Product Monograph

Including Patient Medication Information

[Pr]TECVAYLI®

Teclistamab injection

Solution for subcutaneous injection

153 mg/1.7 mL (90 mg/mL) and 30 mg/3 mL (10 mg/mL)

Professed Standard

Antineoplastic, monoclonal antibody

ATC code: L01FX24

TECVAYLI, indicated for:

- the treatment of adult patients with relapsed or refractory multiple myeloma who have received at least three prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent and an anti-CD38 monoclonal antibody, and who have demonstrated disease progression on the last therapy,

has been issued market 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 TECVAYLI please refer to Health Canada's Notice of Compliance with conditions - drug products web site.

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Date of Authorization:
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Submission Control Number: 295510

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

A 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.

Recent Major Label Changes

4 Dosage and Administration / 4.2 Recommended Dose and Dosage Adjustment	2024/08
7 Warnings and Precautions, Immune	2024/07
7 Warnings and Precautions, Neurologic	2025/06

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Certain sections or subsections that are not applicable at the time of the preparation of the most recent authorized product monograph are not listed.

Part 1: Healthcare Professional Information

1. Indications

TECVAYLI® (teclistamab injection) is indicated for:

- the treatment of adult patients with relapsed or refractory multiple myeloma who have received at least three prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent and an anti-CD38 monoclonal antibody, and who have demonstrated disease progression on the last therapy.

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): Of the 165 patients treated with TECVAYLI in Study MajesTEC-1 at the recommended dose, 48% were 65 years of age or older, and 15% were 75 years of age or older. No overall differences in safety or effectiveness were observed between these patients and younger patients.

2. Contraindications

TECVAYLI 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 6. Dosage Forms, Strengths, Composition and Packaging.

3. Serious Warnings and Precautions Box

Serious Warnings and Precautions

- Cytokine release syndrome (CRS), including life-threatening or fatal reactions, can occur in patients receiving TECVAYLI. Initiate treatment with TECVAYLI step-up dosing schedule to reduce the risk of CRS. Monitor patients for signs or symptoms of CRS. Withhold TECVAYLI until CRS resolves, provide supportive care and treatment as needed or permanently discontinue based on severity (see7. Warnings and Precautions).
- Serious, life-threatening, or fatal neurologic toxicities, including Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS), can occur following treatment with TECVAYLI. The onset of ICANS can be concurrent with CRS, following resolution of CRS, or in the absence of CRS. Monitor patients for signs or symptoms of neurologic toxicity, including ICANS, during treatment. Withhold TECVAYLI until neurologic toxicity resolves or permanently discontinue based on severity (see7. Warnings and Precautions).

4. Dosage and Administration

4.1. Dosing Considerations

- TECVAYLI should be administered by subcutaneous injection only.
- Pregnancy status for females of child-bearing potential should be verified prior to starting treatment with TECVAYLI.
- Do not administer TECVAYLI step-up dosing schedule in patients with active infection.
- Prior to starting treatment with TECVAYLI, anti-viral prophylaxis should be considered for the prevention of herpes zoster virus reactivation per local institutional guidelines.
- Administer pre-treatment medications prior to each dose of the TECVAYLI step-up dosing schedule (see 4.4. Administration).

4.2. Recommended Dose and Dosage Adjustment

Recommended Dose

The recommended dose for TECVAYLI is 1.5 mg/kg actual body weight administered subcutaneously once weekly, preceded by step-up doses of 0.06 mg/kg and 0.3 mg/kg. The dosing schedule is provided in Table 1.

In patients who have a complete response (CR) or better for a minimum of 6 months, a reduced dosing frequency of 1.5 mg/kg actual body weight administered every two weeks may be considered (see 14. Clinical Trials).

Administer TECVAYLI subcutaneously according to the step-up dosing schedule in Table 1 to reduce the incidence and severity of cytokine release syndrome (CRS).

Failure to follow the recommended doses or dosing schedule for initiation of therapy or re-initiation of therapy after dose delays may result in increased frequency and severity of adverse events related to mechanism of action, particularly CRS (see 7. Warnings and Precautions).

Table 1: TECVAYLI Dosing Schedule

Dosing schedule	Day	Dose[a]	
All patients			
Step-up dosing schedule[b]	Day 1	Step-up dose 1	0.06 mg/kg single dose
	Day 3[c]	Step-up dose 2	0.3 mg/kg single dose
	Day 5[d]	First treatment dose	1.5 mg/kg single dose
Weekly dosing schedule[b]	One week after first treatment dose and weekly thereafter[e]	Subsequent treatment doses	1.5 mg/kg once weekly
Patients who have a complete response or better for a minimum of 6 months			
Biweekly (every two weeks) dosing schedule[b]	Consider reducing the dosing frequency to 1.5 mg/kg every two weeks		

[a] Dose is based on actual body weight and should be administered subcutaneously.
[b] See Table 6 for recommendations on restarting TECVAYLI after dose delays.
[c] Step-up dose 2 may be given between 2 to 7 days after Step-up dose 1.
[d] First treatment dose may be given between 2 to 7 days after Step-up dose 2. This is the first full treatment dose (1.5 mg/kg).
[e] Maintain a minimum of five days between weekly treatment doses.

Refer to Table 3, Table 4 and Table 5 to determine the dosage based on predetermined weight ranges.

Patients should be treated with TECVAYLI until disease progression or unacceptable toxicity.

For guidance regarding restarting therapy with TECVAYLI after dose delays, see 4.5. Missed Dose.

Dosage Adjustment

Do not skip step-up doses of TECVAYLI.

Dose reductions of TECVAYLI are not recommended.

Dose delays may be required to manage toxicities related to TECVAYLI (see 7. Warnings and Precautions and 4. Dosage and Administration).

See Table 2 for recommended actions for adverse reactions following administration of TECVAYLI.

Table 2: Recommended Actions for Adverse Reactions Following Administration of TECVAYLI

Adverse Reactions	Grade	Actions
Cytokine Release Syndrome (CRS)[a] (see 7. Warnings and Precautions)	Grade 1	• Withhold TECVAYLI until adverse reaction resolves. • See Table 8 for management of cytokine release syndrome. • Administer pre-treatment medication prior to next dose of TECVAYLI.

Adverse Reactions	Grade	Actions
The presenting symptoms of CRS per grade are included in Table 8.	Grade 2 Grade 3 (Duration: less than 48 hours)	• Withhold TECVAYLI until adverse reaction resolves. • See Table 8 for management of cytokine release syndrome. • Administer pre-treatment medications prior to next dose of TECVAYLI. • Monitor patient daily for 48 hours following the next dose of TECVAYLI. Instruct patients to remain within proximity of a healthcare facility during daily monitoring.
	Grade 3 (Recurrent or duration: more than 48 hours) Grade 4	• Permanently discontinue therapy with TECVAYLI. • See Table 8 for management of cytokine release syndrome.
Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS)[b] (see 7. Warnings and Precautions) The presenting symptoms of ICANS outlined per grade are included in Table 9.	Grade 1	• Withhold TECVAYLI until adverse reaction resolves. • See Table 9 for management of immune effector cell-associated neurotoxicity syndrome.
	Grade 2 Grade 3 (First occurrence)	• Withhold TECVAYLI until adverse reaction resolves. • See Table 9 for management of immune effector cell-associated neurotoxicity syndrome. • Monitor patient daily for 48 hours following the next dose of TECVAYLI. Instruct patients to remain within proximity of a healthcare facility during daily monitoring.
	Grade 3 (Recurrent) Grade 4	• Permanently discontinue therapy with TECVAYLI. • See Table 9 for management of immune effector cell-associated neurotoxicity syndrome.
Infections (see 7. Warnings and Precautions)	All Grades	• Do not administer TECVAYLI step-up dosing schedule in patients with active infection.
	Grade 3 Grade 4	• Withhold subsequent treatment doses of TECVAYLI until infection improves to Grade 1 or better.

Adverse Reactions	Grade	Actions
Hematologic Toxicities (see 7. Warnings and Precautions and 8. Adverse Reactions)	Absolute neutrophil count less than 0.5×10^9/L	• Withhold TECVAYLI until absolute neutrophil count is 0.5×10^9/L or higher.
	Febrile neutropenia	• Withhold TECVAYLI until absolute neutrophil count is 1.0×10^9/L or higher and fever resolves.
	Hemoglobin less than 8 g/dL	• Withhold TECVAYLI until hemoglobin is 8 g/dL or higher.
	Platelet count less than 25000/µL Platelet count between 25000/µL and 50000/µL with bleeding	• Withhold TECVAYLI until platelet count is 25000/µL or higher and no evidence of bleeding.
Other Adverse Reactions (see 8. Adverse Reactions)	Grade 3 Grade 4	• Withhold TECVAYLI until adverse reaction improves to Grade 1 or better. • Consider permanent discontinuation for Grade 4 non-hematologic adverse reactions.

[a] Based on American Society for Transplantation and Cellular Therapy (ASTCT) grading.

[b] Based on American Society for Transplantation and Cellular Therapy (ASTCT) 2019 grading for ICANS.

Renal impairment

No formal studies of TECVAYLI in patients with renal impairment have been conducted. Based on population pharmacokinetic analyses, no dose adjustment is recommended for patients with mild or moderate renal impairment (see 10.3. Pharmacokinetics). Limited data are available for patients with severe renal impairment.

Hepatic impairment

No formal studies of TECVAYLI in patients with hepatic impairment have been conducted. Based on population pharmacokinetic analyses, no dose adjustment is recommended for patients with mild hepatic impairment (see 10.3. Pharmacokinetics). No data are available in patients with moderate and severe hepatic impairment.

Pediatric (<18 years)

Health Canada has not authorized an indication for pediatric use.

