PRE-APPROVAL ACCESS (PAA) Named Patient Program (NPP) TREATMENT GUIDELINES for Teclistamab (JNJ-64007957) for Treating Physician Use 64007957MMY4001

IMPORTANT

Please read the whole document carefully.

Teclistamab (JNJ-64007957) does not have marketing authorization or is not yet commercially available via the local health care system in the country where the treatment is being requested.

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1. Introduction

This document refers to the **PRE-APPROVAL ACCESS** to teclistamab for the treatment of patients with relapsed and refractory multiple myeloma.

Pre-approval access (PAA) pertains to the provision of treatment by use of an investigational product prior to its marketing authorization. Such access may be considered for patients with serious/life-threatening diseases or conditions, where there are no alternative treatments or where alternative treatments have been exhausted.

Teclistamab does not yet have marketing authorization or is not yet commercially available via the local health care system in the country where the treatment is requested.

For further information related to PAA for this investigational product, please contact the local Janssen affiliate or the Janssen Managed Access team: JanssenMAc@its.jnj.com.

2. Safety Data Collection

All relevant safety data of teclistamab must be reported during the duration of the PAA program according to treatment guidelines, local laws/regulations, and any other applicable guidelines.

Safety data reporting must begin as soon as a signed and dated informed consent form is obtained. Safety data reporting must continue till 30 days after last product administration.

PAA to teclistamab allows the collection of pertinent and relevant safety information on the use of teclistamab to ensure optimum usage while allowing its use in patients with serious/life-threatening diseases or conditions. As such, Janssen may request information from treating physicians.

The instructions for safety reporting are included in Section 7.

3. Responsibilities of Physicians

A treating physician participating in the PAA program agrees to accept certain responsibilities. These include, but are not limited to:

- Attending to the care and safety of the patient(s);
- Complying with all sections of this treatment guidelines;
- Developing the informed consent form/age-appropriate assent (based on the Information for Patients document) and securing the patient's/patient's legal representative signature
- Informing patients that the investigational product being used is unlicensed/has not received marketing authorization or is not yet commercially available through the local health care system;
- Understanding the potential risks and side effects of the investigational product;
- Ensuring that the patient is not eligible for a clinical trial;
- Ensuring that any local requirements for treating physicians to comply with health authorities and/or Independent Ethics Committees/Institutional Review Boards, if applicable, are met;
- Reporting safety data in accordance with Section 7 of this document;
- Ensuring that the investigational product provided for PAA is used only for the purpose for which it is ordered and labelled;
- Ensuring that all delegates are trained to ensure that the drug is prepared and administered as per provided instructions;
- Ensuring that the required medical equipment and supplies necessary to safely and effectively treat patients are in place and available for use;
- Informing the patient on how to contact the treating physician in case of urgent medical questions or to report a (serious) adverse event or special situation;

- Ensuring completion of information on the label as applicable;
- Ensuring destruction of any unused or expired product according to local procedures;
- Responding to queries from Janssen related to reported (serious) adverse events or special situations and meeting all other Janssen requirements and conditions for PAA set forth in the provided documents and information, as well as all other applicable local legal and regulatory requirements.

As a Janssen requirement and condition for PAA, Janssen's Global Tracking System for Managed Access (GTS-MAc) (www.janssenmanagedaccess.com) will be used for all of the purposes and functions for which it was designed, including but not limited to registering patients and placing orders.

Please note that in case no medication has been ordered for 6 months after the last order placed, Janssen can remove the patient from the Managed Access program as this would imply the patient no longer requires the treatment offered by Janssen.

4. Guidelines for the Selection of Patients

Certain criteria defining the eligibility of patients have been defined by Janssen which must be carefully assessed prior to the acceptance of a patient. Before registering a patient in teclistamab Named Patient Program, please examine the criteria that have been established for this particular program.

Mandatory questions (marked by an asterisk *) must be answered to complete the patient registration in GTS-MAc.

If your patient meets either of the following criteria, please contact the Janssen Managed Access team: JanssenMAc@its.jnj.com

- Any other malignancy concomitant with Multiple Myeloma
- Creatinine clearance from 30-39ml/min

BASELINE QUESTIONS

1) First line treatment (please select all that apply)* (bortezomib, ixazomib, carfilzomib, thalidomide, lenalidomide, pomalidomide, daratumumab, isatuximab, cyclophosphamide, melphalan, dexamethasone, bendamustine, elotuzumab, belantamab mafodotin, selinexor, BCMA-targeted CAR-T, autologous stem cell transplant, allogenic stem cell transplant, other)
2) Start date first line treatment (Please enter the date in the following format: DD/MM/YYYY)*
3) Stop date first line treatment (Please enter the date in the following format: DD/MM/YYYY)*
4) Second line treatment (please select all that apply)* (bortezomib, ixazomib, carfilzomib, thalidomide, lenalidomide, pomalidomide, daratumumab, isatuximab, cyclophosphamide, melphalan, dexamethasone, bendamustine, elotuzumab, belantamab mafodotin, selinexor, BCMA-targeted CAR-T, autologous stem cell transplant, allogenic stem cell transplant, other)
5) Start date second line treatment (Please enter the date in the following format: DD/MM/YYYY)*
6) Stop date second line treatment (Please enter the date in the following format: DD/MM/YYYY)*
7) Third line treatment (please select all that apply)* (bortezomib, ixazomib, carfilzomib, thalidomide, lenalidomide, pomalidomide, daratumumab, isatuximab, cyclophosphamide, melphalan, dexamethasone, bendamustine, elotuzumab, belantamab mafodotin, selinexor, BCMA-targeted CAR-T, autologous stem cell transplant, allogenic stem cell transplant, other)

