (see Table 1: Dose Modifications in Case of Adverse Reactions). See Table 1 for guidance on when to resume Minjuvi infusion.

If a patient has a Grade 1 to 3 infusion-related reaction, premedication should be administered before every subsequent Minjuvi infusion. See Table 1 for guidance on when to permanently discontinue Minjuvi.

4.2 Recommended Dose and Dosage Adjustment

The recommended dose is 12 mg Minjuvi per kilogram body weight administered as an intravenous infusion according to the following schedule:

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

Each treatment cycle is 28 days long.

Minjuvi is to be administered with lenalidomide for up to 12 cycles. 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 **should be adjusted, as necessary, according to the lenalidomide product monograph**.

After a maximum of twelve cycles of combination therapy, stop treatment with lenalidomide and continue to administer Minjuvi infusions on day 1 and 15 of each 28-day cycle, until disease progression or unacceptable toxicity.

Pediatrics

Health Canada has not authorized an indication for pediatric use.

Dose Modifications

Temporary interruption or definitive discontinuation of Minjuvi treatment may be required for infusion-related reactions (IRRs) or myelosuppression (see Table 1 for guidance).

Recommended Dose Modification for lenalidomide used in combination with Minjuvi: Refer to the manufacturer's Product Monograph for the co-administered product, lenalidomide, for toxicity management, dose adjustment guidelines for special populations, and contraindications (see Section 17 SUPPORTING PRODUCT MONOGRAPHS).

Table 1: Dose modifications in case of adverse reactions

Adverse Reaction	Severity	Minjuvi Dose Modification
Infusion-related reactions	Grade 2 (moderate)	• Interrupt infusion immediately and manage signs and symptoms. • Once signs and symptoms resolve or reduce to Grade 1, resume 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 rate at which the reaction occurred.

Adverse Reaction	Severity	Minjuvi Dose Modification
	Grade 3 (severe)	• Interrupt infusion immediately and manage signs and symptoms. • Once signs and symptoms resolve or reduce to Grade 1, resume 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, manage signs and symptoms, and permanently discontinue Minjuvi.
Myelosuppression	**Thrombocytopenia:** Platelet count of less than 50,000/mcL	• Withhold Minjuvi and lenalidomide and monitor complete blood count (CBC) weekly until platelet count is 50,000/mcL or higher. • When platelet count recovers to at least 50,000/mcL, resume Minjuvi at the same dose and lenalidomide at a reduced dose. **Refer to the lenalidomide product monograph for additional guidance on dosage modifications.**
	Neutropenia: Neutrophil count of less than 1,000/mcL for at least 7 days OR Neutrophil count of 1,000/mcL or less with an increase of body temperature to 38°C or higher OR Neutrophil count less than 500/mcL	• Withhold Minjuvi and lenalidomide and monitor CBC weekly until neutrophil count is 1,000/ mcL or higher. • When neutrophil count recovers to at least 1,000/mcL, resume Minjuvi at the same dose and lenalidomide at a reduced dose. Refer to lenalidomide product monograph for dosage modifications. **Refer to the lenalidomide product monograph for additional guidance on dosage modifications.**

Abbreviations: mcL – microliters, CBC – complete blood count

Dose Modifications for Special Populations

Pediatric use: The safety and effectiveness of Minjuvi have not been established in pediatric patients under 18 years of age. Health Canada has not authorized an indication for pediatric use (see Section 1.1 INDICATIONS, Pediatrics).

Geriatric patients: No dose adjustment is needed for elderly patients ≥ 65 years (see Section 10.3 CLINICAL PHARMACOLOGY, Pharmacokinetics, Special Populations and Conditions, Geriatrics).

Renal impairment: No dose adjustment of Minjuvi is required in patients with mild or moderate 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 (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 (see Section 10.3 CLINICAL PHARMACOLOGY, Pharmacokinetics, Special Populations and Conditions, Renal Insufficiency).

Hepatic impairment: No dose adjustment of Minjuvi is required in patients with mild 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 ≤ ULN and 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 (see Section 10.3 CLINICAL PHARMACOLOGY, Pharmacokinetics, Special Populations and Conditions, Hepatic Insufficiency).

4.3 Reconstitution

Table 2: Reconstitution

Vial Size (mg/vial)	Volume of Diluent to be Added to Vial	Approximate Available Volume	Concentration per mL
200 mg	5 mL sterile water for injection	5 mL	40 mg/mL

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.

1. Determine the dose of Minjuvi based on patient weight (measured prior to each cycle) by multiplying 12 mg/kg by the patient weight (kg).
2. Calculate the number of Minjuvi vials needed (each vial contains 200 mg tafasitamab).
3. Using a sterile syringe, gently add 5 mL sterile water for injection into each tafasitamab vial. Direct the stream toward the walls of each vial and not directly on the lyophilized powder. The resulting solution contains Minjuvi at a concentration of 40 mg/mL.
4. Gently swirl the reconstituted vial(s) to aid the dissolution of the lyophilized powder. **Do not shake or swirl vigorously**. Do not remove the contents until all of the solids have been completely dissolved. The lyophilized powder should completely dissolve within 5 minutes.
5. The reconstituted Minjuvi solution should appear as a colourless to slightly yellow solution. Before proceeding, ensure there is no particulate matter or discolouration by visually inspecting the vials. If the solution is cloudy, discoloured or contains visible particles, discard the vial(s) and prepare freshly reconstituted Minjuvi.
6. The reconstituted Minjuvi solution contains no preservative and should be used as soon as possible after reconstitution. If not used immediately, the reconstituted product may be stored

prior to dilution for up to 24 hours at 2°C – 25°C. Do not freeze or shake. Protect from light during storage.