Geriatrics (≥65 years of age)

No dose adjustment is required in patients over 65 years of age (see 10. Clinical Pharmacology).

4.3. Administration

TECVAYLI should be administered by healthcare professionals at treatment centres with adequate medical equipment and personnel to manage severe reactions, including CRS and neurologic toxicities. Educational materials related to the risks of CRS and neurologic toxicities, including ICANS, are available for healthcare professionals through the manufacturer.

It is very important that the instructions for preparation and administration provided in this section are strictly followed to minimize potential dosing errors with TECVAYLI 30 mg/3 mL (10 mg/mL) vial and TECVAYLI 153 mg/1.7 mL (90 mg/mL) vial.

TECVAYLI should be administered via subcutaneous injection only. Do not administer TECVAYLI intravenously.

Pre-treatment Medications

Administer the following pre-treatment medications 1 to 3 hours before each dose of the TECVAYLI step-up dosing schedule, which includes step-up dose 1, step-up dose 2, and the first treatment dose (Table 1) to reduce the risk of cytokine release syndrome (see 7. Warnings and Precautions).

- Corticosteroid (oral or intravenous dexamethasone, 16 mg)
- Antihistamine (oral or intravenous diphenhydramine, 50 mg or equivalent)
- Antipyretics (oral or intravenous acetaminophen, 650 mg to 1000 mg or equivalent)

Administration of pre-treatment medications may be required prior to the administration of subsequent doses of TECVAYLI in the following patients:

- Patients who repeat doses within the TECVAYLI step-up dosing schedule following a dose delay (see Table 6).
- Patients who experienced CRS following the prior dose of TECVAYLI (see Table 2).

Preparation of TECVAYLI

- TECVAYLI is available in two strengths, 30 mg/3 mL (10 mg/mL) in a 3 mL glass vial with a blue colour cap, and 153 mg/1.7 mL (90 mg/mL) in a 1.7 mL glass vial with an orange colour cap (see 6. Dosage Forms, Strengths, Composition and Packaging). Use TECVAYLI 30 mg/3 mL (10 mg/mL) vial for Step-up dose 1 and Step-up dose 2, and TECVAYLI 153 mg/1.7 mL (90 mg/mL) vial for treatment dose.

- TECVAYLI 10 mg/mL and TECVAYLI 90 mg/mL are supplied as ready-to-use solutions for injection that do not need dilution prior to administration.

- TECVAYLI vials of different concentrations should not be combined to achieve treatment dose.

- Use aseptic technique to prepare and administer TECVAYLI.
- TECVAYLI solution for injection is clear to slightly opalescent, colourless to light yellow. Visually inspect TECVAYLI for particulate matter and discolouration prior to administration. Do not use if the solution is discoloured, or cloudy, or if foreign particles are present. Verify the prescribed dose for each TECVAYLI injection. To minimize errors, use the following tables to prepare TECVAYLI injection.
- Use Table 3 to determine total dose, injection volume, and number of vials required based on patient's actual body weight for **Step-up Dose 1 using TECVAYLI 30 mg/3 mL (10 mg/mL) vial**.

Table 3: Step-up Dose 1 Injection Volumes Using TECVAYLI 30 mg/3 mL (10 mg/mL) Vial

	Body Weight (kg)	Total Dose (mg)	Volume of Injection (mL)	Number of Vials (1 vial=3 mL)
Step-Up Dose 1 (0.06 mg/kg)	35-39	2.2	0.22	1
	40-44	2.5	0.25	1
	45-49	2.8	0.28	1
	50-59	3.3	0.33	1
	60-69	3.9	0.39	1
	70-79	4.5	0.45	1
	80-89	5.1	0.51	1
	90-99	5.7	0.57	1
	100-109	6.3	0.63	1
	110-119	6.9	0.69	1
	120-129	7.5	0.75	1
	130-139	8.1	0.81	1
	140-149	8.7	0.87	1
	150-160	9.3	0.93	1

- Use Table 4 to determine total dose, injection volume and number of vials required based on patient's actual body weight for **Step-up Dose 2 using TECVAYLI 30 mg/3 mL (10 mg/mL) vial**.

Table 4: Step-up Dose 2 Injection Volumes Using TECVAYLI 30mg/3 mL (10 mg/mL) Vial

	Body Weight (kg)	Total Dose (mg)	Volume of Injection (mL)	Number of Vials (1 vial=3 mL)
Step-up Dose 2 (0.3 mg/kg)	35-39	11	1.1	1
	40-44	13	1.3	1
	45-49	14	1.4	1
	50-59	16	1.6	1
	60-69	19	1.9	1
	70-79	22	2.2	1
	80-89	25	2.5	1
	90-99	28	2.8	1
	100-109	31	3.1	2
	110-119	34	3.4	2
	120-129	37	3.7	2
	130-139	40	4	2
	140-149	43	4.3	2
	150-160	47	4.7	2

Use Table 5 to determine total dose, injection volume and number of vials required based on patient's actual body weight for the **Treatment Dose using TECVAYLI 153 mg/1.7 mL (90 mg/mL) vial**.

Table 5: Treatment Dose Injection Volumes Using TECVAYLI 153 mg/1.7 mL (90 mg/mL) Vial

	Body Weight (kg)	Total Dose (mg)	Volume of Injection (mL)	Number of Vials (1 vial=1.7 mL)
Treatment Dose (1.5 mg/kg)	35-39	56	0.62	1
	40-44	63	0.7	1
	45-49	70	0.78	1
	50-59	82	0.91	1
	60-69	99	1.1	1
	70-79	108	1.2	1
	80-89	126	1.4	1
	90-99	144	1.6	1
	100-109	153	1.7	1
	110-119	171	1.9	2
	120-129	189	2.1	2
	130-139	198	2.2	2
	140-149	216	2.4	2
	150-160	234	2.6	2

- Remove the appropriate strength TECVAYLI vial from refrigerated storage (2°C to 8°C) and equilibrate to ambient temperature (15°C to 30°C), as needed, for at least 15 minutes. Do not warm TECVAYLI in any other way.

- Once equilibrated, gently swirl the vial for approximately 10 seconds to mix. Do not shake.
- Withdraw the required injection volume of TECVAYLI from the vial(s) into an appropriately sized syringe using a transfer needle.
    - Each injection volume should not exceed 2.0 mL. Divide doses requiring greater than 2.0 mL equally into multiple syringes.
- TECVAYLI is compatible with stainless steel injection needles and polypropylene or polycarbonate syringe material.
- Replace the transfer needle with an appropriately sized needle for injection.

Administration of TECVAYLI

- Inject the required volume of TECVAYLI into the subcutaneous tissue of the abdomen (preferred injection site). Alternatively, TECVAYLI may be injected into the subcutaneous tissue at other sites (e.g., thigh). If multiple injections are required, TECVAYLI injections should be at least 2 cm apart.
- Do not inject into tattoos or scars or areas where the skin is red, bruised, tender, hard or not intact.
- If TECVAYLI is not used immediately, store at 2 to 8°C or at ambient temperature for a maximum of 20 hours. Discard after 20 hours, if not used.
- Any unused medicinal product or waste material should be disposed in accordance with local requirements.

Monitoring

Instruct the patients to remain within proximity of a healthcare facility and monitor daily for 48 hours for signs and symptoms of CRS after administration of all doses within the TECVAYLI step-up dosing schedule, or alternatively consider hospitalization for patients (see 4. Dosage and Administration and 7. Warnings and Precautions).

4.4. Missed Dose

Restarting TECVAYLI after dose delays

If a dose of TECVAYLI is delayed, restart therapy based on the recommendations listed in Table 6 and resume the treatment schedule accordingly (see 4.2. Recommended Dose and Dosage Adjustment). Administer pre-treatment medications as indicated and monitor patients following administration of TECVAYLI accordingly (see 4.4. Administration).

Table 6: Recommendations for Restarting TECVAYLI after Dose Delay

Last Dose Administered	Duration of Delay from the Last Dose Administered	Action
Step-up Dose 1	7 days or less	Resume TECVAYLI step-up dosing schedule at Step-up Dose 2 (0.3 mg/kg).[a]
	More than 7 days	Restart TECVAYLI step-up dosing schedule at Step-up Dose 1 (0.06 mg/kg).[a]
Step-up Dose 2	7 days or less	Resume TECVAYLI step-up dosing schedule at Treatment Dose (1.5 mg/kg).[a]
	8 days to 28 days	Resume TECVAYLI step-up dosing schedule at Step-up Dose 2 (0.3 mg/kg).[a]
	More than 28 days	Restart TECVAYLI step-up dosing schedule at Step-up Dose 1 (0.06 mg/kg).[a]
Any Treatment Dose	28 days or less	Resume TECVAYLI at last Treatment Dose and schedule (1.5 mg/kg once weekly or 1.5 mg/kg every two weeks).
	More than 28 days	Restart TECVAYLI step-up dosing schedule at Step-up Dose 1 (0.06 mg/kg).[a]

[a] Administer pre-treatment medications prior to TECVAYLI dose and monitor accordingly (see 4.4 Administration).

5. Overdosage

The maximum tolerated dose of teclistamab has not been determined. In clinical trials, doses of up to 6 mg/kg have been administered.

In the event of an overdose, the patient should be monitored for any signs or symptoms of adverse effects and appropriate symptomatic treatment should be instituted immediately.