8) Start date third line treatment (Please enter the date in the following format: DD/MM/YYYY)*
9) Stop date third line treatment (Please enter the date in the following format: DD/MM/YYYY)*
10) Fourth line treatment (please select all that apply)* (bortezomib, ixazomib, carfilzomib, thalidomide, lenalidomide, pomalidomide, daratumumab, isatuximab, cyclophosphamide, melphalan, dexamethasone, bendamustine, elotuzumab, belantamab mafodotin, selinexor, BCMA-targeted CAR-T, autologous stem cell transplant, allogenic stem cell transplant, other, no 4th line treatment)
11) Start date fourth line treatment.
(Enter “not applicable” if there is no fourth line treatment, otherwise please enter the date in the following format: DD/MM/YYYY)*
12) Stop date fourth line treatment.
(Enter “not applicable” if there is no fourth line treatment, otherwise please enter the date in the following format: DD/MM/YYYY)*
13) Fifth line treatment (please select all that apply)* (bortezomib, ixazomib, carfilzomib, thalidomide, lenalidomide, pomalidomide, daratumumab, isatuximab, cyclophosphamide, melphalan, dexamethasone, bendamustine, elotuzumab, belantamab mafodotin, selinexor, BCMA-targeted CAR-T, autologous stem cell transplant, allogenic stem cell transplant, other, no 5th line treatment)
14) Start date fifth line treatment. (Enter “not applicable” if there is no fifth line treatment, otherwise please enter the date in the following format: DD/MM/YYYY)*
15) Stop date fifth line treatment. (Enter “not applicable” if there is no fifth line treatment, otherwise please enter the date in the following format: DD/MM/YYYY)*
16) Sixth line treatment (please select all that apply)* (bortezomib, ixazomib, carfilzomib, thalidomide, lenalidomide, pomalidomide, daratumumab, isatuximab, cyclophosphamide, melphalan, dexamethasone, bendamustine, elotuzumab, belantamab mafodotin, selinexor, BCMA-targeted CAR-T, autologous stem cell transplant, allogenic stem cell transplant, other, no 6th line treatment)
17) Start date sixth line treatment. (Enter “not applicable” if there is no sixth line treatment, otherwise please enter the date in the following format: DD/MM/YYYY)*
18) Stop date sixth line treatment. (Enter “not applicable” if there is no sixth line treatment, otherwise please enter the date in the following format: DD/MM/YYYY)*
19) Most recent line treatment (if the previous line of treatment is the most recent line treatment, enter it again; please select all that apply)* (bortezomib, ixazomib, carfilzomib, thalidomide, lenalidomide, pomalidomide, daratumumab, isatuximab, cyclophosphamide, melphalan, dexamethasone, bendamustine, elotuzumab, belantamab mafodotin, selinexor, BCMA-targeted CAR-T, autologous stem cell transplant, allogenic stem cell transplant, other).
20) Start date most recent line treatment (Please enter the date in the following format: DD/MM/YYYY)*
21) Stop date most recent line treatment (Please enter the date in the following format: DD/MM/YYYY)*
22) Has the patient received any treatment regimens other than those listed above?*
23) How many lines of treatment has the patient received for MM?* (<3, 3, 4, 5, 6, 7, 8, 9, 10, >10)
24) What is your patient’s Eastern Cooperative Oncology Group (ECOG) performance status score?* (0, 1, 2)
25) Does your patient have extramedullary disease (EMD)?* (Yes, No)

INCLUSION CRITERIA

1) Is your patient aged 18 or older?*
2) Does your patient have a diagnosis of Relapsed and Refractory Multiple Myeloma?*
3) Has your patient been previously exposed to at least 1 proteosome inhibitor, at least 1 immunomodulatory agent, and an anti-CD38 monoclonal antibody?*
4) Has your patient exhausted all commercially approved and clinically appropriate (not patient or physician preference) treatment options, and is ineligible for a clinical trial?*
5) Does your patient have evidence of disease progression on the last line of therapy?*
6) I confirm I have obtained written consent from my patient or my patient's legal representative to be treated with teclistamab as well as permitting use of all patient's personal information provided to Janssen as part of the program.*
7) I confirm I will follow the management of my patient in accordance with the Treatment Guidelines.*
8) I confirm the patient is willing and able to comply with the lifestyle recommendations specified in the Treatment Guidelines (Appendix 2).*
9) I confirm my patient will have access to the required ICU facilities and treatments required for the initial teclistamab priming dosing and at any time during the treatment if needed including the treatment of CRS.*
10) I confirm the following wash-out period from the last line of treatment, where applicable, will be met before starting the patient on teclistamab:*

Targeted therapy, epigenetic therapy, or treatment with an investigational drug or used an invasive investigational medical device	21 days or at least 5 half-lives, whichever is less
Monoclonal antibody treatment for multiple myeloma	21 days
Cytotoxic therapy	21 days
Proteasome inhibitor therapy	14 days
Immunomodulatory agent therapy	7 days
Gene modified adoptive cell therapy (e.g., chimeric antigen receptor modified T cells, natural killer [NK] cells)	3 months
Radiotherapy	14 days
Focal radiation	7 days
ASCT (autologous stem cell transplant)	12 weeks

EXCLUSION CRITERIA

1) Has your patient ever been enrolled in a teclistamab trial (teclistamab or control arm) or teclistamab Single Patient Request (SPR) program?*
2) Within the 14-day period before the first anticipated dose of teclistamab, will your patient have exceeded a maximum cumulative dose of corticosteroids equivalent to ≥140 mg of prednisone? (see Appendix 3 for guidance)*
3) Does your patient have any history of autoimmune disorder or active systemic infection?*
4) Does your patient have any clinically significant cardiac disease? (see Appendix 4 for guidance)*
5) Does your patient have active plasma cell leukemia, Waldenström's macroglobulinemia, POEMS syndrome (polyneuropathy, organomegaly, endocrinopathy, M-protein, and skin changes)?*
6) Does your patient have known active CNS involvement or exhibit clinical signs of meningeal involvement of multiple myeloma?*
7) Does your patient have myelodysplastic syndrome or active malignancies (ie, progressing or requiring treatment change in the last 24 months) other than relapsed and refractory multiple myeloma? If patient has one of the allowed malignancies listed in Appendix 5, please answer with No*
8) Has your patient had a stroke or seizure within the last 6 months?*

9) Does your patient have active hepatitis B or C infection defined as a positive antigen or positive PCR test OR a history of HBV infection with serologies concurrent with infection? (see Special Warnings and Precautions for Use: HBV Reactivation)?*
10) Does your patient have any other medical condition or disease that in the opinion of the physician would constitute a hazard for participating in this NPP?*
11) Does your patient have any of the following laboratory test results:*

Absolute neutrophil count ≤1.0 × 10^9/L;
Hemoglobin level ≤8 g/dL (≤4.65 mmol/L);
Platelet count <50 x 10^9/L (transfusion support within 7 days before the laboratory test is not permitted);
Alanine aminotransferase and aspartate aminotransferase level ≥2.5 times the upper limit of normal (ULN);
Total bilirubin level >2 × ULN, (except for Gilbert Syndrome: direct bilirubin >1.5 × ULN);
Creatinine clearance <40 mL/min/1.73 m^2;
Corrected serum calcium >14.0 mg/dL (>3.5 mmol/L).