Dilution

1. Obtain an infusion bag containing 250 mL sodium chloride 9 mg/mL (0.9%) solution for injection.
2. Calculate the total volume of the 40 mg/mL reconstituted Minjuvi solution needed based on the patient's weight prior to each cycle.

$$Volume = \frac{Minjuvi\ dose\ (12mg/kg) \times patient's\ weight\ (kg)}{Reconstituted\ vial\ concentration\ (40\ mg/mL)}$$

3. Withdraw saline solution equal to the calculated volume from the infusion bag and discard the withdrawn volume.
4. 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 tafasitamab remaining in the vial.
5. 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 inverting the bag slowly. Do not shake.
6. Once diluted, the product should be used immediately. If not used immediately, the infusion solution may be stored for a maximum of 36 hours at 2°C - 8°C followed by up to 24 hours at up to 25°C. Do not freeze or shake. Protect from light during storage.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements (see Section 11 STORAGE, STABILITY and DISPOSAL).

Incompatibilities

No incompatibilities have been observed between Minjuvi infusion solutions with standard infusion materials.

4.4 Administration

Do not administer Minjuvi as an intravenous push or bolus.

Recommended supplies: 250 mL 0.9% NaCl infusion bag or bottle; standard IV infusion administration set, and 0.2 µm in-line filter. No incompatibilities have been observed between Minjuvi with infusion containers made of polypropylene (PP), polyvinylchloride (PVC), polyethylene (PE), polyethylenterephthalate (PET), or glass and infusion sets made of polyurethane (PUR) or PVC. No incompatibilities were observed with terminal in-line filters with neutral or positively charged polyethersulfone (PES) membrane, 0.2 µm.

- Administer Minjuvi as an intravenous infusion after reconstitution and dilution.
- For the first infusion of cycle 1, the intravenous infusion rate should be 70 mL/h for the first 30 minutes. Afterwards, increase the rate so that the first infusion is complete within a 2.5-hour period.

- Monitor patients during the entire infusion for infusion-related reactions. Most infusion-related reactions occur in the first 15 minutes of the first dose. Follow standard care measures for monitoring after the infusion is complete. Advise patients to contact their healthcare professional if they experience signs and symptoms of infusion-related reactions including fever, chills, rash or breathing problems within 24 hours of infusion.

- In the absence of any prior infusion-related reaction, subsequent infusions may be administered within a 1.5 - 2-hour period.

- Do not co-administer other medicines through the same infusion line.

- After the infusion is complete, flush the tubing with 0.9% NaCl injection to ensure the entire dose is administered.

5 OVERDOSAGE

There is no information on overdose with Minjuvi. The recommended dose of Minjuvi is 12 mg/kg, which is the highest dose that has been tested in clinical studies. 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.

For management of a suspected drug overdose, contact your regional poison control centre.

6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

Table 3: Dosage Forms, Strengths, Composition and Packaging

Route of Administration	Dosage Form / Strength/Composition	Non-medicinal Ingredients
Intravenous Infusion	lyophilized powder, 200 mg	citric acid monohydrate, polysorbate 20, sodium citrate dihydrate, and trehalose dihydrate

Minjuvi for injection: 200 mg of tafasitamab as white to slightly yellowish lyophilized powder in single-dose vial for reconstitution and further dilution.

Packaging: Minjuvi (tafasitamab) is supplied as a vial containing 200 mg per vial with an outer carton.

7 WARNINGS AND PRECAUTIONS

General

Infusion-related reactions

Infusion-related reactions may occur and have been reported in clinical studies with Minjuvi. Infusion-related reactions may occur more frequently during the first infusion, but can occur during or after any infusion. Patients should be monitored closely throughout the infusion. Advise patients to contact their healthcare professionals if they experience signs and symptoms of infusion-related reactions including fever, chills, rash or breathing problems within 24 hours of infusion (see Section 8.2 ADVERSE REACTIONS, Clinical Trial Adverse Reactions).

Premedicate patients prior to starting tafasitamab infusion. Monitor patients frequently during infusion. If infusion reaction occurs or is suspected, immediately interrupt or discontinue Minjuvi based on the severity of the infusion-related reaction. Institute appropriate medical management (see Section 4.1 DOSAGE AND ADMINISTRATION, Dosing Considerations).

Endocrine and Metabolism

Tumor Lysis Syndrome

Patients with high tumor burden and rapidly proliferative tumor may be at increased risk of tumor lysis syndrome. In patients with R/R-DLBCL who received Minjuvi in clinical studies, tumor lysis syndrome has been observed. Measures/prophylaxis appropriate for TLS should be instituted in accordance with local guidelines prior to treatment with Minjuvi. Patients should be monitored closely for tumor lysis syndrome during treatment with tafasitamab.

Hematology

Myelosuppression

Treatment with Minjuvi can cause serious and/or severe myelosuppression including neutropenia, thrombocytopenia, and anemia. Monitor complete blood counts throughout treatment and prior to administration of each treatment cycle. Withhold Minjuvi based on the severity of the adverse reaction (see Section 4.2 DOSAGE AND ADMINISTRATION, Recommended Dose and Dosage Adjustment, and Section 8.2 ADVERSE REACTIONS, Clinical Trial Adverse Reactions). Minjuvi is given in combination with lenalidomide, which may also cause myelosuppression, refer to the lenalidomide product monograph for guidance on lenalidomide related toxicity management.

Neutropenia

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

Thrombocytopenia

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

Immune

Immunizations

The safety of immunization with live vaccines following Minjuvi therapy has not been investigated, and vaccination with live vaccines is not recommended concurrently with Minjuvi therapy.