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

6. Dosage Forms, Strengths, Composition and Packaging

Table 7: Dosage Forms, Strengths, Composition and Packaging

Route of Administration	Dosage Form / Strength/Composition	Non-medicinal Ingredients
Subcutaneous injection	Solution for injection 10 mg/mL strength: each 3 mL solution for injection contains 30 mg of teclistamab (10 mg	EDTA disodium salt dihydrate Glacial acetic acid Polysorbate 20 Sodium acetate trihydrate Sucrose

	teclistamab per mL) 90 mg/mL strength: each 1.7 mL solution for injection contains 153 mg of teclistamab (90 mg of teclistamab per mL)	Water for injection

TECVAYLI is a clear to slightly opalescent, colourless to light yellow preservative-free solution for injection.

TECVAYLI is available in a 3 mL glass vial (10 mg teclistamab per mL) with a blue-coloured cap and a 1.7 mL glass vial (90 mg of teclistamab per mL) with an orange-coloured cap.

7. Warnings and Precautions

Please see 3. Serious Warnings and Precautions Box.

The data described in this section reflects the safety profile of 165 patients with relapsed or refractory multiple myeloma who received the recommended dose regimen of subcutaneous TECVAYLI monotherapy in MajesTEC-1, unless otherwise noted.

Driving and Operating Machinery

Due to the potential for ICANS, patients receiving TECVAYLI are at risk of a depressed level of consciousness. Patients should avoid driving or operating heavy or potentially dangerous machinery during and for 48 hours after completion of TECVAYLI step-up dosing schedule (Table 1) and in the event of new onset of any neurological symptoms (see 4. Dosage and Administration).

Hematologic

Hypogammaglobulinemia

Hypogammaglobulinemia has been reported in patients receiving TECVAYLI (see 8. Adverse Reactions).

Monitor immunoglobulin levels during treatment with TECVAYLI and treat according to local institutional guidelines, including infection precautions, antibiotic or antiviral prophylaxis, and administration of immunoglobulin replacement therapy.

Neutropenia

Neutropenia and febrile neutropenia have been reported in patients who received TECVAYLI (see 8. Adverse Reactions).

Monitor complete blood cell counts at baseline and periodically during treatment and provide supportive care per local institutional guidelines.

Patients with neutropenia should be monitored for signs of infection.

Withhold treatment with TECVAYLI based on severity as indicated in Table 2 (see- 4. Dosage and Administration – Dosage Adjustment).

Immune

Cytokine release syndrome

Cytokine release syndrome (CRS), including life-threatening or fatal reactions, can occur in patients receiving TECVAYLI. The majority of CRS events observed following TECVAYLI administration were Grade 1 and Grade 2 (see 8. Adverse Reactions). The median time to onset of CRS was 2 (range: 1 to 6) days after the most recent dose with a median duration of 2 (range: 1 to 9) days.

Clinical signs and symptoms of CRS may include, but are not limited to, fever, chills, hypotension, tachycardia, hypoxia, headache, and elevated liver enzymes. Potentially life-threatening complications of CRS may include cardiac dysfunction, adult respiratory distress syndrome, neurologic toxicity, renal and/or hepatic failure, and disseminated intravascular coagulation (DIC).

Initiate therapy according to TECVAYLI step-up dosing schedule to reduce risk of CRS (see Table 1). Failure to follow the recommended doses or dosing schedule for initiation of therapy or re-initiation of therapy after dose delays may result in increased frequency and severity of adverse events related to mechanism of action. Administer pre-treatment medications (corticosteroids, antihistamine, and antipyretics) prior to each dose of the TECVAYLI step-up dosing schedule to reduce the risk of CRS and monitor patients following administration accordingly (see 4. Dosage and Administration). In patients who experienced CRS following their previous dose, administer pre-treatment medications prior to the next dose of TECVAYLI.

In MajesTEC-1, tocilizumab, corticosteroids, and tocilizumab in combination with corticosteroids were used to treat 32%, 11% and 3% of CRS events, respectively. The use of myeloid growth factors, particularly granulocyte macrophage-colony stimulating factor (GM-CSF), should be avoided during CRS.

Identify CRS based on clinical presentation. Evaluate and treat other causes of fever, hypoxia, and hypotension. Counsel patients to seek medical attention should signs and symptoms of CRS occur. If CRS is suspected, immediately evaluate patients for hospitalization, administer supportive care (including but not limited to anti-pyretic agents, intravenous fluid support, vasopressors, supplemental oxygen, etc.) as appropriate, and treat CRS per institutional guidelines. Table 8 describes the CRS management in Study MajesTEC-1. Withhold TECVAYLI until CRS resolves (see Table 2). Consider laboratory testing to monitor for disseminated intravascular coagulation (DIC), hematology parameters, as well as pulmonary, cardiac, renal, and hepatic function.

Table 8: Recommendations for Management of Cytokine Release Syndrome

Grade[e]	Presenting Symptoms	Tocilizumab[a]	Corticosteroids[b]
Grade 1	Temperature ≥ 38°C (100.4°F)[c]	May be considered.	Not applicable.

Grade[e]	Presenting Symptoms	Tocilizumab[a]	Corticosteroids[b]
Grade 2	Temperature ≥ 38°C (100.4°F)[c] with either: Hypotension responsive to fluids and not requiring vasopressors. Or, oxygen requirement of low-flow nasal cannula[d] or blow-by.	Administer tocilizumab[b] 8 mg/kg intravenously over 1 hour (not to exceed 800 mg). Repeat tocilizumab every 8 hours as needed, if not responsive to intravenous fluids or increasing supplemental oxygen. Limit to a maximum of 3 doses in a 24-hour period; maximum total of 4 doses.	Manage per guidance below, if no improvement within 24 hours of starting tocilizumab.
Grade 3	Temperature ≥ 38°C (100.4°F)[c] with either: Hypotension requiring one vasopressor, with or without vasopressin. Or, oxygen requirement of high-flow nasal cannula[d], facemask, non-rebreather mask, or Venturi mask	Administer tocilizumab 8 mg/kg intravenously over 1 hour (not to exceed 800 mg). Repeat tocilizumab every 8 hours as needed if not responsive to intravenous fluids or increasing supplemental oxygen. Limit to a maximum of 3 doses in a 24-hour period; maximum total of 4 doses.	If no improvement, administer methylprednisolone 1 mg/kg intravenously twice daily or equivalent dexamethasone (e.g., 10 mg intravenously every 6 hours). Continue corticosteroids use until the event is Grade 1 or less, then taper over 3 days.
Grade 4	Temperature ≥ 38°C (100.4°F)[c] with either: Hypotension requiring multiple vasopressors (excluding vasopressin). Or, oxygen requirement of positive pressure (e.g., continuous positive airway pressure (CPAP), bilevel positive airway pressure (BiPAP), intubation, and mechanical ventilation)	Administer tocilizumab 8 mg/kg intravenously over 1 hour (not to exceed 800 mg). Repeat tocilizumab every 8 hours as needed if not responsive to intravenous fluids or increasing supplemental oxygen. Limit to a maximum of 3 doses in a 24-hour period; maximum total of 4 doses.	As above or administer methylprednisolone 1000 mg intravenously per day for 3 days, per physician discretion. If no improvement or if condition worsens, consider alternate immunosuppressants.[b]

Grade[e]	Presenting Symptoms	Tocilizumab[a]	Corticosteroids[b]

[a] The recommendations describe the CRS management in Study MajesTEC-1. Treat CRS per institutional guidelines.
[b] Treat unresponsive CRS per institutional guidelines.
[c] Attributed to CRS. Fever may not always be present concurrently with hypotension or hypoxia as it may be masked by interventions such as antipyretics or anticytokine therapy (e.g., tocilizumab or steroids).
[d] Low-flow nasal cannula is ≤6 L/min, and high-flow nasal cannula is >6 L/min.
[e] Based on American Society for Transplantation and Cellular Therapy (ASTCT) grading (Lee et al 2019).

Infections

Severe, life-threatening or fatal infections have been reported in patients receiving TECVAYLI (see 8. Adverse Reactions). New or reactivated viral infections and opportunistic infections occurred during therapy with TECVAYLI.

Monitor patients for signs and symptoms of infection prior to and during treatment with TECVAYLI and treat appropriately. Prophylactic antimicrobials should be administered according to local institutional guidelines.

Withhold treatment with TECVAYLI as indicated in Table 2 (see 4. Dosage and Administration).

Progressive Multifocal Leukoencephalopathy (PML), which can be fatal, has also been reported in patients receiving TECVAYLI (see 8. Adverse Reactions). Monitor any new onset of or changes in pre-existing neurological signs or symptoms. If PML is suspected, withhold treatment with TECVAYLI and initiate appropriate diagnostic testing. Discontinue TECVAYLI if PML is confirmed.

Hepatitis B Virus reactivation

Hepatitis B virus reactivation has been reported in patients treated with drugs directed against B-cells, and in some cases, may result in fulminant hepatitis, hepatic failure, and death.

Patients with evidence of positive HBV serology should be monitored for clinical and laboratory signs of HBV reactivation while receiving TECVAYLI, and for at least six months following the end of treatment.

In patients who develop reactivation of HBV while on TECVAYLI, withhold treatment with TECVAYLI as indicated in Table 2 and manage per local institutional guidelines (see 4. Dosage and Administration).

Vaccines

Immune response to vaccines may be reduced when taking TECVAYLI.

The safety of immunization with live viral vaccines during or following TECVAYLI treatment has not been studied. Vaccination with live virus vaccines is not recommended for at least 4 weeks prior to the start of treatment, during treatment, and at least 4 weeks after treatment.

Neurologic

Neurologic toxicities

Serious, life-threatening or fatal neurologic toxicities, including encephalopathy and Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS), can occur following treatment with TECVAYLI. One case of Guillain-Barré syndrome occurred in a patient treated with TECVAYLI. The majority of neurologic toxicity events were Grade 1 and Grade 2 (see 8. Adverse Reactions). The onset of ICANS can be concurrent with CRS, following resolution of CRS, or in the absence of CRS.