12) Does your patient have contraindications or life-threatening allergies, hypersensitivity, or intolerance to teclistamab or its excipients as listed in the Investigator's Brochure?*
13) Will your patient have had an allogeneic stem cell transplant within last 6 months or autologous stem cell transplant within 12 weeks of teclistamab treatment initiation?*
14) Will your patient have undergone major surgery within 2 weeks of starting teclistamab or have major surgery planned during teclistamab treatment?*
15) Is your patient pregnant or breastfeeding or planning to become pregnant (female) or father a child (male) during their participation in this program and/or for 3 months following treatment discontinuation (see Appendix 2 protocol/treatment guideline for all restrictions)?*
16) Has your patient been exposed to investigational or live, attenuated vaccine(s) within the last 4 weeks?*
NOTE: For COVID vaccine recommendations, please see Appendix 9

5. Treatment Guidance

a) BASIC DRUG INFORMATION

Teclistamab is a humanized IgG-4 PAA bispecific antibody targeting the CD3 receptor complex on T cells and BCMA on B cells. It is hypothesized that teclistamab will be an effective therapy for multiple myeloma by promoting enhanced T cell-mediated cytotoxicity through recruitment of CD3-expressing T cells to the BCMA-expressing cells. This will lead to the activation of T cells and induce subsequent BCMA+ cell lysis, which is mediated by secreted perforin and various granzymes stored in the secretory vesicles of cytotoxic T cells.

Janssen will be responsible for the manufacturing of the product, teclistamab.

The labels will specify that teclistamab is an ‘unlicensed medicinal product’ or ‘not for commercial purposes’. The physician should ensure that information on the clinical label is completed before providing the medication to the patient. A clinical label may require completion of information such as (but not limited to) patient identification and name, address, and telephone number of treating physician.

Teclistamab is supplied as Investigational Product (IP) vials (JNJ-64007957) for subcutaneous administration.

Teclistamab will be provided as final vialed product that must be stored refrigerated between 2°C to 8°C and protected from light during storage.

It is recommended that teclistamab is dispensed in a manner that ensures that supplies with the nearest expiry date are used first.

Teclistamab is supplied in two (2) different concentrations as single-use, sterile, solutions in glass vials closed with stopper and aluminum seal with plastic flip off cap. The IP does not contain any preservatives and is designed for use with a single patient. The drug product configurations provided are shown below:

Table 1. Presentations of Teclistamab (JNJ-64007957) vials

IP Strength (mg)	IP Concentration (mg/mL)	Extractable Volume (mL)	Fill Volume (mL)	Vial Presentation	Storage Conditions	When to use IP vial
30 mg	**10 mg/mL**	**3.0 mL**	**3.5 mL**	Glass vial with a **blue** flip top cap	**Refrigerated** between 2°C to 8°C	For **60 mcg/kg** and **300 mcg/kg Step up** doses
150 mg	**90 mg/mL**	**1.7 mL**	**2.0 mL**	Glass vial with an **orange** flip top cap	**Refrigerated** between 2°C to 8°C	For **1500 mcg/kg Treatment** doses

Prior to dose preparation, the vials should be visually inspected for particulate matter and discoloration. It should be **colorless to light yellow**. The drug product should not be used if it is discolored or cloudy, or if any particulate matter is present.

Store vials at 2ºC to 8ºC and protected from light. Keep the vials in original package until dose preparation.

In case of a Temperature Excursion, teclistamab should be placed in quarantine and the Janssen MAc Team should be notified immediately to evaluate if teclistamab can still be used. Please report the Temperature Excursion to JanssenMAc@its.jnj.com.

The treating physician/pharmacist should keep a log of teclistamab dispensed to patients. The log should contain, for each patient, the number of vials dispensed, the date on which they were dispensed, and the batch or lot number. The treating physician should ensure that traceability is in place between the patient identifier in the program and their own patient identification details.

Teclistamab is provided on an individual patient basis and supplies provided should not be given to other patients. In case the patient stops treatment, unused drug should be destroyed per health care professional site's procedures.

b) BENEFIT/RISK PROFILE

Teclistamab has undergone nonclinical and clinical studies and has shown promising early results in patients with relapsed/refractory multiple myeloma. Clinical data from the first in human trial (Study 64007957MMY1001), support targeting-B Cell Maturation Antigen (BCMA) in patients with heavily pretreated multiple myeloma (median of 5 prior lines of therapy) and have been presented at key international congresses (including ASCO, EHA and ASH) since 2020. Study 64007957MMY1001 supports further evaluation of teclistamab in our ongoing comprehensive Clinical Development Plan.

On 28th Dec, 2021, Janssen submitted a Biologics License Application (BLA) to the U.S. Food and Drug Administration (FDA) for teclistamab, a BCMAxCD3 bispecific antibody for the treatment of patients with relapsed or refractory multiple myeloma who have received at least three prior therapies, including a proteasome inhibitor, an immunomodulatory agent and an anti-CD38 monoclonal antibody. This follows the Breakthrough Therapy Designation (BTD) granted by the FDA earlier in 2021.

On 31st Jan 2022, Janssen announced the submission of a Marketing Authorization Application (MAA) to the European Medicines Agency (EMA) seeking approval of teclistamab as monotherapy for the treatment of adult patients with relapsed and refractory multiple myeloma who have received at least three prior therapies, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 antibody and have demonstrated disease progression on the last therapy.

This Named Patient Program is open for patients who have been previously exposed to at least 1 proteasome inhibitor, at least 1 immunomodulatory agent, and an anti-CD38 monoclonal antibody, have exhausted all commercially approved and clinically appropriate treatment options, are ineligible for a clinical trial and have evidence of disease progression after the last therapy.

Potential risks of treatment with teclistamab, are addressed in the Warnings and Precautions section. Adverse events must be carefully monitored by the treating physician.

For the most comprehensive nonclinical and clinical information regarding teclistamab, refer to the latest version of the Investigator's Brochure.

c) DOSAGE AND ADMINISTRATION

Please ensure that the dosing instructions detailed in this Guideline are followed.

Patients in this PAA program must receive pretreatment medication below:

Administer the following pretreatment medications 1 to 3 hours before each dose of the teclistamab step-up dosing schedule to reduce the risk of cytokine release syndrome (see Warnings and Precautions - Cytokine Release Syndrome).

- 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 pretreatment medications may be required for subsequent doses after dose delays.

Teclistamab should be administered as described in the Investigational Product Preparation Instructions (IPPI). Please check the latest version of the IPPI for the Managed Access Program available in Janssen's Global Tracking System for Managed Access (GTS-MAc).