Infections

Serious and/or fatal bacterial, fungal and new or reactivated viral infections, including opportunistic infections, can occur in patients treated with Minjuvi.

Patients with a history of recurring or chronic infections may be at increased risk of infection and should be monitored appropriately (see Section 8.2 ADVERSE REACTIONS, Clinical Trial Adverse Reactions).

Advise patients to contact their healthcare professionals if fever or other evidence of potential infection such as chills, cough or pain on urination develops.

Hepatitis B Virus (HBV) Reactivation

Hepatitis B virus (HBV) reactivation, in some cases resulting in fulminant hepatitis, hepatic failure and death, can occur in patients treated with monoclonal antibodies that target B-lymphocytes. Reactivation of HBV replication is often followed by hepatitis, i.e., increase in transaminase levels and, in severe cases, increase in bilirubin levels, liver failure, and death. Screen all patients for HBV infection by measuring HBsAg and anti-HBc before initiating treatment with Minjuvi.

Patients with active hepatitis B disease should not be treated with Minjuvi. Patients with positive hepatitis B serology (HBsAg positive [regardless of antibody status] or HBsAg negative but anti-HBc positive), should consult physicians with expertise in managing hepatitis B regarding monitoring and consideration for HBV antiviral therapy.

Monitor patients with evidence of current or prior HBV infection for clinical and laboratory signs of hepatitis or HBV reactivation during and for several months following treatment with Minjuvi. HBV reactivation has been reported for other B-cell cytolytic antibodies following completion of therapy. In patients who develop reactivation of HBV while receiving Minjuvi, immediately discontinue Minjuvi and any concomitant anti-neoplastic therapy, and institute appropriate treatment. Resumption of Minjuvi in patients whose HBV reactivation resolves should be discussed with physicians with expertise in managing hepatitis B.

Progressive Multifocal Leukoencephalopathy (PML)

PML has been observed in clinical studies of Minjuvi. The diagnosis of PML should be considered in any patient presenting with new-onset or changes to pre-existing neurologic manifestations. The symptoms of PML are non-specific and can vary. Common symptoms include muscular weakness, paralysis, sensory abnormalities, cerebellar symptoms, and visual field defects. Evaluation of PML includes consultation with a neurologist, brain magnetic resonance imaging (MRI), and lumbar puncture (CSF testing for JC viral DNA). Therapy with Minjuvi should be withheld during the investigation of potential PML. Discontinue Minjuvi therapy and consider discontinuation or reduction of any concomitant anti-neoplastic treatment or immunosuppressive therapy in patients who develop PML.

Reproductive Health: Female and Male Potential

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

Fertility

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

Teratogenicity

Based on its mechanism of action, Minjuvi may cause fetal B-cell depletion when administered to a pregnant woman. Minjuvi in combination with lenalidomide should not be initiated in female patients unless pregnancy has been excluded (see Section 7.1.1 WARNINGS AND PRECAUTIONS, Special Populations, Pregnant Women).

Minjuvi may cause fetal harm. Advise females of reproductive potential to use effective contraception during Minjuvi treatment and for at least 3 months after the end of treatment.

Lenalidomide has been found to be teratogenic. Please refer to the lenalidomide product monograph.

7.1 Special Populations

7.1.1 Pregnant Women

There are no data on the use of Minjuvi in pregnant women. However, IgG is known to cross the placenta and Minjuvi may cause fetal B-cell depletion based on the mechanism of action (see Section 10.1 CLINICAL PHARMACOLOGY, Mechanism of Action).

Minjuvi is not recommended during pregnancy and in women of childbearing potential not using contraception. Advise patients to notify their doctor if they become pregnant or intend to become pregnant during Minjuvi therapy, as it may cause harm to the unborn baby.

Minjuvi is administered in combination with lenalidomide for up to 12 cycles. Lenalidomide can cause embryo-fetal harm and is contraindicated for use in pregnancy and in women of childbearing potential unless all of the conditions of the lenalidomide pregnancy prevention program are met.

7.1.2 Breast-feeding

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

7.1.3 Pediatrics (< 18 years of age)

No data are available to Health Canada; therefore, Health Canada has not authorized an indication for pediatric use.

7.1.4 Geriatrics (≥ 65 years of age)

Among 81 patients treated in the L-MIND study, 72% were 65 years and older. No overall differences in efficacy were observed in patients above 70 years of age or younger (see Section 1.2 INDICATIONS, Geriatrics).

8 ADVERSE REACTIONS

8.1 Adverse Reactions Overview

In the clinical development program of Minjuvi, 427 patients have received Minjuvi, either as monotherapy or in combination with other treatments. Of these, 35 patients with relapsed or refractory DLBCL were treated with Minjuvi monotherapy (MOR208C201 study) and 80 patients with relapsed or refractory DLBCL were treated with Minjuvi in combination with lenalidomide (MOR208C203 [L-MIND] study).

8.2 Clinical Trial Adverse Reactions

Clinical trials are conducted under very specific conditions, the adverse reaction rates observed in the clinical trials may not reflect the rates observed in practice and should not be compared to the rates in the clinical trials of another drug. Adverse reaction information from clinical trials may be useful for identifying and approximating rates of adverse drug-reactions in real-world use.

The safety of Minjuvi has been evaluated in 81 patients with non-transplant eligible relapsed or refractory DLBCL in the MOR208C203 (L-MIND) study in which Minjuvi was used in combination with lenalidomide. One patient received tafasitamab, but not lenalidomide. The remaining 80 patients received at least one dose of tafasitamab and lenalidomide.