Monitor patients for signs or symptoms of neurologic toxicities during treatment and treat promptly. Counsel patients to seek medical attention should signs or symptoms of neurologic toxicity occur.

At the first sign of neurologic toxicity, including ICANS, immediately evaluate patient (e.g., consider neurology evaluation, and rule out other causes of neurologic symptoms) and institute treatment based on severity per institutional guidelines. Table 9 describes the ICANS management in Study MajesTEC-1. Provide intensive care and supportive therapy for severe or life-threatening neurologic toxicities. Withhold treatment with TECVAYLI as indicated in Table 2 (see 4. Dosage and Administration).

Table 9: Recommendations for Management of Immune Effector Cell-Associated Neurotoxicity Syndrome

<table>
<tr><th>Grade</th><th>Presenting Symptoms[a]</th><th>Concurrent CRS[b]</th><th>No Concurrent CRS</th></tr>
<tr><td rowspan="2">Grade 1</td><td rowspan="2">ICE score 7-9[c]

or depressed level of consciousness[d]: awakens spontaneously.</td><td>Management of CRS (see Table 8).

Monitor neurologic symptoms and consider neurology consultation and evaluation, per physician discretion.</td><td>Monitor neurologic symptoms and consider neurology consultation and evaluation, per physician discretion.</td></tr>
<tr><td colspan="2">Consider non-sedating, anti-seizure medicines (e.g., levetiracetam) for seizure prophylaxis.</td></tr>
<tr><td rowspan="2">Grade 2</td><td rowspan="2">ICE score 3-6[c]

or depressed level of consciousness[d]: awakens to voice.</td><td>Management of CRS (see Table 8).

If no improvement after starting tocilizumab, administer dexamethasone[e] 10 mg intravenously every 6 hours if not already taking other corticosteroids. Continue dexamethasone use until resolution to Grade 1 or less, then taper.</td><td>Administer dexamethasone[e] 10 mg intravenously every 6 hours.

Continue dexamethasone use until resolution to Grade 1 or less, then taper.</td></tr>
<tr><td colspan="2">Consider non-sedating, anti-seizure medicines (e.g., levetiracetam) for seizure prophylaxis. Consider neurology consultation and other specialists for further evaluation, as needed.</td></tr>
</table>

Grade	Presenting Symptoms[a]	Concurrent CRS[b]	No Concurrent CRS
Grade 3	ICE score 0-2[c] or depressed level of consciousness[d]: awakens only to tactile stimulus, or seizures[d], either: • any clinical seizure, focal or generalized, that resolves rapidly, or • non-convulsive seizures on electroencephalogram (EEG) that resolve with intervention, • or raised intracranial pressure: focal/local edema on neuroimaging[d].	Management of CRS (see Table 8). In addition, administer dexamethasone[e] 10 mg intravenously with the first dose of tocilizumab and repeat dose every 6 hours. Continue dexamethasone use until resolution to Grade 1 or less, then taper.	Administer dexamethasone[e] 10 mg intravenously every 6 hours. Continue dexamethasone use until resolution to Grade 1 or less, then taper.
		Consider non-sedating, anti-seizure medicines (e.g., levetiracetam) for seizure prophylaxis. Consider neurology consultation and other specialists for further evaluation, as needed.	

<table>
<tr><th>Grade</th><th>Presenting Symptoms[a]</th><th>Concurrent CRS[b]</th><th>No Concurrent CRS</th></tr>
<tr><td rowspan="2">Grade 4</td><td>ICE score-0[c]

or depressed level of consciousness[d] either:
• patient is unarousable or requires vigorous or repetitive tactile stimuli to arouse, or
• stupor or coma,

or seizures[d], either:
• life-threatening prolonged seizure (>5 minutes), or
• repetitive clinical or electrical seizures without return to baseline in between,

or motor findings[d]:
• deep focal motor weakness such as hemiparesis or paraparesis,

or raised intracranial pressure/cerebral edema[d], with signs/symptoms such as:
• diffuse cerebral edema on neuroimaging, or
• decerebrate or decorticate posturing, or
• cranial nerve VI palsy, or
• papilledema, or
• Cushing’s triad.</td><td>Management of CRS (see Table 8).

Administer dexamethasone[e] 10 mg intravenously with the first dose of tocilizumab and repeat dose every 6 hours. Continue dexamethasone use until resolution to Grade 1 or less, then taper.

Alternatively, consider administration of methylprednisolone 1000 mg per day intravenously with first dose of tocilizumab, and continue methylprednisolone 1000 mg per day intravenously for 2 or more days.</td><td>Administer dexamethasone[e] 10 mg and repeat dose every 6 hours. Continue dexamethasone use until resolution to Grade 1 or less, then taper.

Alternatively, consider administration of methylprednisolone 1000 mg per day intravenously for 3 days; if improves, then manage as above.</td></tr>
<tr><td colspan="2">Consider non-sedating, anti-seizure medicines (e.g., levetiracetam) for seizure prophylaxis. Consider neurology consultation and other specialists for further evaluation, as needed. In case of raised intracranial pressure/cerebral edema, refer to local institutional guidelines for management.</td></tr>
</table>

[a] Management is determined by the most severe event, not attributable to any other cause.

[b] The recommendations describe the ICANS management in Study MajesTEC-1. Treat ICANS per institutional guidelines.

[c] If patient is arousable and able to perform Immune Effector Cell-Associated Encephalopathy (ICE) Assessment, assess: **Orientation** (oriented to year, month, city, hospital = 4 points); **Naming** (name 3 objects, e.g., point to clock, pen, button = 3 points); **Following Commands** (e.g., “show me 2 fingers” or “close your eyes and stick out your tongue” = 1 point); **Writing** (ability to write a standard sentence = 1 point; and **Attention** (count backwards from 100 by ten = 1 point). If patient is unarousable and unable to perform ICE Assessment (Grade 4 ICANS) = 0 points.

[d] Attributable to no other cause.

[e] All references to dexamethasone administration are dexamethasone or equivalent

Reproductive Health

Fertility

There are no data on the effect of TECVAYLI on fertility. Effects of TECVAYLI on male and female fertility have not been evaluated in animal studies.

7.1. Special Populations

7.1.1. Pregnant Women

There are no available data on the use of TECVAYLI in pregnant women or animal data to assess the risk of TECVAYLI in pregnancy. Human IgG is known to cross the placenta after the first trimester of pregnancy. Therefore, teclistamab has the potential to be transmitted from the mother to the developing fetus. TECVAYLI is not recommended for women who are pregnant.

TECVAYLI is associated with hypogammaglobulinemia, therefore, assessment of immunoglobulin levels in newborns of mothers treated with TECVAYLI should be considered.

Contraception

Advise females of reproductive potential to use effective contraception during treatment and for five months after the final dose of TECVAYLI.

Advise male patients with a female partner of reproductive potential to use effective contraception during treatment and for three months after the last dose of TECVAYLI.

7.1.2. Breast-feeding

It is not known whether teclistamab is excreted in human or animal milk, affects breastfed infants, or affects milk production. Because of the potential for serious adverse reactions in breastfed infants from TECVAYLI, advise patients not to breastfeed during treatment with TECVAYLI and for at least five months after the last dose.

7.1.3. Pediatrics

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

Geriatrics (≥ 65 years of age): Of the 165 patients treated with TECVAYLI in MajesTEC-1 at the recommended dose, 48% were 65 years of age or older, and 15% were 75 years of age or older. No overall differences in safety or effectiveness were observed between these patients and younger patients. No dose adjustment is necessary.

8. Adverse Reactions

8.1. Adverse Reaction Overview

The safety data of TECVAYLI was evaluated in MajesTEC-1, which included 165 adult patients with relapsed or refractory multiple myeloma who received the recommended dose regimen of subcutaneous TECVAYLI as monotherapy. The median duration of TECVAYLI treatment was 8.5 (range: 0.2 to 24.4) months.

The most frequent adverse reactions of any grade (≥ 20%) in patients were hypogammaglobulinemia, cytokine release syndrome, neutropenia, anemia, musculoskeletal pain, fatigue, thrombocytopenia, injection site reaction, upper respiratory tract infection, lymphopenia, diarrhea, pneumonia, nausea, pyrexia, headache, cough, constipation, hypotension and pain.

Serious adverse reactions were reported in 65% patients who received TECVAYLI. Serious adverse reactions reported in ≥ 2% of patients included pneumonia (16%), COVID 19 (15%), cytokine release syndrome (8%), sepsis (7%), pyrexia (5%), musculoskeletal pain (5%), acute kidney injury (4.8%), diarrhea (3.0%), cellulitis (2.4%), hypoxia (2.4%), febrile neutropenia (2.4%), and encephalopathy (2.4%). Fatal adverse events were reported in 18 patients (10.9%), and the most commonly reported fatal adverse event was infection (15 patients [9.1%], including 12 patients [7.3%] with fatal COVID-19 infection).

Dose interruptions (dose delays and dose skips) of TECVAYLI due to adverse reactions occurred in 65% of patients. The most frequent adverse reactions (≥ 5%) leading to dose interruptions were neutropenia (26%), COVID-19 (12%), pneumonia (10%), cytokine release syndrome (8%), and pyrexia (7%).

Dose reduction of TECVAYLI due to adverse reaction occurred in one patient (0.6%) due to neutropenia.

Permanent discontinuation of TECVAYLI due to adverse reactions occurred in two patients (1.2%), both due to infections.

8.2. Clinical Trial Adverse Reactions

Clinical trials are conducted under very specific conditions. The adverse reaction rates observed in the clinical trials; therefore, 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 in identifying and approximating rates of adverse drug reactions in real-world use.