Table 2 - Teclistamab Administration

Dosing Instructions	Teclistamab will be administered using a weight-based dosing-approach (see IPPI). SC injections will be prepared as described in the IPPI and administered with the use of a syringe and needle by a manual push. Required pretreatment medications must be administered per guidance above.
Schedule of Administration	**Step-up Dose Schedule:** The step-up schedule consists of 2 step-up doses: a first step-up dose of 60 µg/kg followed by a second step-up dose of 300 µg/kg. Each step-up dose is separated by 2 to 4 days and the second step-up dose is to be completed 2 to 4 days prior to the first treatment dose. If there are no delays in treatment, the first treatment dose should be administered 4-8 days after the first step-up dose and 2-4 days after the second step-up dose.

Step-up doses MUST be delayed until CRS and/or immune-effector cell associated neurotoxicity syndrome (ICANS) associated with prior dose have fully resolved.

Treatment Dose Schedule: full doses on each dosing day.
Weekly dosing: Days 1, 8, 15, and 22 of a 28-day cycle.
A change from the dosing schedule of 1500 µg/kg weekly to dosing schedule of 1500 µg/kg biweekly (Day 1 and Day 15, ±7 days), may occur, if approved by Janssen, when a patient has had a response of CR or better for a minimum of 6 months.

Table 2a - Teclistamab Dose ScheduleTeclistamab dose	**Schedule**
60 µg/kg (1st step-up dose)	Day 1
300 µg/kg (2nd step-up dose)	Separated 2 to 4 days from the 1st step-up dose
1500 µg/kg (1st treatment dose)	Separated 2 to 4 days from the 2nd step-up dose
1500 µg/kg (following treatment doses)	Weekly until disease progression

If a dose is delayed, please follow the recommendations in the table below:

Table 2b - Recommendations for restarting teclistamab after dose delay

Delayed Dose	**Duration of Delay from the Last Dose Administered**	**Action**
Step-up Dose 2	7 days or less	Restart teclistamab at Step-up Dose 2 (300 µg/kg).*
	More than 7 days	Restart teclistamab at Step-up Dose 1 (60 µg/kg).*
Initial Treatment Dose	7 days or less	Restart teclistamab at Treatment Dose (1500 µg/kg).*
	8 days to 28 days	Restart teclistamab at Step-up Dose 2 (300 µg/kg).*
	More than 28 days	Restart teclistamab at Step-up Dose 1 (60 µg/kg).*
Subsequent Treatment Doses	28 days or less	Restart teclistamab at Treatment Dose (1500 µg/kg).
	More than 28 days	Restart teclistamab at Step-up Dose 1 (60 µg/kg).*

* Administered pretreatment medications prior to teclistamab dose and monitor accordingly. (see *Dosage and Administration above* – section *5c*)

Hospitalization Requirements

Hospitalization is required for all patients as follows:

Step-up Dose Schedule:

– For step-up dosing days, hospitalize for at least 48 hours from the start of administration.

Treatment Dose Schedule:

– 1st treatment dose; hospitalize for at least 48 hours from the start of administration.

	If the patient experiences any signs of CRS, ICANS, or other clinically significant event(s), they must be hospitalized until 48 hours after administration of the first treatment dose. For the subsequent treatment doses, hospitalization is required as follows: • Following prior sARR Grade 3: at least 24 hours after administration of next dose of teclistamab.Following prior Grade 2 or 3 CRS, or Grade 2 or 3 ICANS at least 48 hours after administration of next dose of teclistamab.

Dose Modification Guidance

Dose delays are the primary method for managing teclistamab-related toxicities in this PAA. If dosing of teclistamab is interrupted for >4 weeks, dosing re-initiation should be discussed with Janssen. Note that sARRs or CRS may occur upon re-initiation of teclistamab after a prolonged dosing interruption. Repeat of step-up dose(s) and pretreatment medication may be required after a delay more than 28 days and should be discussed with Janssen.

The criteria for a dose delay are:

- Grade 4 hematologic toxicity except lymphopenia
- Grade 3 thrombocytopenia with bleeding
- Febrile neutropenia
- Grade 3 neutropenia with infection
- Grade 3 or higher non-hematologic toxicities that are clinically significant except of disease-related pain
- First sign of CRS
  - Treatment with the drug must be withheld until resolution of CRS.
- First sign of ICANS
  - Treatment with the drug must be withheld until resolution of ICANS.

Following a dose delay, any non-hematologic toxicity other than CRS or ICANS must resolve to Grade ≤1 or to baseline and there must be no evidence of a serious bacterial, viral, or fungal infection before proceeding to the next dose. CRS and ICANS must fully resolve before preceding to the next dose.

Guidance for Skipped Doses

Step-up doses should not be skipped but may be delayed.

If the step-up dose schedule is interrupted due to toxicity and later reinitiated, the dose and schedule must be discussed with Janssen before resuming treatment.

Day 1 of a cycle should not be skipped; however, Day 1 of a cycle may be delayed. Other than on Day 1 of a cycle, if a teclistamab administration does not commence within the prespecified window of the scheduled administration date, then the dose will be considered a missed dose. Administration may resume at the next planned dosing date. A missed treatment dose will not be made up.

d) DRUG DESTRUCTION

Any unused or expired product must be destroyed according to local policy and procedures.

e) SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Teclistamab is an investigational drug with limited safety data available from ongoing clinical studies. As with any new product, administration of teclistamab may involve risks that are currently unforeseen. Potential safety risks are based on clinical safety data from the FIH clinical study of teclistamab, in vitro cytokine data, the known MoA (e.g., T cell activation and tumor cell lysis), the route of administration, and class effects of other bispecific T cell engagers.

Patients with known hypersensitivity to any component of the drug formulation for teclistamab should not receive teclistamab. The formulation components of the 10 and 90 mg/mL drug products include teclistamab, sodium acetate trihydrate, glacial acetic acid, sucrose, polysorbate 20, ethylenediaminetetraacetic acid (EDTA), and water for injection and is at pH 5.2.

Please refer to the Precautions and Warnings section of the Summary of Data and Guidance for Investigators in the current Investigator's Brochure.

Management and prevention of Cytokine Release Syndrome (CRS)

As the specific mechanism of action of teclistamab is based on the binding and activation of T cells and the release of cytokines in the tumor environment, CRS is anticipated. CRS is most likely to occur during step-up dosing and the first treatment dose of teclistamab or potentially after a prolonged interruption in dosing of teclistamab and has been observed mainly as Grade 1 or 2. To reduce the risk of CRS, patients receive step-up doses of teclistamab. Patients should also receive premedications (glucocorticoid, antihistamine, and antipyretic) prior to each step-up dose and the first treatment dose of teclistamab as described in Dosage and Administration.