Serious adverse events occurred in 52% of patients who received tafasitamab. Serious adverse events in ≥6% of patients included infections (26%) including pneumonia (7%), and febrile neutropenia (6%). Fatal adverse events occurred in 5% of patients who received tafasitamab, including cerebrovascular accident (1.2%), respiratory failure (1.2%), progressive multifocal leukoencephalopathy (1.2%) and sudden death (1.2%).

Permanent discontinuation of tafasitamab or lenalidomide due to an adverse event occurred in 25% of patients and permanent discontinuation of tafasitamab due to an adverse event occurred in 15%. The most frequent adverse event which resulted in permanent discontinuation of tafasitamab were infections (5%), nervous system disorders (2.5%), respiratory, thoracic and mediastinal disorders (2.5%).

The adverse reactions from L-MIND are presented in Table 4.

Table 4: Adverse Reactions (≥10%) in Patients with Relapsed or Refractory Diffuse Large B-Cell Lymphoma Who Received Minjuvi in L-MIND

Adverse Reaction	Minjuvi (N=81)	
	All Grades n (%)	Grade 3 or 4 n (%)
Blood and lymphatic system disorders		
Neutropenia	41 (51)	40 (49)
Anemia	29 (36)	6 (7)
Thrombocytopenia	25 (31)	14 (17)
Leukopenia	12 (15)	9 (11)
Febrile neutropenia	10 (12)	10 (12)
General disorders and administration site conditions		
Asthenia[1]	32 (39.5)	3 (3.7)
Pyrexia	(19) 24	(1) 1.2
Peripheral edema	19 (24)	0
Gastrointestinal disorders		
Diarrhea	29 (36)	1 (1.2)
Constipation	14 (17)	0
Nausea	12 (15)	0
Vomiting	12 (15)	0
Respiratory, thoracic and mediastinal disorders		
Cough	21 (26)	1 (1.2)
Dyspnea	10 (12)	1 (1.2)
Infections		
Respiratory tract infection[2]	43 (53.1)	11 (13.6)
Urinary tract infection[3]	14 (17)	4 (4.9)
Metabolism and nutrition disorders		
Decreased appetite	18 (22)	0
Hypokalemia	15 (19)	5 (6)
Musculoskeletal and connective tissue disorders		
Back pain	15 (19)	2 (2.5)
Muscle spasms	12 (15)	0
Skin and subcutaneous tissue disorders		
Rash[4]	13 (16)	2 (2.5)

[1] Includes fatigue and malaise

[2] Respiratory tract infection includes bronchitis, bronchopulmonary aspergillosis, influenza, lower respiratory tract infection, nasopharyngitis, parainfluenzae virus infection, pharyngitis, pharyngitis streptococcal, pneumonia, respiratory syncytial virus infection, respiratory tract infection, rhinitis, sinusitis, tonsillitis, upper respiratory tract infection, upper respiratory tract infection bacterial, viral pharyngitis

[3] Urinary tract infection includes: urinary tract infection, Escherichia urinary tract infection, urinary tract infection bacterial, and urinary tract infection enterococcal

[4] Rash includes rash, rash maculopapular, rash pruritus, rash erythematous

Description of selected adverse reactions

Myelosuppression

Treatment with Minjuvi can cause serious or severe myelosuppression including neutropenia, thrombocytopenia and anaemia (see Section 4.2 DOSAGE AND ADMINISTRATION, Recommended Dose and Dosage Adjustment, and Section 7 WARNINGS AND PRECAUTIONS, Hematology). In patients treated with Minjuvi and lenalidomide, Grade 3 or higher hematological adverse reactions (in 59% of patients) included neutropenia (49%), thrombocytopenia (17%), febrile neutropenia (12%), leukopenia and anemia (7%). Grade 4 hematological adverse reactions (in 31% of patients) included neutropenia (including agranulocytosis), thrombocytopenia, febrile neutropenia, and leukopenia.

When patients in MOR208C203 (L-MIND) were switched from tafasitamab and lenalidomide in the combination therapy phase to tafasitamab alone in the extended monotherapy phase, the incidences of hematological events decreased by at least 20% for neutropenia, anaemia and thrombocytopenia; no incidences of febrile neutropenia were reported with tafasitamab monotherapy.

Infections

Bacterial, fungal, and new or reactivation of viral infections can occur during and following Minjuvi therapy (see Section 7 WARNINGS AND PRECAUTIONS, Immune). Grade 3 or higher infections occurred in 30% of patients treated with Minjuvi and lenalidomide. The most frequently reported Grade 3 or higher infections were pneumonia (7%), respiratory tract infections (4.9%), urinary tract infection (4.9%) and sepsis (4.9%). Infection-related death was reported in 1% of patients (pneumonia) within 30 days of last treatment.

Infusion-related reactions

In the MOR208C203 (L-MIND) study, 6% of patients experienced an infusion-related reaction; Eighty percent of these reactions occurred during cycle 1 or 2; all were Grade 1 and resolved on the day of occurrence. Symptoms included chills, flushing, dyspnea and hypertension.