Table 10 lists adverse reactions reported in ≥5% of patients who received TECVAYLI in MajesTEC-1.

Table 10: Adverse Reactions (≥5%) in Patients with Multiple Myeloma Treated with TECVAYLI in MajesTEC-1

System Organ Class	Adverse Reaction	N=165	
		Incidence (%)	
		Any Grade	Grade 3 or 4
Blood and lymphatic system disorders	Neutropenia	117 (71%)	106 (64%)
	Anemia[1]	90 (55%)	61 (37%)
	Thrombocytopenia	66 (40%)	35 (21%)
	Lymphopenia	57 (35%)	54 (33%)
	Leukopenia	29 (18%)	12 (7%)
Cardiac disorders	Cardiac arrhythmias[2]	29 (18%)	4 (2.4%)
Gastrointestinal disorders	Diarrhoea	47 (28%)	6 (3.6%)
	Nausea	46 (28%)	1 (0.6%)
	Constipation	34 (21%)	0
	Vomiting	22 (13%)	1 (0.6%)
General disorders and administration site conditions	Pyrexia	130 (79%)	5 (3.0%)
	Fatigue[3]	67 (41%)	5 (3.0%)
	Injection site reaction[4]	62 (38%)	1 (0.6%)
	Pain[5]	34 (21%)	3 (1.8%)
	Chills	30 (18%)	0
	Edema[6]	23 (14%)	0
Immune system disorders	Hypogammaglobulinaemia[7]	123 (75%)	3 (1.8%)
	Cytokine release syndrome^	119 (72%)	1 (0.6%)
Infections and infestations	Upper respiratory tract infection[8]	61 (37%)	4 (2.4%)
	Pneumonia[9]*	46 (28%)	32 (19%)
	COVID-19[10]*	30 (18%)	20 (12%)
	Sepsis[11]	13 (8%)	11 (7%)
Metabolism and nutrition disorders	Decreased appetite	20 (12%)	1 (0.6%)
Musculoskeletal and connective tissue disorders	Musculoskeletal pain[12]	86 (52%)	14 (8%)

Nervous system disorders	Headache	44 (27%)	1 (0.6%)
	Motor dysfunction[13]	31 (19%)	0
	Neuropathy peripheral[14]	26 (16%)	1 (0.6%)
	Encephalopathy[15]	17 (10%)	0
Renal and urinary disorders	Acute kidney injury[16]	18 (11%)	6 (3.6%)
Respiratory, thoracic and mediastinal disorders	Cough[17]	39 (24%)	0
	Hypoxia	33 (20%)	6 (3.6%)
	Dyspnea[18]	22 (13%)	3 (1.8%)
Vascular disorders	Hypotension	34 (21%)	4 (2.4%)
	Hypertension[19]	22 (13%)	9 (5%)
	Hemorrhage[20]*	20 (12%)	5 (3.0%)

CRS = cytokine release syndrome.
CRS was graded by ASTCT consensus grading system (Lee et al 2019).
Adverse events are coded using MedDRA Version 24.0.

* Includes fatal events

^ CRS-related symptoms reported in MajesTEC-1 include pyrexia, hypoxia, chills, hypertension, sinus tachycardia, headache, nausea, myalgia, fatigue, back pain, hypotension, vomiting.

1 Anemia includes Anaemia, Iron deficiency and Iron deficiency Anaemia.

2 Cardiac arrhythmias includes Atrial flutter, Cardiac arrest, Sinus bradycardia, Sinus tachycardia, Supraventricular tachycardia and Tachycardia.

3 Fatigue includes Asthenia, Fatigue and Malaise.

4 Injection site reaction includes Injection site bruising, Injection site cellulitis, Injection site discomfort, Injection site erythema, Injection site haematoma, Injection site induration, Injection site inflammation, Injection site oedema, Injection site pruritus, Injection site rash, Injection site reaction and Injection site swelling.

5 Pain includes Ear pain, Flank pain, Groin pain, Non-cardiac chest pain, Oropharyngeal pain, Pain, Pain in jaw, Toothache and Tumour pain.

6 Edema includes Face oedema, Fluid overload, Oedema peripheral and Peripheral swelling.

7 Hypogammaglobulinaemia includes patients with adverse events of hypogammaglobulinaemia, hypoglobulinaemia, immunoglobulins decreased; and/or patients with laboratory IgG levels below 500 mg/dL following treatment with Teclistamab.

8 Upper respiratory tract infection includes Bronchitis, Nasopharyngitis, Pharyngitis, Respiratory tract infection, Respiratory tract infection bacterial, Rhinitis, Rhinovirus infection, Sinusitis, Tracheitis, Upper respiratory tract infection and Viral upper respiratory tract infection.

9 Pneumonia includes Enterobacter pneumonia, Lower respiratory tract infection, Lower respiratory tract infection viral, Metapneumovirus pneumonia, Pneumocystis jirovecii pneumonia, Pneumonia, Pneumonia adenoviral, Pneumonia bacterial, Pneumonia klebsiella, Pneumonia moraxella, Pneumonia pneumococcal, Pneumonia pseudomonal, Pneumonia respiratory syncytial viral, Pneumonia staphylococcal and Pneumonia viral.

10 COVID-19 includes Asymptomatic COVID-19 and COVID-19.

11 Sepsis includes Bacteraemia, Meningococcal sepsis, Neutropenic sepsis, Pseudomonal bacteraemia, Pseudomonal sepsis, Sepsis and Staphylococcal bacteraemia.

12 Musculoskeletal pain includes Arthralgia, Back pain, Bone pain, Musculoskeletal chest pain, Musculoskeletal pain, Myalgia, Neck pain and Pain in extremity.

13 Motor dysfunction includes Cogwheel rigidity, Dysgraphia, Dysphonia, Gait disturbance, Hypokinesia, Muscle rigidity, Muscle spasms, Muscular weakness, Peroneal nerve palsy, Psychomotor hyperactivity, Tremor and VIth nerve paralysis.

14 Neuropathy peripheral includes Dysaesthesia, Hypoaesthesia, Hypoaesthesia oral, Neuralgia, Paraesthesia, Paraesthesia oral, Peripheral sensory neuropathy and Sciatica.

15 Encephalopathy includes Confusional state, Depressed level of consciousness, Lethargy, Memory impairment and Somnolence.

16 Acute kidney injury includes Acute kidney injury and Renal impairment.

[17] Cough includes Allergic cough, Cough, Productive cough and Upper-airway cough syndrome.
[18] Dyspnea includes Acute respiratory failure, Dyspnoea and Dyspnoea exertional
[19] Hypertension includes Essential hypertension and Hypertension.
[20] Hemorrhage includes Conjunctival haemorrhage, Epistaxis, Haematoma, Haematuria, Haemoperitoneum, Haemorrhoidal haemorrhage, Lower gastrointestinal haemorrhage, Melaena, Mouth haemorrhage and Subdural haematoma.

Description of Selected Adverse Reactions

Cytokine Release Syndrome

In MajesTEC-1 (N=165), CRS was reported in 72% of patients following treatment with TECVAYLI. One-third (33%) of patients experienced more than one CRS event. Most patients experienced CRS following Step-up Dose 1 (44%), Step-up Dose 2 (35%), or the initial treatment dose (24%). Less than 3% of patients developed first occurrence of CRS following subsequent doses of TECVAYLI. Most CRS events were Grade 1 (50%) and Grade 2 (21%). Less than one percent (0.6%) of CRS events were Grade 3, and no Grade 4 or fatal events occurred.

The most frequent (≥ 3%) signs and symptoms associated with CRS were fever (72%), hypoxia (13%), chills (12%), hypotension (12%), sinus tachycardia (7%), headache (7%), and elevated liver enzymes (aspartate aminotransferase and alanine aminotransferase elevation) (3.6% each).

Neurologic Toxicities

In MajesTEC-1 (N=165), neurologic toxicities were reported in 15% of patients receiving TECVAYLI (Grade 1 [8.5%], Grade 2 [5.5%] and Grade 4 [0.6%]). The most frequently reported neurologic toxicity was headache (8.5%). One case of Guillain-Barré syndrome occurred in a patient treated with TECVAYLI.

ICANS was reported in 3% of patients receiving TECVAYLI at the recommended dose. The most frequent clinical manifestations of ICANS reported were confusional state (1.2%) and dysgraphia (1.2%).

Longer-term Follow-up

In MajesTEC-1 (N=165), based on an updated safety analysis with a median follow-up of 30.4 months (median treatment duration of 9.3 months) additional adverse reactions occurring in ≥10% of patients were: abdominal pain (Any Grade: 12%, Grade 3 or 4: 1.2%), urinary tract infection (Any Grade: 14%, Grade 3 or 4: 6%), and hypoglycemia (Any Grade: 23%, Grade 3 or 4: 0%). Grade 5 treatment-emergent adverse events were reported in 7 additional patients (including COVID-19 in 6 patients and 1 patient each for Guillain Barré syndrome and influenza). Six additional patients discontinued study treatment due to adverse events (including 2 patients with COVID-19, and 1 patient each: sepsis, arthralgia, arthritis, and brain neoplasm).

8.3. Less Common Clinical Trial Adverse Reactions

Clinically relevant adverse reactions reported in less than 5% of patients who received TECVAYLI in MajesTEC-1 are summarized below:

Blood and lymphatic system disorders: Febrile neutropenia (3.6%)

Infections and infestations: Cellulitis (4.2%), herpes simplex (2.4%), herpes zoster (1.2%), hepatitis B reactivation (0.6%), adenovirus reactivation (0.6%), BK virus infection (0.6%), cytomegalovirus infection reactivation (0.6%), progressive multifocal leukoencephalopathy (0.6%)

Nervous system disorders: Immune effector cell-associated neurotoxicity syndrome (3%)

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

Clinical Trial Findings

Table 11 lists laboratory abnormalities that worsened from baseline in patients who received TECVAYLI in MajesTEC-1.