Clinical symptoms indicative of CRS may include, but are not limited to, fever (with or without rigors), arthralgia, nausea, vomiting, tachypnea, hypoxia, tachycardia, hypotension, headache, confusion, tremor, delirium, dyspnea, pulmonary edema and capillary leak. 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.

CRS and CRS symptoms will be captured as an adverse event of special interest and graded per the American Society for Transplantation and Cellular Therapy (ASTCT) grading system provided in Appendix 6.

Trained clinical personnel should be prepared to intervene in the event of CRS. Table 3 provides recommendations for the clinical management of CRS. At the first sign of CRS (such as fever), dosing of teclistamab should be interrupted and the patient should be hospitalized immediately for evaluation, if not already hospitalized.

Infection and CRS may have a similar presentation. Therefore, physicians are strongly encouraged to evaluate for an infection at the first signs or symptoms of CRS. However, treatment for CRS should not be delayed. Cultures and imaging should be obtained; the clinical signs and symptoms should determine which tests are appropriate.

Supportive care for CRS (including but not limited to antipyretic agents, IV fluid support, vasopressors, supplemental oxygen, etc) should be administered according to the clinical manifestations of the patient's illness (see Table 3). Coagulation laboratory tests should be performed; pulmonary, renal, and hepatic function must be monitored closely.

Tocilizumab intervention should be considered in response to a presenting symptom of fever per physician discretion if infection is not suspected or in the presence of persistent (>24 hours)

fever. Early administration of tocilizumab should be considered in patients at high risk of severe CRS (eg, high baseline tumor burden or early fever onset). The use of growth factors, particularly G-CSF and GM-CSF, should be avoided during CRS.

Recommendations for the clinical management of CRS are provided in the table below and are symptom-driven. See Table 3 for hospitalization requirements after specified CRS events. Recommendations for the clinical management of CRS are provided below:

Table 3 - Recommended Management of Cytokine Release Syndrome

Presenting Symptoms	Treatment Options	
	Tocilizumab[a]	Corticosteroids[b]
Temperature ≥38°C[c]	May be considered	Not applicable
Temperature ≥38°C[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 IV over 1 hour (not to exceed 800 mg). Repeat tocilizumab every 8 hours as needed if not responsive to IV 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.
Temperature ≥38°C[c] with either: Hypotension requiring 1 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 IV over 1 hour (not to exceed 800 mg). Repeat tocilizumab every 8 hours as needed if not responsive to IV 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 IV twice daily or equivalent dexamethasone (eg, 10 mg IV every 6 hours). Continue corticosteroids use until the event is Grade 1 or less, then taper over 3 days.
Temperature ≥38°C[c] with either: Hypotension requiring multiple vasopressors (excluding vasopressin). Or, oxygen requirement of positive pressure (eg, CPAP, BiPAP, intubation, and mechanical ventilation)	Administer tocilizumab 8 mg/kg IV over 1 hour (not to exceed 800 mg). Repeat tocilizumab every 8 hours as needed if not responsive to IV 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 IV per day for 3 days per physician discretion. If no improvement or if condition worsens, consider alternate immunosuppressants.[b]

a. Refer to tocilizumab prescribing information for details.
b. Monoclonal antibodies targeting cytokines may be considered based on institutional practice for unresponsive CRS.
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.

Immune-effector cell associated neurotoxicity syndrome (ICANS)

Based on the specific mode-of-action of teclistamab severe or serious neurological toxicities (including immune effector cell-associated neurotoxicity syndrome - ICANS) may occur. Patients should be monitored for neurological toxicities including, but not restricted to, speech disorders, convulsions, disturbances in consciousness, confusion, disorientation, or coordination and balance disorders. Patients should be advised to seek medical evaluation if they notice impairment in motor function (e.g., weakness); changes in sensation (e.g., numbness); or symptoms suggestive of possible CNS abnormalities, such as new onset of headache or mental status changes.

ICANS events will be graded per the ASTCT guidelines (Appendix 8), including administration of the ICE tool (Appendix 7) to assess encephalopathy and evaluation of other neurologic domains.

At the first sign of ICANS, dosing of teclistamab should be interrupted, and the patient should be hospitalized immediately for evaluation, if not already hospitalized (see Table 4). Table 5 summarizes recommendations for the management of ICANS. Table 5 presents guidelines for the management of increased ICP/cerebral edema.

Table 4 - Recommended Management of ICANS

Presenting Symptoms[a]	**Concurrent CRS**	**No Concurrent CRS**
ICE score 7-9[b] or depressed level of consciousness[c]: awakens spontaneously.	Management of CRS as appropriate per Table 3. Monitoring of neurologic symptoms and consider neurology consultation and evaluation, per physician discretion.	Monitor neurologic symptoms and consider neurology consultation and evaluation, per physician discretion.
	Consider non-sedating, anti-seizure medicines (eg, levetiracetam) for seizure prophylaxis.	
ICE score-3-6[b] or depressed level of consciousness[c]: awakens to voice.	Management of CRS as appropriate per Table 3. If no improvement after starting tocilizumab, administer dexamethasone[d] 10 mg IV every 6 hours if not already taking other corticosteroids. Continue dexamethasone use until the event is Grade 1 or less, then taper.	Administer dexamethasone[d] 10 mg intravenously every 6 hours. Continue dexamethasone use until the event is Grade 1 or less, then taper.
	Consider non-sedating, anti-seizure medicines (eg, levetiracetam) for seizure prophylaxis. Consider neurology consultation and other specialists (ie, intensivists) for further evaluation, as needed.	
ICE score-0-2[b] or depressed level of consciousness[c]: awakens only to tactile stimulus, or seizures[c], either: • any clinical seizure, focal or	Management of CRS as appropriate per Table 3. In addition, administer dexamethasone[d] 10 mg IV with the first dose of tocilizumab and repeat dose every 6 hours. Continue dexamethasone use until the	Administer dexamethasone[d] 10 mg IV every 6 hours. Continue dexamethasone use until the event is Grade 1 or less, then taper.