8.3 Less Common Clinical Trial Adverse Reactions

Blood and lymphatic system disorders: lymphopenia (6.2%)

General disorders and administration site conditions: infusion-related reaction (6.2%)

Infections: sepsis, including Klebsiella sepsis, neutropenic sepsis and streptococcal sepsis (4.9%)

Investigations: weight decreased (4.9%)

Musculoskeletal and connective tissue disorders: arthralgia (8.6%), pain in extremity (8.6%), musculoskeletal pain (1.2%)

Neoplasms benign, malignant, and unspecified: basal cell carcinoma (1.2%)

Nervous system disorders: headache (9%), paresthesia (7%), dysgeusia (6%)

Respiratory, thoracic and mediastinal disorders: nasal congestion (4.9%), exacerbation of chronic obstructive pulmonary disease (1.2%)

Skin and subcutaneous tissue disorders: pruritus (9.9%), erythema (3.7%), alopecia (2.5%), hyperhidrosis (2.5%)

8.4 Abnormal Laboratory Findings: Hematologic, Clinical Chemistry and Other Quantitative Data

Table 5: Select Laboratory Abnormalities (>20%) Worsening from Baseline in Patients with Relapsed or Refractory Diffuse Large B-Cell Lymphoma Who Received Minjuvi in L-MIND

Laboratory Abnormality	Minjuvi[1]	
	All Grades n (%)	Grade 3 or 4 n (%)
Chemistry		
Glucose increased	36 (49)	4 (5)
Calcium decreased	35 (47)	1 (1.4)
Gamma glutamyl transferase increased	25 (34)	4 (5)
Albumin decreased	19 (26)	0
Magnesium decreased	16 (22)	0
Urate increased	15 (20)	5 (7)
Phosphate decreased	15 (20)	4 (5)
Creatinine increased	15 (20)	1 (1.4)
Aspartate aminotransferase increased	15 (20)	0
Coagulation		
Activated partial thromboplastin time increased	34 (46)	3 (4.1)

[1] The denominator used to calculate the rate was 74 based on the number of patients with a baseline value and at least one post-treatment value.

9 DRUG INTERACTIONS

9.2 Drug Interactions Overview

No formal drug-drug interaction studies have been performed. In a population-pharmacokinetic analysis, concomitant administration of lenalidomide had no clinically meaningful effect on Minjuvi pharmacokinetics.

9.3 Drug-Behavioral Interactions

Women of child-bearing potential should use contraception while undergoing treatment with Minjuvi and for at least 3 months after end of treatment. (see Section 7.1 WARNINGS AND PRECAUTIONS, Special Populations).

9.4 Drug-Drug Interactions

Interactions with other drugs have not been established.

9.5 Drug-Food Interactions

Minjuvi can be administered with or without food (see Section 10.3 CLINICAL PHARMACOLOGY, Pharmacokinetics).

9.6 Drug-Herb Interactions

Drug-herb interactions have not been studied

9.7 Drug-Laboratory Test Interactions

Interactions with laboratory tests have not been established.

10 CLINICAL PHARMACOLOGY

10.1 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 and on several B-cell malignancies, including diffuse large B-cell lymphoma.

Upon binding to CD19, tafasitamab mediates B-cell lysis through apoptosis and immune effector mechanisms including antibody-dependent cellular cytotoxicity (ADCC) and antibody-dependent cellular phagocytosis (ADCP). In *in vitro* laboratory studies conducted in DLBCL tumour cell lines, tafasitamab, in combination with lenalidomide, was associated with greater cytotoxicity than observed when cells were treated with either agent alone.

10.2 Pharmacodynamics

In patients with relapsed or refractory DLBCL, tafasitamab led to a reduction in peripheral blood B-cell counts. The reduction relative to baseline B-cell count reached 97% after eight days of treatment in the MOR208C203 (L-MIND) study. The maximum B-cell reduction at approximately 100% (median) was reached within 16 weeks of treatment.

Although the depletion of B-cells in the peripheral blood is a measurable pharmacodynamic effect, it is not directly correlated with the depletion of B-cells in solid organs or in malignant deposits.

10.3 Pharmacokinetics

Absorption: Based on a population pharmacokinetic analysis of Minjuvi in combination with lenalidomide, tafasitamab average serum trough concentrations (± standard deviation) were 179 (± 53) µg/mL during weekly intravenous administrations of 12 mg/kg (plus an additional dose on day 4 of cycle 1). During administration every 14 days from cycle 4 to cycle 23 onwards, average trough serum

concentrations were 153 (± 68) µg/mL. Overall, maximum Minjuvi serum concentrations were 483 (± 109) µg/mL.

Distribution: The total volume of distribution for tafasitamab was 9.3 L (95% CI 8.59, 10.0 L).

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

Elimination: The clearance of tafasitamab was 0.41 L/day and terminal elimination half-life was 16.9 days (95% CI 15.4, 18.4 days). Following long-term observations, tafasitamab clearance was found to decrease over time to 0.19 L/day after two years.

Special Populations and Conditions

- **Pediatrics (< 18 years of age):** The pharmacokinetics of Minjuvi has not been studied in pediatric patients.
- **Geriatrics (≥ 65 years of age):** Age had no relevant effect on the pharmacokinetics of Minjuvi.
- **Sex:** Sex had no relevant effect on the pharmacokinetics of Minjuvi.
- **Pregnancy and Breast-feeding:** The pharmacokinetics of Minjuvi in patients who are pregnant or breast-feeding has not been studied.
- **Ethnic Origin:** The pharmacokinetics of Minjuvi has not evaluated based on ethnic origin.
- **Hepatic Insufficiency:** 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 ≤ ULN and 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) on the pharmacokinetics of Minjuvi is unknown.
- **Renal Insufficiency:** 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 (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) on the pharmacokinetics of Minjuvi is unknown.
- **Obesity:** Weight had a statistically significant effect on the pharmacokinetics of Minjuvi in a population pharmacokinetic model; however, the effect was not considered clinically relevant in patients who weigh less than 163 kg. The clinical relevance in patients who weigh 163 kgs or greater is unknown.

11 STORAGE, STABILITY AND DISPOSAL

Store in a refrigerator (2°C – 8°C).

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

Reconstituted solution (prior to dilution)

From a microbiological point of view, the reconstituted Minjuvi solution should be used as soon as possible after reconstitution. If not used immediately, the reconstituted product may be stored prior to dilution for up to 24 hours at 2°C - 25°C. Do not freeze or shake. Protect from light during storage.