Table 11: Laboratory Abnormalities Worsening from Baseline in at least 20% of Patients with Multiple Myeloma Treated with TECVAYLI in MajesTEC-1

	N=165	
	n (%)	
Laboratory Abnormality	**Any Grade**	**Grade 3 or 4**
Lymphocyte count decreased	151 (92%)	137 (83%)
White blood cell decreased	147 (89%)	72 (44%)
Neutrophil count decreased	143 (87%)	104 (63%)
Platelet count decreased	120 (73%)	38 (23%)
Hypoalbuminemia	118 (72%)	10 (6%)
Anemia	117 (71%)	61 (37%)
Alkaline phosphatase increased	71 (43%)	5 (3.0%)
Hypophosphatemia	71 (43%)	24 (15%)
Aspartate aminotransferase increased	67 (41%)	5 (3.0%)
Gamma-glutamyltransferase increased	63 (38%)	15 (9%)
Hyponatremia	59 (36%)	20 (12%)
Alanine aminotransferase increased	57 (35%)	7 (4.2%)
Hypocalcemia (Corrected)	57 (35%)	3 (1.8%)
Creatinine increased	56 (34%)	5 (3.0%)
Hypokalemia	51 (31%)	8 (4.8%)
Hypomagnesemia	47 (28%)	0
Hypercalcemia (Corrected)	46 (28%)	7 (4.2%)
Lipase increased	42 (25%)	9 (5%)
Serum amylase increased	39 (24%)	7 (4.2%)
Hyperkalemia	33 (20%)	3 (1.8%)

Laboratory toxicity grades are derived based on the NCI CTCAE (National Cancer Institute Common Terminology Criteria for Adverse Events) Version 4.03.

8.5. Post-Market Adverse Reactions

The following adverse reactions have been reported during post-marketing experience. As limited relevant information is available from voluntary reporting, meaningful estimates of frequency and a robust data review and analysis is not always possible.

Nervous system disorders: Immune effector cell-associated neurotoxicity syndrome (includes events with fatal outcome) (see 7. Warnings and Precautions)

9. Drug Interactions

9.2. Drug Interactions Overview

No drug interaction studies have been performed with TECVAYLI.

9.4. Drug-Drug Interactions

The initial release of cytokines associated with the start of TECVAYLI treatment could suppress CYP450 enzymes. Based on physiologically based pharmacokinetic (PBPK) modelling, the highest risk of drug-drug interaction is predicted to be from initiation of TECVAYLI step-up dosing schedule up to 7 days after the first Treatment Dose or during a CRS event. During this time period, monitor for toxicity or drug concentrations (e.g., cyclosporine) in patients who are receiving concomitant CYP450 substrates with a narrow therapeutic index. The dose of the concomitant drug should be adjusted as needed.

9.5. Drug-Food Interactions

Interactions with food have not been established.

9.6. Drug-Herb Interactions

Interactions with herbal products have not been established.

9.7. Drug-Laboratory Test Interactions

Interactions with laboratory tests have not been established.

10. Clinical Pharmacology

10.1. Mechanism of Action

Teclistamab is a full-size, IgG4-PAA bispecific antibody that targets the CD3 receptor expressed on the surface of T-cells and B-cell maturation antigen (BCMA) expressed on the surface of malignant multiple myeloma and healthy B-lineage cells and plasma cells. With its dual binding sites, teclistamab is able to draw CD3+ T-cells in close proximity to BCMA+ cells, resulting in T-cell activation and subsequent lysis and death of BCMA+ cells, which is mediated by secreted perforin and various granzymes stored in the secretory vesicles of cytotoxic T-cells. This effect occurs without regard to T-cell receptor specificity or reliance on major histocompatibility complex (MHC) Class 1 molecules on the surface of antigen presenting cells.

10.2. Pharmacodynamics

Within the first month of treatment with teclistamab, activation and redistribution of T-cells, reduction of B-cells and induction of serum cytokines were observed.

T-cell redistribution was demonstrated by reduction in peripheral CD4+ and CD8+ T-cells after the initial doses (step up and first full treatment dose) of teclistamab, followed by T-cell recovery beginning by C1D15. Reduction of CD19+ B-cells was observed in patients treated at pivotal recommended Phase II dose (RP2D) within the first cycle (beginning after the initial step-up doses) with persistent decreased levels observed at Cycle 3. Non-myeloma IgG had an initial decrease followed by a slight and gradual increase over time, which likely reflects increased use of IVIG during treatment. Induction of IL-10, IFN-g, TNF-α or IL-6 was observed following teclistamab administration. There was heterogeneity in the kinetics of cytokine increase, with considerable variability between patients when maximum induction occurred.

10.3. Pharmacokinetics

Teclistamab exhibited approximately dose-proportional pharmacokinetics following subcutaneous administration across a dose range of 0.08 mg/kg to 3 mg/kg (0.05 to 2.0 times the recommended dose). Ninety percent of steady state exposure was achieved after 12 weekly treatment doses. The mean accumulation ratio between the first and 13th weekly maintenance dose of teclistamab 1.5 mg/kg was 4.2-fold for C_{max}, 4.1-fold for C_{trough}, and 5.3-fold for AUC_{tau}. The C_{max}, C_{trough}, and AUC_{tau} of teclistamab are presented in Table 12.

Table 12: Pharmacokinetic Parameters of Teclistamab for the 13th Recommended Weekly Treatment Dose (1.5 mg/kg) in Patients with Relapsed or Refractory Multiple Myeloma (MajesTEC-1)

Pharmacokinetic Parameters	Teclistamab Geometric Mean (CV%)
C_{max} (µg/mL)	23.8 (55%)
C_{trough} (µg/mL)	21.1 (63%)
AUC_{tau} (µg·h/mL)	3 838 (57%)

C_{max} = Maximum serum teclistamab concentration; C_{trough} = Serum teclistamab concentration prior to next dose; CV = geometric coefficient of variation; AUC_{tau} = Area under the concentration-time curve over the weekly dosing interval.

Absorption

The mean bioavailability of teclistamab was 72% when administered subcutaneously. The median (range) T_{max} of teclistamab after the first and 13th weekly maintenance doses were 139 (19 to 168) hours and 72 (24 to 168) hours, respectively.

Distribution

The mean volume of distribution was 5.63 L (29% coefficient of variation [CV]).

Elimination

Teclistamab clearance decreases over time, with a mean (CV%) maximal reduction from

baseline to the 13th weekly treatment dose of 40.8% (56%). The geometric mean (CV%) clearance is 0.472 L/day (64%) at the 13th weekly treatment dose. Patients who discontinue teclistamab after the 13th weekly treatment dose are expected to have a 50% reduction from C_{max} in teclistamab concentration at a median (5th to 95th percentile) time of 15 (7 to 33) days after T_{max} and a 97% reduction from C_{max} in teclistamab concentration at a median time of 69 (32 to 163) days after T_{max}.

Population pharmacokinetic analysis (based on MajesTEC-1) showed that soluble BCMA did not impact teclistamab serum concentrations.

Special Populations and Conditions

- **Pediatrics:** The pharmacokinetics of teclistamab in pediatric patients have not been investigated.
- **Geriatrics:** Results of population pharmacokinetic analyses indicate that age (24 to 84 years) did not significantly influence the pharmacokinetics of teclistamab.
- **Sex:** Results of population pharmacokinetic analyses indicate that sex did not influence the pharmacokinetics of teclistamab.
- **Hepatic Insufficiency:** No formal studies of TECVAYLI in patients with hepatic impairment have been conducted.

  Results of population pharmacokinetic analyses indicate that mild hepatic impairment (total bilirubin less than or equal to upper limit of normal [ULN] with AST greater than ULN or total bilirubin greater than 1 to 1.5 times ULN with any AST) did not significantly influence the pharmacokinetics of teclistamab. No data are available in patients with moderate and severe hepatic impairment.
- **Renal Insufficiency:** No formal studies of TECVAYLI in patients with renal impairment have been conducted.

  Results of population pharmacokinetic analyses indicate that mild or moderate renal impairment (estimated glomerular filtration rate [eGFR] by Modification of Diet in Renal Disease [MDRD] method: 30 to 89 mL/min) did not significantly influence the pharmacokinetics of teclistamab. Limited data are available from patients with severe renal impairment.

10.4. Immunogenicity

All therapeutic proteins have the potential for immunogenicity.

The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody (including neutralizing antibody) positivity in an assay may be influenced by several factors including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of incidence of antibodies in the studies described below with the incidences of antibodies in other studies or to other products may be misleading.

Patients treated with subcutaneous teclistamab monotherapy (N=238) in MajesTEC-1 were evaluated for antibodies to teclistamab using an electrochemiluminescence-based immunoassay. One patient (0.4%) developed antibodies to teclistamab of low-titer which were neutralizing.

11. Storage, Stability and Disposal

Store refrigerated at 2°C to 8°C. Do not freeze.

Store in the original carton in order to protect from light.

Keep out of the sight and reach of children.

12. Special Handling Instructions

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

Part 2: Scientific Information

13. Pharmaceutical Information

Drug Substance

Non-proprietary name of the drug substance: teclistamab

Molecular formula and molecular mass: approximately 146 kDa

Structure: TECVAYLI (teclistamab) is a humanized immunoglobulin G4-proline, alanine, alanine (IgG4-PAA) bispecific antibody targeting the B cell maturation antigen (BCMA) and CD3 receptors.

Physicochemical properties: TECVAYLI is a clear to slightly opalescent, colourless to light yellow preservative-free solution for injection.