generalized, that resolves rapidly, or • non-convulsive seizures on EEG that resolve with intervention, or • raised ICP: focal/local edema on neuroimaging[c].	event is Grade 1 or less, then taper.	
	Consider non-sedating, anti-seizure medicines (eg, levetiracetam) for seizure prophylaxis. Consider neurology consultation and other specialists (ie, intensivists) for further evaluation, as needed.	
ICE score-0[b] or depressed level of consciousness[c] either: • patient is unarousable or requires vigorous or repetitive tactile stimuli to arouse, or • stupor or coma, or seizures[c], either: • life-threatening prolonged seizure (>5 min), or	Management of CRS as appropriate per Table 3. As above, or consider administration of methylprednisolone 1000 mg IV per day with first dose of tocilizumab and continue methylprednisolone 1000 mg IV per day for 2 or more days, per physician discretion.	As above, or consider administration of methylprednisolone 1000 mg IV per day for 3 days; if improves, then manage as above.
• repetitive clinical or electrical seizures without return to baseline in between, or motor findings[c]: • deep focal motor weakness such as hemiparesis or paraparesis, or raised ICP/cerebral edema[c], 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.	Consider non-sedating, anti-seizure medicines (eg, levetiracetam) for seizure prophylaxis. Consider neurology consultation and other specialists (ie, intensivists) for further evaluation, as needed. In case of raised ICP/cerebral edema, refer to Table 5 for additional management guidelines.	

a. Management is determined by the most severe event, not attributable to any other cause
b. If patient is arousable and able to perform Mental Status assessment, the following domains should be tested: orientation, naming, following commands, writing, and attention (see Appendix 7; ICE Tool).
c. Attributable to no other cause.
d. All references to dexamethasone administration are dexamethasone or equivalent

Table 5 - Guidelines for the Management of Raised ICP/Cerebral Edema
• Elevate head of patient's bed to an angle of 30 degrees. • If patient has an Ommaya reservoir, drain cerebrospinal fluid (CSF) to target opening pressure of <20 mmHg. • Hyperventilation to achieve target $PaCO_2$ of 28 to 30 mm Hg but maintained for no longer than 24 hours. • Consider neurology and/or neurosurgery consultation. • Use high-dose corticosteroids with methylprednisolone IV 1 g/day, as recommended above. • Hyperosmolar therapy with either mannitol (20 g/dL solution) or hypertonic saline (3% or 23.4%, as detailed below):

- Mannitol: initial dose 0.5 to 1 g/kg; maintenance at 0.25 to 1 g/kg every 6 hours while monitoring metabolic profile and serum osmolality every 6 hours and withhold mannitol if serum osmolality is ≥320 mOsm/kg, or the osmolality gap is ≥40.
- Hypertonic saline: initial 250 mL of 3% hypertonic saline; maintenance at 50 to 75 mL/hr while monitoring electrolytes every 4 hours, and withhold infusion if serum Na levels reach ≥155 mEq/L.
- For patients with imminent herniation: initial 30 ml of 23.4% hypertonic saline; repeat after 15 min, if needed.

- Consider IV anesthetics for burst-suppression pattern on electroencephalography.

Systemic Administration-Related Reactions (sARRs)

sARRs may manifest as wheezing, flushing, hypoxemia, fever, chills, rigors, bronchospasm, headache, rash, pruritus, arthralgia, hypo- or hypertension or other symptoms and may occur with SC administration of teclistamab. If sARR occurs during the administration of teclistamab, the injection should be interrupted immediately if possible. Symptoms of sARRs should be managed per the recommendations provided in Table 6.

After a sARR event, patients being treated with teclistamab should receive pretreatment medication per Dosage and Administration instructions for at least the subsequent dose of teclistamab.

Table 6- Guidelines for the Management of sARRs

NCI-CTCAE Grade	Treatment/Intervention
Grade 1 or Grade 2 Mild or moderate reaction; requires therapy or infusion interruption but responds promptly to symptomatic treatment	**SC administration:** Start IV fluids; give diphenhydramine 50 mg (or equivalent) IV and/or paracetamol 650 to 1000 mg (acetaminophen); consider corticosteroids and bronchodilator therapy; monitor patient closely until recovery from symptoms. Consider hospitalization if Grade 2 laryngeal edema or Grade 2 bronchospasm occurs.
Grade 3 Severe, prolonged (ie, not rapidly responsive to symptomatic medication; recurrence of symptoms following initial improvement; hospitalization indicated for other clinical sequelae [eg, renal impairment, pulmonary infiltrates])	Start IV saline infusion; recommend bronchodilators (if indicated), epinephrine 0.2 to 1 mg of a 1:1000 solution for subcutaneous administration or 0.1 to 0.25 mg of a 1:10000 solution injected slowly for IV administration, and/or diphenhydramine 50 mg IV with methylprednisolone 100 mg IV (or equivalent), as needed, and other drugs as appropriate. Treating Physician should follow their institutional guidelines for the treatment of anaphylaxis. Monitored until medically stable, per Treating Physician medical judgment.
Grade 4: life-threatening; pressor or ventilator support indicated	See Dosage and Administration for required hospitalization for subsequent administration(s) of teclistamab after a Grade 3 sARR related to teclistamab. Patients who experience a Grade 4 sARR must discontinue teclistamab.
General	**Prophylactic medications (after initial event)** must be used as described in Dosage and Administration.

	In the case of late-occurring hypersensitivity symptoms (eg, appearance of a localized or generalized pruritis within 1 week after treatment), symptomatic treatment must be given (eg, oral antihistamine or corticosteroids), as appropriate.

Injection Site Reactions

SC administration of any medication can be associated with local injection site reactions including, but not limited to, induration and erythema. Injection site reactions should be managed per institutional standards.

Tumor Lysis Syndrome (TLS)

Patients should be monitored for evidence of TLS. Management of TLS including forced diuresis and correction of electrolyte disturbances such as hyperkalemia, hyperuricemia, and hypocalcemia, is highly recommended. It is also recommended that high-risk patients, (ie, those with a high tumor burden, [a patient with ≥80% plasma cell infiltrate on the bone marrow biopsy or aspirate, whichever is higher, SPEP ≥5 g/dL; FLC ≥5000 mg/L; multiple soft-tissue plasmacytomas]), be treated prophylactically in accordance with local standards (eg, rehydration, diuretics, allopurinol 300 mg daily and medication to increase urate excretion).

Immune-related Adverse Events (irAEs)

Treatment with teclistamab may lead to specific irAEs. Continuous, careful monitoring and timely management of irAEs may help to mitigate more severe toxicity. Symptomatic and best supportive care measures for potential irAEs should be in progress as soon as clinically indicated in accordance with institutional standards. These treatments may include corticosteroids and/or other immunosuppressive agents as required and interrupting or discontinuing teclistamab.