Diluted solution (solution for infusion)

From a microbiological point of view, once diluted, the product should be used immediately. If not used immediately, the infusion solution may be stored for a maximum of 36 hours at 2°C - 8°C followed by up to 24 hours at up to 25°C. Do not freeze or shake. Protect from light during storage.

PART II: SCIENTIFIC INFORMATION

13 PHARMACEUTICAL INFORMATION

Drug Substance

Proper name: tafasitamab for injection

Molecular mass: Tafasitamab has a molecular weight of approximately 150 kDa.

Molecular formula: $C_{6538}H_{10068}N_{1720}O_{2046}S_{52}$

Structure: Tafasitamab is a fragment crystallizable (Fc)-engineered humanized monoclonal antibody. It is derived from the murine monoclonal antibody (mAb) 4G7 by humanization of the variable domain.

Drug Product Characteristics

Tafasitamab is expressed in Chinese hamster ovary (CHO) cells. Tafasitamab drug product (DP) is a lyophilized powder for reconstitution and intravenous infusion. Tafasitamab DP is a white to slightly yellowish lyophilizate for reconstitution. After reconstitution, tafasitamab is presented at a concentration of 40 mg/mL in a 25 mM citrate buffered, isotonic solution at pH 6.0 supplied in single-use 20 R glass vials.

14 CLINICAL TRIALS

14.1 Trial Design and Study Demographics

Tafasitamab plus lenalidomide followed by tafasitamab monotherapy was studied in the MOR208C203 (L-MIND) study (NCT02399085), an open-label multicentre single-arm study. Adult patients were eligible for the study if they had relapsed or refractory DLBCL, had received 1 to 3 prior systemic DLBCL therapies, and, who at the time of the trial, were not candidates for high dose chemotherapy followed by ASCT. At least one of the prior systemic therapies had to include a CD20 targeted therapy. Patients were not eligible if they had other types of lymphoma including primary mediastinal B-cell lymphoma (PMBCL) or Burkitt lymphoma or if they had a history of double/triple hit genetics (i.e., detection of MYC with BCL2 and/or BCL6 translocations). Patients with a history of CNS lymphoma involvement were also excluded.

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. Pre-medication, including antipyretics, histamine H1 and H2 receptor blockers and glucocorticosteroids, was given 30 to 120 minutes prior to the first three tafasitamab infusions.

Patients self-administered 25 mg lenalidomide daily on days 1 to 21 of each 28-day cycle, for up to 12 cycles.

A total of 81 patients were enrolled in the study. Seventy-one of the enrolled patients had DLBCL confirmed by a central laboratory, and received combination treatment on study. The median age was 71 years (range 41 to 86 years), 87% were white and 55% were male. The median number of prior

therapies was two and all patients had received a prior CD20-containing therapy. Fourteen patients (19.7%) had a primary refractory disease, 32 (45.1%) were refractory to their last prior therapy and 30 (42.3%) were refractory to rituximab. Nine patients (12.7%) had received prior ASCT. The primary reasons for patients (full analysis set) not being candidates for ASCT included age (46.5%), refractory to salvage chemotherapy (26.8%), comorbidities (12.7%) and refusal of high dose chemotherapy/ASCT (12.7%).

The median duration of exposure to tafasitamab and lenalidomide was 6.7 months. Twenty-six (36.6%) patients completed 12 cycles of tafasitamab. Twenty-three (32.4%) patients completed 12 cycles of lenalidomide.

14.2 Study Results

The primary efficacy outcome in the L-MIND study was the best Overall Response Rate (ORR), defined as the sum of the proportions of patients who were complete or partial responders as assessed by an independent review committee who applied the International Working Group Response Criteria (Cheson 2007). Study Results are summarized in Table 6.

Table 6: Efficacy Results in L-MIND

	(N = 71)
Best objective response rate[1]	
Overall response rate, n (%) (95% CI)	38 (53.5) (41.3,65.5)
Complete response rate, n (%) (95% CI)	25 (35.2) (24.2,47.5)
Partial response rate, n (%) (95% CI)	13 (18.3) (10.1,29.3)
Overall duration of response (complete + partial response)	
Median, months[2] (95% CI) (range, months)	34.6 (21.7, not reached) 0, 34.6
Duration of response in patients with complete response as best response	
Median, months[2] (95% CI) (range, months)	NR (26.1, NR) 0+, 34.1+
Duration of response in patients with partial response as best response	
Median, months[2] (95% CI) (range, months)	5.7 (1.8, NR) 0+, 34.6

[1] Confidence interval based on the Clopper-Pearson method.

[2] Kaplan-Meier estimates. Confidence interval based on the Brookmeyer and Crowley method.

+ Denotes a censored observation.

14.4 Immunogenicity

As with all therapeutic proteins, there is the potential for immunogenicity. The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay.

Seventeen of 245 evaluable subjects (6.9%) tested ADA-positive before start of tafasitamab treatment suggesting the presence of pre-existing antibodies. Six subjects who had pre-existing ADAs were ADA-positive on an intermittent basis also after start of tafasitamab treatment. The remaining 11 of baseline ADA-positive subjects did not test positive for ADA during treatment. No baseline ADA-negative subjects tested positive for ADA during treatment. Thus, no treatment-emergent or treatment-boosted ADAs were detected. The ADA titers were low and there was no apparent clinical impact of ADAs on PK, safety or efficacy.

15 MICROBIOLOGY

No microbiological information is required for this drug product.

16 NON-CLINICAL TOXICOLOGY

General Toxicology: 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.