Product Characteristics:

TECVAYLI is produced in a mammalian cell line (Chinese Hamster Ovary [CHO]) using recombinant DNA technology.

14. Clinical Trials

14.1. Clinical Trials by Indication

Multiple Myeloma after Three or More Prior Lines of Therapy

Table 13: Summary of patient demographics for clinical trials in adult patients with relapsed or refractory multiple myeloma who have received at least three prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent and an anti-CD38 monoclonal antibody.

Study # Trial design	Dosage, route of administration and duration	Study subjects (n)	Median age (range)	Sex
Study MMY1001 (MajesTEC-1) Phase 1/2, open-label, multicenter study to evaluate the safety and efficacy of teclistamab in adult patients with relapsed or refractory multiple myeloma, including those who have received at least three prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent and an anti-CD38 monoclonal antibody	Initial step-up doses of 0.06 mg/kg and 0.3 mg/kg of TECVAYLI administered subcutaneously followed by the treatment dose of 1.5 mg/kg administered subcutaneously once weekly until disease progression or unacceptable toxicity Patients who had a complete response or better for a minimum of 6 months were eligible to reduce dosing frequency to once every two weeks	Efficacy population treated at the pivotal dose in Phase 2 (n = 110)	66.0 years (range: 33-82 years)	56% male, 44% female

See Table 13 for a summary of study design and dosing.

MajesTEC-1 is a single-arm, open-label, multicenter, study that included patients with relapsed or refractory multiple myeloma. The study included patients who had received at least three prior therapies, including a proteasome inhibitor (PI), an immunomodulatory agent (IMiD) and an anti-CD38 monoclonal antibody. The study excluded patients who had stroke, seizure, allogeneic stem cell transplant within the past 6 months, Eastern Cooperative Oncology Group (ECOG) performance status score 2 or higher, known central nervous system (CNS) involvement or clinical signs of meningeal involvement of multiple myeloma, and active or documented history of autoimmune disease (with the exception of vitiligo, Type 1 diabetes and prior autoimmune thyroiditis).

Patients received initial step-up doses of 0.06 mg/kg and 0.3 mg/kg of TECVAYLI administered subcutaneously, followed by the treatment dose of 1.5 mg/kg administered subcutaneously once weekly thereafter until disease progression or unacceptable toxicity (see 4.2. Recommended Dose and Dosage Adjustment).

Patients who had a complete response (CR) or better for a minimum of 6 months were eligible to reduce dosing frequency to 1.5 mg/kg subcutaneously every two weeks until disease progression or unacceptable toxicity (see 4.2. Recommended Dose and Dosage Adjustment).

The median duration between Step-up Dose 1 and Step-up Dose 2 was 2.9 (range: 2-7) days. The median duration between Step-up Dose 2 and the initial treatment dose was 3.9 (range: 2-9) days. Patients were hospitalized for monitoring for at least 48 hours after administration of each dose of the TECVAYLI step-up dosing schedule.

The efficacy population treated at the pivotal dose in Phase 2 included 110 patients. The median age was 66.0 (range: 33-82) years with: 16% of patients ≥ 75 years of age; 56% were male; 91% were White; 5% were Black; and 3% were Asian. The International Staging System (ISS) at study entry was 51% in Stage I, 38% in Stage II, and 12% in Stage III. High-risk cytogenetics (presence of del(17p). t(4;14) or t(14; 16)) were present in 25% of patients. Seventeen percent of patients had extramedullary plasmacytomas.

The median time since initial diagnosis of multiple myeloma to enrollment was 6.4 (range: 1.1-22.7) years. The median number of prior therapies was 5 (range: 2-14) with 20% of patients who received 3 prior lines of therapy. Eighty-one percent of patients received prior stem cell transplantation. All patients had received prior therapy with a proteasome inhibitor, an immunomodulatory agent and an anti-CD38 monoclonal antibody, and 76% were triple-class refractory (refractory to a PI, an IMiD and an anti-CD38 monoclonal antibody). Nine-two percent of patients were refractory to the last prior line of myeloma therapy.

Study Results

Efficacy results were based on overall response rate as determined by the Independent Review Committee (IRC) assessment using International Myeloma Working Group (IMWG) 2016 criteria (see Table 14).

Table 14: Efficacy results of study MajesTEC-1 in adult patients with relapsed or refractory multiple myeloma who have received at least three prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent and an anti-CD38 monoclonal antibody.

	N=110[a]
Overall response rate (ORR: sCR+CR+VGPR+PR) n(%)	68 (61.8%)
95% CI (%)	(52.1%, 70.9%)
Stringent complete response (sCR)	25 (22.7%)
Complete response (CR)	6 (5.5%)
Very good partial response (VGPR)	32 (29.1%)
Partial response (PR)	5 (4.5%)

Number of responders	68
Duration of Response (Months): Median (95% CI)	NE (9.0, NE)

CI = confidence interval; NE = not estimable

[a] Efficacy population treated at the pivotal dose in Phase 2 with had a median duration of follow-up at the primary analysis: 8.8 months.

The median time to first response was 1.2 months (range 0.2 - 5.5 months) for responders treated at the pivotal dose in Phase 2 of the MajesTEC-1 study (N=68).

After a median follow-up of 29.5 months, the ORR was 62.4% (95% CI: 53.3%, 70.9%) for patients treated at the recommended dose in Phase 2 of MajesTEC-1 (N=125) with 36.8% of patients achieving sCR, 7.2% of patients achieving CR, 14.4% of patients achieving VGPR and 4.0% of patients achieving a PR. The median duration of response was 21.6 months (95% CI: 14.9 months, NE) for responders (N=78). Forty-three of the 78 responders (55.1%) switched from weekly to Q2W dosing during the study.

15. Microbiology

No microbiological information is required for this drug product.

16. Non-Clinical Toxicology

Carcinogenicity: No carcinogenicity studies have been performed to assess the carcinogenic potential of teclistamab.

Genotoxicity: No genotoxicity studies have been performed to assess the genotoxic potential of teclistamab.

Reproductive and Developmental Toxicology: No reproductive and developmental toxicity animal studies have been conducted to evaluate the potential effects of teclistamab.

No studies have been conducted to evaluate the effects of teclistamab on fertility in males or females. In the 5-week repeat-dose toxicity study in cynomolgus monkeys, there were no notable effects in the male and female reproductive organs at doses up to 30 mg/kg/week (approximately 22 times the maximum recommended human dose based on AUC exposure) intravenously for five weeks.

Patient Medication Information

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

PrTECVAYLI®

(teclistamab injection)

This Patient Medication Information is written for the person who will be taking **TECVAYLI** (Tek vay' lee). This may be you or a person you are caring for. Read this information carefully. Keep it as you may need to read it again.

This Patient Medication Information is a summary. It will not tell you everything about this medication. If you have more questions about this medication or want more information about **TECVAYLI**, talk to a healthcare professional.

Serious warnings and precautions box

- Fever and chills which may be symptoms of a serious side effect called cytokine release syndrome (CRS), which can be severe or fatal. Other symptoms of CRS may include difficulty in breathing, dizziness or feeling light-headed, feeling the need to throw up, headache, fast heartbeat, low blood pressure, feeling tired, vomiting, muscle pain and joint pain.

- Neurologic problems which may include symptoms like headache, confusion, difficulty with memory, difficulty speaking or slow speech, difficulty understanding speech, difficulty in writing, confused about time or surroundings, being less alert, or excessive sleepiness, and seizures (fits) which can be serious, life-threatening, or fatal. Some of these may be signs of a serious immune reaction called 'immune effector cell associated neurotoxicity syndrome' (ICANS). These effects can occur days or weeks after you receive the injection, and may initially be subtle.

- Your healthcare professional will monitor for signs and symptoms of CRS and neurological problems during treatment with TECVAYLI. You should call your healthcare professional right away if you develop any of the signs and symptoms of CRS or neurologic problems at any time during your treatment with TECVAYLI.

What is TECVAYLI used for:

TECVAYLI is used to treat patients with a type of cancer of the bone marrow called multiple myeloma. It is given when your cancer has not responded to or has come back after at least three different treatments, and your cancer is not responding to your most recent therapy.

TECVAYLI is given alone to treat multiple myeloma.

For the following indication TECVAYLI 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.

- The treatment of adult patients with relapsed or refractory multiple myeloma who have received at least three prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent and an anti-CD38 monoclonal antibody, and who have demonstrated disease progression on the last therapy.

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

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 TECVAYLI work:

TECVAYLI is a cancer medicine that contains the active substance 'teclistamab'.

TECVAYLI is an antibody, which is a type of protein. It has been designed to recognize and attach to specific targets in your body. TECVAYLI targets the following proteins found on cells in the blood:

- BCMA (B-cell maturation antigen), found on cancer cells, and on some healthy cells.
- CD3 (cluster of differentiation 3), found in your immune system.

TECVAYLI works by attaching to these proteins so that your immune system can destroy the multiple myeloma cancer cells.

The ingredients in TECVAYLI are:

Medicinal ingredient: teclistamab

Non-medicinal ingredients: EDTA disodium salt dihydrate, glacial acetic acid, polysorbate 20, sodium acetate trihydrate, sucrose and water for injection

TECVAYLI comes in the following dosage forms:

TECVAYLI comes in two different strengths:

- teclistamab 30 mg/3 mL (10 mg/mL).
- teclistamab 153 mg/1.7 mL (90 mg/mL).

TECVAYLI is a solution for injection and is a clear to slightly opalescent, colourless to light yellow liquid. TECVAYLI is supplied as a carton pack containing 1 glass vial.