HBV Reactivation

HBV reactivation is a potential risk of teclistamab. All patients should undergo HBV serology testing. For patients with a clinical history of or serology testing indicating prior HBV infection, antiviral prophylaxis can be considered and serial HBV-DNA monitoring by PCR is required every 12 weeks while on treatment and for 6 months following end of treatment. For patients who are diagnosed with HBV reactivation (ie, HBV-DNA becomes detectable) while on treatment, suspend treatment and any steroids and institute appropriate treatment. Resumption of treatment with concomitant antiviral prophylaxis as per standard of care in patients whose HBV reactivation is adequately controlled should be discussed with physicians with expertise in managing HBV and approved by Janssen.

f) CONCOMITANT MEDICATION

The following list details disallowed medications while taking teclistamab based on known or theoretical drug-drug interactions. Janssen must be consulted prior to initiation of any disallowed medication.

- Any chemotherapy, anticancer immunotherapy, experimental therapy, or radiotherapy (except as noted below).
- Continuation of the treatment after emergency orthopedic surgery or radiotherapy is allowed only in the absence of disease progression and after consultation with and approval by Janssen. For patients where a delay of systemic therapy is not appropriate, emergency radiotherapy may consist of localized radiotherapy for pain control or for stabilization of an extensive bone lesion at high risk of pathologic fracture or damage to surrounding tissues.

The circumstances must be reviewed by Janssen to determine whether study treatment may be continued. Radiotherapy should not be given within 7 days of Cycle 1 Day 1 and through the end of Cycle 1.

- Medications used for other indications that have antimyeloma properties (eg, IFN and clarithromycin; Joshi 2006).
  - As an exception, clarithromycin that is prescribed for a course of ≤14 days to treat an infection for which there is no therapeutic alternative is allowed.
- Systemic corticosteroids should be avoided other than for management of AEs and pretreatment medication as specified in Dosage and Administration paragraph.
  - Corticosteroids may be administered for the management of AEs if there is not another therapeutic option; the dose regimen is not to exceed a cumulative dose of 140 mg of prednisone or equivalent within 14 days.
- Other immunosuppressant agents unless used as pretreatment medications or medications to treat an AE (eg, CRS, ICANS).
- Nonsteroidal anti-inflammatory agents should be avoided to minimize the risk of exacerbation of potential sub-clinical myeloma-related kidney disease.
- The use of IV contrast infusions should be avoided to prevent myeloma-related kidney disease. If administration of IV contrast is necessary, then adequate precautions including hydration are indicated.
- Vaccination with live, attenuated vaccines is prohibited during treatment and for 30 days after the last dose of teclistamab. Annual inactivated influenza or SARS CoV-2 vaccines are allowed. Note that antibody responses to vaccines may be suboptimal during treatment with teclistamab (Ariza-Heredia and Chemaly 2015).
- Routine transfusions should not be given on dosing days for teclistamab administration.
- The use of transdermal patches at the injection site should be avoided.
- CYP450 substrates with narrow therapeutic index should be used with caution during the first 48 hours after administration of step-up doses and the first treatment dose of teclistamab SC, as well as during any event of CRS.
- Use of warfarin during Cycle 1 is prohibited unless no other therapeutic option is available. For patients who cannot switch to a different anticoagulant and who experience CRS, coagulation parameters should be monitored closely during a CRS event and until CRS symptoms resolve.

g) TREATMENT WITHDRAWAL CRITERIA

The patient can at any time decide to stop treatment with teclistamab.

It is strongly recommended that the patient be withdrawn from treatment if:

- The patient starts treatment with one of the medications reported on the list of disallowed medications (see Section 5f); Janssen must be consulted prior to initiation of any disallowed medication(s)
- The treating physician considers it to be in the best interest of the patient for safety reasons to be withdrawn;
- Pregnancy has been confirmed;
- The patient receives concurrent (non-protocol) anticancer treatment;

- The patient has an intercurrent illness that prevents further administration of treatment;
- The patient refuses further treatment with the drug;
- Noncompliance with pre-approval access treatment guidelines;
- First event of Grade ≥3 CRS if unresolved in ≥48 hours
- Second event of Grade 3 CRS or any event Grade 4 CRS
- Second event of Grade 3 ICANS or any event Grade 4 ICANS
- Second event of Grade 3 sARR or any event Grade 4 sARR associated with administration of teclistamab SC
- Grade ≥3 injection-site reaction associated with administration of teclistamab SC

Date of stop treatment must be recorded in GTS-MAc (www.janssenmanagedaccess.com). Date of stop treatment corresponds with the date of the last treatment administration.

TREATMENT STOP QUESTIONS

The reason for withdrawal ("stop treatment") must be recorded in GTS-MAc (www.janssenmanagedaccess.com).

- Date of last teclistamab administration*
- Why has treatment been discontinued *? (Progression, Patient withdrew consent, Did not follow treatment guidelines / Physician decision, Patient passed away, AE/ SAE, Transitioned to another source of teclistamab, Duplicate request, Lost to follow-up, Patient never started on teclistamab, other).
- If other, please specify

The program ends for enrolled patients when patients can be transitioned to an available source of teclistamab at the time teclistamab becomes commercially available to the patient in the country and/or reimbursement is granted per local regulations, or the patient can be safely transitioned to other therapies/clinical management at physician's judgement.

Janssen reserves the right to discontinue PAA before patients can be transitioned to commercially available teclistamab, if such discontinuation is necessary based upon considerations of patient safety or upon receipt of data suggesting lack of sufficient efficacy, regulatory decision, drug manufacturing or supply issues or discontinuation of teclistamab development.

Contact the local Janssen affiliate or the Janssen Managed Access Team (JanssenMAc@its.jnj.com) for further guidance.

6. Patient Registration and Supply of Medication

a) PATIENT REGISTRATION

Teclistamab is an unlicensed investigational product. Patients for whom the treating physician wishes to provide teclistamab must be fully informed and written consent of the patient or the patient's legal representative must be obtained prior to PAA treatment. Please refer to the Information for Patients document to develop the Informed Consent Form.

Patients that are provided teclistamab must be registered via GTS-MAc (www.janssenmanagedaccess.com).

Janssen is making every effort to avoid collection and processing Personal Information e.g., identifiable information about patients such as (but not limited to) a patient's name or a combination of initials and date of birth.

For instructions on how to de-identify personal identifiable information from documents, please contact your local Janssen affiliate or JanssenMAc@its.jnj.com.

b) SUPPLY AND RE-SUPPLY OF MEDICATION

Prior to shipment of the initial supply of medication and any re-supply (if applicable), the treating physician will be required to complete a physician declaration in GTS-MAc (please see Appendix 1). Please read all documents available in GTS-MAc (www.janssenmanagedaccess.com) (which may include training materials on safety, compound training, GTS-MAc user guide, reference safety information (SmPC/IB), investigational product preparation instruction and current treatment guidelines) before completing the physician declaration. The physician declaration at the ordering of initial and subsequent supply of medication must be completed via Janssen's GTS-MAc (www.janssenmanagedaccess.com). If there are any questions, please contact the local Janssen affiliate or the Janssen Managed Access Team (JanssenMAc@its.jnj.com).