Carcinogenicity: Carcinogenicity studies have not been conducted with tafasitamab; consistent with health authority guidelines for therapeutics intended for the treatment of cancer, carcinogenicity studies are generally not warranted.

Genotoxicity: Genotoxicity studies have not been conducted with tafasitamab; consistent with health authority guidelines for biotechnology products, genotoxicity studies are generally not needed.

Reproductive and Developmental Toxicology: No specific studies of fertility or reproductive and developmental toxicity were conducted with tafasitamab. In the 13-week repeat-dose general toxicity study in cynomolgus monkeys, no adverse effects on male and female reproductive organs were observed up to the highest dose tested, 100 mg/kg/week (approximately 9 times the human exposure based on AUC at the clinical dose of 12 mg/kg/week).

Immunogenicity: In the 13-week repeat-dose general toxicity study in cynomolgus monkeys, there was evidence for anti-drug antibody formation but no evidence for cytokine release. There was a reversible reduction in a primary antibody response to antigens in a T-cell dependent antibody response assessment.

17 SUPPORTING PRODUCT MONOGRAPHS

1. Product Monograph, REVLIMID (lenalidomide) Capsules, 2.5 mg, 5 mg, 10 mg, 20 mg, 25 mg, Antineoplastic Agent, Immunomodulatory Agent, Celgene Inc. Control No. 229241, Revision Date: 20 August 2019

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

[PR]Minjuvi™

tafasitamab for injection

Read this carefully before you start taking Minjuvi and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about Minjuvi.

Serious Warnings and Precautions

- Infections: Fatal, life threatening, or serious infections have been reported in patients treated with Minjuvi (see Section *What are possible side effects from using Minjuvi?*)
- Decreased production of blood cells: Serious and severe reduction in blood cells have been reported in patients treated with Minjuvi (see Section *What are possible side effects from using Minjuvi?*)
- A serious and life-threatening brain condition called progressive multifocal leukoencephalopathy (PML) has been observed after treatment with Minjuvi (see Section *What are possible side effects from using Minjuvi?*)
- Recurrence of hepatitis B viral infection can occur with Minjuvi treatment (see Section *What are possible side effects from using Minjuvi?*)

What is Minjuvi used for?

- Diffuse large B-cell lymphoma (DLBCL) – a type of cancer found mainly in the lymph nodes made up of white blood cells that have become malignant. Minjuvi can be used to treat adult patients who have had their cancer return after other treatments or when other treatments did not work.

"For the following indication, Minjuvi™ has been approved *with conditions* (NOC/c). This means it has passed Health Canada's review and can be bought and sold in Canada, but the manufacturer has agreed to complete more studies to make sure the drug works the way it should. For more information, talk to your healthcare professional."

- Minjuvi (tafasitamab for injection) is indicated in combination with lenalidomide for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) not otherwise specified, including DLBCL arising from low grade lymphoma, who are not eligible for autologous stem cell transplant (ASCT).

A Notice of Compliance with Conditions (NOC/c) is a type of approval to sell a drug in Canada.

Health Canada only gives an NOC/c to a drug that treats, prevents, or helps identify a serious or life-threatening illness. The drug must show promising proof that it works well, is of high quality, and is reasonably safe. Also, the drug must either respond to a serious medical need in Canada, or be much safer than existing treatments.

Drug makers must agree in writing to clearly state on the label that the drug was given an NOC/c, to complete more testing to make sure the drug works the way it should, to actively monitor the drug's performance after it has been sold, and to report their findings to Health Canada.

How does Minjuvi work?

Minjuvi contains the active substance tafasitamab, an anti-cancer agent, which is a monoclonal antibody that has been designed to kill cancer cells. The monoclonal antibody acts by binding to a protein on the surface of cancerous B cells in order to kill the cells and to recruit normal immune cells, which also can target and kill the cancer cells. A monoclonal antibody is a protein that binds to a specific protein target.

Minjuvi is given with another drug called lenalidomide. Minjuvi in combination with lenalidomide resulted in better cancer cell toxicity in laboratory studies than when either drug was used by itself.

What are the ingredients in Minjuvi?

Medicinal ingredients: tafasitamab

Non-medicinal ingredients: citric acid monohydrate, polysorbate 20, sodium citrate dihydrate, and trehalose dihydrate.

Minjuvi comes in the following dosage forms:

For injection: 200 mg of tafasitamab as white to slightly yellowish lyophilized powder in single-dose vial for reconstitution and further dilution

Do not use Minjuvi if:

You are allergic to tafasitamab or to any of the other ingredients in the medicine.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take Minjuvi. Talk about any health conditions or problems you may have, including if you:

- have an active infection or have had one recently.
- have hepatitis B or have recovered from hepatitis B in the past.
- are pregnant or plan to become pregnant. Minjuvi may harm your unborn baby. You should not become pregnant during treatment with Minjuvi. Do not receive treatment with Minjuvi in combination with lenalidomide if you are pregnant because lenalidomide can cause birth defects and death of your unborn baby.
    - you should use an effective method of birth control (contraception) during treatment and for at least 3 months after your last dose of Minjuvi.
    - tell your healthcare professional right away if you become pregnant or think you may be pregnant during treatment with Minjuvi.
- are breast-feeding or plan to breast-feed. It is not known if Minjuvi passes into your breast-milk. Do not breast-feed during treatment and for at least 3 months after your last dose of Minjuvi.

Other warnings you should know about:

- Infusion-related reactions
    - Your healthcare provider will monitor you for infusion reactions during your infusion of Minjuvi. Tell your health care provider right away if you get chills, flushing, headache, or shortness of breath during an infusion with Minjuvi.
- Low blood cell counts (platelets, red blood cells, and white blood cells)

- Low blood cell counts are common with Minjuvi, but can also be serious or severe. Your healthcare provider will monitor your blood counts during treatment with Minjuvi. Tell your healthcare provider right away if you get a fever of 38°C or above, or any bruising or bleeding.