Do not use TECVAYLI if:

You are allergic to TECVAYLI or any of the other ingredients of this medicine (listed in "The ingredients in TECVAYLI are:"). If you think you may be allergic, ask your doctor for advice.

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

- have an infection, or have ever had or might now have a hepatitis B infection. This is because TECVAYLI could cause hepatitis B virus to become active again. Your healthcare professional will check you for signs of this infection before, during and for some time after treatment with TECVAYLI. Tell your healthcare professional if you get worsening tiredness, or yellowing of your skin or white part of your eyes.
- have had a stroke or seizure, or any other types of neurological problems within the past 6 months.
- notice any new or worsening symptoms of Progressive Multifocal Leukoencephalopathy (PML). PML is a serious and potentially fatal brain infection. Symptoms may include, but are not limited to, blurred, loss of or double vision, difficulty speaking, weakness in an arm or a leg, a change in the way you walk or problems with your balance, persistent numbness, decreased sensation or loss of sensation, memory loss or confusion.
- have had a recent vaccination or are going to have a vaccination.
- are pregnant, think you might be pregnant or are planning a baby. If you could become pregnant, you must use effective contraception during and for 5 months after stopping treatment with TECVAYLI. If your partner could become pregnant, you must use effective contraception during and for 3 months after stopping treatment with TECVAYLI. If you or your partner become pregnant while being treated with this medicine, tell your healthcare professional right away.
- are producing breastmilk. You and your doctor will decide if the benefit of breastfeeding is greater than the risk to your baby. If you and your doctor decide to stop taking this medicine, you should not breastfeed for 5 months after stopping treatment.

Other warnings you should know about:

Do not receive live vaccines:

- four weeks before beginning treatment with TECVAYLI.
- during treatment with TECVAYLI.
- four weeks after your final dose of TECVAYLI.

Driving and using machines:

- Some people may feel tired, dizzy, or confused while taking TECVAYLI. Do not drive, use tools, or operate heavy machinery. Also, do not do things that could pose a danger to yourself or others.
- Wait until at least 48 hours after receiving your third dose of TECVAYLI or as instructed by your doctor.

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

Interactions with other drugs, vitamins, minerals, natural supplements or alternative medicines have not been established with TECVAYLI.

How to take TECVAYLI:

TECVAYLI will be given to you by your healthcare professional. It will be given as an injection under the skin (subcutaneous injection) in your stomach area or thigh.

Before you have TECVAYLI your healthcare professional will check:

- Your blood counts.
- For signs of infection - an infection will be treated before you have TECVAYLI.
- If you are pregnant or breastfeeding.

Before each of your first three injections of TECVAYLI, you will be given medicines to help lower the chance of side effects. These may include:

- Medicines for an allergic reaction (antihistamines).
- Medicines for inflammation (corticosteroids).
- Medicines for fever (such as acetaminophen/paracetamol).

You may be given these medicines for later doses of TECVAYLI based on any symptoms you have. You may be given additional medicines based on any symptoms you experience or your medical history.

Your healthcare professional will provide you with a Patient Card containing important safety information for patients receiving treatment with TECVAYLI.

Usual dose:

Your healthcare professional will determine your dose of TECVAYLI. The dose of TECVAYLI will depend on your body weight. The recommended dose of TECVAYLI is:

- First dose is 0.06 mg for each kilogram of body weight.
- Second dose is 0.3 mg for each kilogram of body weight.
- Treatment dose is 1.5 mg for each kilogram of body weight.

TECVAYLI is given as follows:

- You will receive your first dose of TECVAYLI to begin treatment.
- You will receive your second dose 2-4 days later.
- You will then start a 'Treatment dose' 2-4 days after your second dose.
- You will continue receiving a 'Treatment dose' once a week for as long as you are getting benefit from TECVAYLI.

If you are continuing to receive benefit from TECVAYLI after 6 months, your healthcare professional may decide that you will receive a 'Treatment dose' every two weeks.

After you have TECVAYLI your healthcare professional will monitor you for side effects and regularly check your blood counts as the number of blood cells and other blood components may decrease.

After each of your first three doses, your healthcare professional will closely monitor you for side effects for 2 days after each dose. You should plan to stay near a healthcare facility after each of the first three doses in case you have side effects. It is also possible that your healthcare professional decides to hospitalize you after each of the first three doses. Your healthcare professional will tell you if you will need to be monitored after other doses.

Overdose:

This medicine will be given by your healthcare professional. In the unlikely event that you are given too much (an overdose) your doctor will check you for side effects.

If you think you, or a person you are caring for, have taken too much TECVAYLI, contact a healthcare professional, hospital emergency department, or regional poison control centre or Health Canada's toll-free number, 1-844 POISON-X (1-844-764-7669) immediately, even if there are no symptoms.

Missed Dose:

It is very important to go to all your appointments. If you miss an appointment, tell your doctor and make another appointment as soon as possible.

Possible side effects from using TECVAYLI:

Like all medicines, this medicine can cause side effects, although not everybody gets them. These are not all the possible side effects you may have when taking TECVAYLI. If you experience any side effects not listed here, tell your healthcare professional.

Very Common (may affect more than 1 in 10 people):

- Infected nose, sinuses or throat (upper respiratory tract infection)
- Unrinary tract infection
- Low levels of red blood cells (anemia)
- Low levels of 'platelets' (cells that help blood to clot)
- Low number of white blood cells (leukopenia)
- Low levels of a type of white blood cells (lymphopenia)
- Low level of antibodies called 'immunoglobulins' in the blood, which may make infections more likely (hypogammaglobulinemia)
- Low level of 'phosphate', 'magnesium' or 'potassium' in the blood (hypophosphatemia, hypomagnesemia or hypokalemia)
- Increased level of 'calcium' in the blood (hypercalcemia)
- Increased 'alkaline phosphatase' in the blood
- Decreased appetite
- Nausea, diarrhea, constipation, vomiting or abdominal pain
- Headache
- Nerve damage that may cause tingling, numbness, pain or loss of pain sensation
- Muscle spasms
- High blood pressure (hypertension)
- Bleeding, which can be severe (hemorrhage)
- Low blood pressure (hypotension)
- Cough
- Being short of breath (dyspnea)
- Fever
- Feeling very tired
- Pain or muscle aches
- Swollen hands, ankles or feet (edema)
- Skin reactions at or near the injection site, including redness of the skin, itching, swelling, pain, bruising, rash, bleeding
- Increased level of 'gamma-glutamyltransferase' in the blood

Common (may affect up to 1 in 10 people)

- Infections caused by herpes viruses including shingles or cold sores
- Low level of 'calcium' or 'sodium'in the blood (hypocalcemia or hyponatremia)
- High level of 'potassium' in the blood (hyperkalemia)
- Low level of 'albumin' in the blood (hypoalbuminemia)
- Low level of 'sugar' in the blood (hypoglycemia)
- Increased level of liver enzymes 'transaminases' in the blood
- Increased level of 'creatinine' in the blood and decreased kidney function
- Increased level of 'amylase' in the blood
- Increased level of 'lipase' in the blood

Uncommon (may affect up to 1 in 100 people)

- Viruses may become active again ('viral reactivation' including adenovirus activation, BK virus infection, cytomegalovirus infection)

Serious side effects and what to do about them

Frequency/Side Effect/Symptom	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
Very Common (more than 1 in 10)			
Fever, chills, nausea, headache, fast heartbeat, feeling dizzy, low blood pressure, vomiting, muscle or joint pain, difficulty breathing, low level of oxygen in the blood (all possible symptoms of a serious immune reaction called 'cytokine release syndrome' [CRS]).		✓	✓
Serious infection, such as lung infections, COVID-19 infection, skin infections, infection in the blood (sepsis). Symptoms may include fever, chills or shivering, cough, shortness of breath, rapid breathing, rapid pulse, red swollen painful area of skin, low blood pressure, liver failure, and respiratory failure.		✓	✓

Frequency/Side Effect/Symptom	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
Muscle weakness or stiffness, muscle tremors, difficulty writing or speaking, inability to produce movement (all possible symptoms of a condition called 'motor dysfunction').		✓	✓
Headache, feeling confused, feeling less alert or excessive sleepiness, speaking slowly, having difficulty writing, reading and understanding words, difficulty with memory, fits (seizures), shaking, or weakness with loss of movement on one side of the body (all possible symptoms of serious side effects of the brain, including encephalopathy and in some cases 'immune effector cell-associated neurotoxicity syndrome [ICANS]).		✓	✓
Common (less than 1 in 10 but more than 1 in 100)			
Low levels of a type of white blood cells with a fever (febrile neutropenia).		✓	✓
Uncommon (less than 1 in 100 but more than 1 in 1000)			
Feeling very tired, loss of appetite, nausea, vomiting, abdominal pain, a swollen belly, yellowing of your skin or eyeballs, bruising or bleeding, confusion or sleepiness (all possible symptoms of hepatitis and liver failure, as a result of re-activation of hepatitis B virus [HBV] if you have a previous infection with the virus).		✓	✓
Progressive weakness on one side of the body, clumsiness of limbs, disturbance of vision, changes in thinking, memory and orientation, confusion, personality changes (all possible symptoms of a rare type of brain infection called 'progressive multifocal leukoencephalopathy' [PML]).		✓	✓

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell 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 (canada.ca/drug-device-reporting) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

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

Storage

TECVAYLI is stored at the hospital or clinic.

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

If you want more information about TECVAYLI:

- Talk to your healthcare professional.
- Find the full product monograph that is prepared for healthcare professionals and includes the Patient Medication Information by visiting the Health Canada Drug Product Database website: (Drug Product Database: Access the database); the manufacturer's website innovativemedicine.jnj.com/canada, or by calling 1-800-567-3331 or 1-800-387-8781.

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