- Infections
  - Serious infections, including infections that can cause death, have happened in people during treatment with Minjuvi and after the last dose. Tell your healthcare provider right away if you get a fever of 38°C or above, or develop any signs or symptoms of infection.
- Hepatitis B reactivation
  - Patients who have previously had hepatitis B may be at greater risk of hepatitis B reactivation after receiving Minjuvi. Hepatitis B reactivation has been observed after treatment with Minjuvi. Your doctor will monitor you for hepatitis B and may make changes to your treatment if necessary.
- Progressive multifocal leukoencephalopathy
  - A serious and life-threatening brain condition called progressive multifocal leukoencephalopathy (PML) has been observed after treatment with Minjuvi. Tell your doctor immediately if you have memory loss, trouble thinking, difficulty with walking, clumsiness, experience falls or weakness on one side of the body, changes in mood or loss of vision. Your doctor will check if you need to see a neurologist.
- Tumor Lysis Syndrome (also called TLS) (the development of unusual levels of some chemicals such as potassium and uric acid, in the blood caused by fast breakdown of cancer cells during treatment)
  - Your healthcare provider will do blood tests to check for TLS.
  - Tell your doctor immediately if you have palpitations/irregular heartbeats; vomiting; fatigue/weakness; difficulty concentrating/trouble thinking; swelling, numbness or tingling in hands, face or feet; back pain; muscle cramps; fainting or trouble breathing.
- Sexual Health
  - Women should use an effective method of birth control during treatment and for 3 months after your final dose of Minjuvi.
  - No information is available to evaluate the potential effects of Minjuvi on fertility.
- Pregnancy
  - Your healthcare professional should do a pregnancy test before you start treatment with Minjuvi. Minjuvi can harm your unborn baby or cause loss of your pregnancy (miscarriage). You should not become pregnant during treatment with Minjuvi. Tell your healthcare professional right away if you become pregnant or think that you may be pregnant.
- Breast-feeding
  - It is unknown if Minjuvi can pass into breast-milk. Do not breastfeed for at least 3 months after your final dose of Minjuvi.

- Immunizations
    - The safety of immunization with live vaccines following tafasitamab therapy has not been investigated, and vaccination with live vaccines is not recommended concurrently with tafasitamab therapy.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with Minjuvi:
No known interactions

How to take Minjuvi:

- Minjuvi will be given to you by your healthcare professional in a healthcare setting. Minjuvi is given as an intravenous infusion.

Usual dose:

- Minjuvi 12 mg per kilogram (mg/kg) body weight is given as an intravenous infusion according to the dosing schedule in Table 7.
- You will receive other medications prior to each dose of Minjuvi to reduce the chances of an infusion reaction. Your health care professional may decide you do not need these medicines after several infusions if you do not have any reactions to the infusion.
- Minjuvi is given while you are taking another drug called lenalidomide. The dose of lenalidomide is 25 mg and it is taken by mouth once a day for the first 21 days of each cycle for a maximum of 12 cycles. You should also read the PATIENT MEDICATION INFORMATION for lenalidomide before starting treatment.
- After a maximum of 12 cycles of Minjuvi and lenalidomide, Minjuvi is given alone. Treatment is usually continued until disease progression or unacceptable toxicity.

Table 7: Minjuvi Dosing Schedule

Cycle	**Dosing Schedule**
Cycle 1	Days 1, 4, 8, 15 and 22
Cycles 2 and 3	Days 1, 8, 15 and 22
Cycle 4 and beyond	Days 1 and 15

Overdose:

Minjuvi is administered by your healthcare professional. There is no information on overdose with Minjuvi. For management of a suspected drug overdose contact your healthcare professional, hospital emergency department or regional poison control centre immediately, even if there are no symptoms.

What are possible side effects from using Minjuvi?

These are not all the possible side affects you may feel when taking Minjuvi. If you experience any side effects not listed here, contact your healthcare professional.

The most common side effects of Minjuvi include:

- decreased blood count (certain white blood cells and red blood cells)
- feeling tired or weak
- decreased platelets
- diarrhea, constipation, nausea, vomiting
- cough
- trouble breathing
- fever
- swelling of lower legs or hands
- respiratory tract infection
- urinary tract infections
- decreased appetite

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
VERY COMMON			
Infections - symptoms may include, fever, chills, sore throat, cough, shortness of breath, nausea, vomiting, diarrhea		√	
Low blood cell counts - symptoms may include feeling tired or weak, fever, bleeding or bruising		√	
COMMON			
Infusion reactions - symptoms include fever, chills, rash, flushing, headache, or shortness of breath within 24 hours of infusion		√	
Hepatitis B reactivation - symptoms may include mild fever, feeling of sickness, fatigue, loss of appetite, joint and/or abdominal pain and yellowing of whites of the eyes, skin and tongue.		√	
Progressive multifocal leukoencephalopathy (PML)		√	

- symptoms may include increasing weakness or numbness of part or all of one side of the body, loss of vision or blurred vision, unexplained dizziness and/or clumsiness or sudden falls, trouble with thinking or memory, changes in mood, change in vision, change in mental status (for example, confusion), seizures.			

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, talk to your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada.html) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

Minjuvi is stored refrigerated at 2°C to 8°C in the original carton to protect from light. Do not shake. Do not freeze.

Keep out of reach and sight of children.

If you want more information about Minjuvi:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website: (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html), the manufacturer's website (www.incytebiosciences.ca), or by calling 1-833-309-2759.

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