RE-SUPPLY QUESTIONS

The treating physician will be asked to answer the following resupply questions in GTS-MAc before the drug order can be finalized.

1. Patient weight in kg*
2. Which teclistamab vials are you requesting for your patient?* (90 mg/ml treatment vials, 10 mg/ml priming vials and 90 mg/ml treatment vials)
3. Which dosing schedule is the patient currently on?* (weekly, biweekly)
4. Does the patient continue to show clinical benefit from treatment with teclistamab*?
5. Any changes with the patient medical status (e.g. Performance, status change, new significant comorbidities, including the ones listed in the Treatment Withdrawal criteria - see protocol/treatment guideline for guidance)?*
6. Is the patient pregnant or breastfeeding? In case you have a male patient, please answer with 'No'*
7. Please enter date of the most recent response assessment on teclistamab (Please enter the date in the following format: DD/MM/YYYY. Please enter "not applicable" if this re-supply is to replace a previous initial supply).*
8. Please enter outcome* (Stringent complete response, Complete response, Very good partial response, Partial response, Stable disease, Progressive disease, Not applicable)

7. Safety Reporting

All safety data (including adverse events and pregnancy exposure and other special situations) received by Janssen during the PAA will be evaluated by Janssen for potential reporting to health authorities and for consideration in the overall safety profile of the product.

a) SAFETY REPORTING DEFINITIONS AND CLASSIFICATIONS

Adverse Event

Any untoward medical occurrence in a patient administered a pharmaceutical product, and which does not necessarily have to have a causal relationship with this treatment. An adverse event can therefore be any unfavorable and unintended sign (including an abnormal finding), symptom, or disease temporally associated with the use of a pharmaceutical product, whether or not related to that pharmaceutical product.

This includes any occurrence that is new in onset or aggravated in severity or frequency from the baseline condition, or abnormal results of diagnostic procedures, including laboratory test abnormalities.

Serious Adverse Event

A serious adverse event is any untoward medical occurrence that at any dose:

- Results in death
- Is life-threatening (The patient was at risk of death at the time of the event. It does not refer to an event that hypothetically might have caused death if it were more severe.)
- Requires inpatient hospitalization or prolongation of existing hospitalization
- Results in persistent or significant disability/incapacity
- Is a congenital anomaly/birth defect
- Is a suspected transmission of any infectious agent via a pharmaceutical product (medically significant)
- Is Medically Important *

  ** Medical and scientific judgment should be exercised in deciding whether other situations should be considered serious, such as important medical events that might not be immediately life-threatening or result in death or hospitalization but may jeopardize the patient or may require intervention to prevent one of the other outcomes listed in the definition above. These should usually be considered serious.*

Attribution Definitions

Assessment of Causality: The causal relationship to the investigational product is determined by the treating physician. The following selection should be used to assess all adverse events.

Related: There is a reasonable causal relationship between investigational product administration and the adverse event.

Not Related: There is not a reasonable causal relationship between investigational product administration and the adverse event.

The term “reasonable causal relationship” means there is evidence to support a causal relationship.

Severity Criteria

An assessment of severity grade will be made by the physician according to the NCI-CTCAE Version 5.0, except as noted for CRS and ICANS. Any AEs or SAEs not listed in the NCI-CTCAE Version 5.0 or evaluable by ASTCT criteria should be evaluated for severity/intensity by using the standard grades as follows:

- **Grade 1** Mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated.
- **Grade 2** Moderate; minimal, local or noninvasive intervention indicated; limiting

age-appropriate instrumental ADL.[a]

- **Grade 3** Severe or medically significant but not immediately life threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care ADL.[b]
- **Grade 4** Life-threatening consequences; urgent intervention indicated.
- **Grade 5** Death related to AE.

[a]Instrumental ADL refers to preparing meals, shopping for groceries or clothes, using the telephone, managing money, etc.
[b]Self-care ADL refers to bathing, dressing and undressing, feeding self, using the toilet, taking medications, and not confined to bed.

The treating physician should use clinical judgment in assessing the severity of events not directly experienced by the patient (e.g., laboratory abnormalities).

Adverse Drug Reaction (ADR)

A noxious and unintended response to a medicinal product for which there is a reasonable possibility that the product caused the response. The phrase “response to a medicinal product” means that a causal relationship between a medicinal product and an adverse event is at least a reasonable possibility. The phrase “a reasonable possibility” means that there are facts, evidence, or arguments to support a causal association with the medicinal product.

Special Situations

Safety events of interest for a Janssen product that require reporting for safety evaluation by Janssen include, but are not limited to:

- Overdose of a Janssen product
- Exposure to a Janssen product from breastfeeding
- Product exposure during pregnancy (maternal and paternal)
- Suspected abuse/misuse of a Janssen product
- Accidental or occupational exposure to a Janssen product
- Any failure of expected pharmacological action (i.e., lack of effect) of a Janssen product
- Unexpected therapeutic or clinical benefit from use of a Janssen product
- Medication error, intercepted medication error, or potential medication error involving a Janssen product (with or without patient exposure to the Janssen product, e.g., name confusion, product label confusion, intercepted prescribing or dispensing errors)
- Suspected transmission of any infectious agent via a Janssen product

Although these safety events do not meet the definition of an adverse event, they are reported in the same manner as adverse events.

Product Quality Complaint

A product quality complaint (PQC) is defined as any suspicion of a product defect related to manufacturing, labeling, or packaging, i.e., any dissatisfaction relative to the identity, quality, durability, reliability, or performance of a distributed product, including its labeling, drug delivery system, or package integrity. A PQC may have an impact on the safety and efficacy of the product. In addition, it includes any technical complaints, defined as any complaint that indicates a potential quality issue during manufacturing, packaging, release testing, stability monitoring, dose preparation, storage or distribution of the product or the drug delivery system.

b) HOW TO REPORT (SERIOUS) ADVERSE EVENTS [(S)AEs] AND SPECIAL SITUATIONS

All adverse events, serious and non-serious, and special situations experienced by a patient must be reported to Janssen within 24 hours of the treating physician's knowledge of the event.

The physician must complete and sign TV-FRM-04813: Pre-Approval Access (Serious) Adverse Event Form (this form can be accessed from GTS-MAc [www.janssenmanagedaccess.com]). The completed and signed form must be submitted to the local safety unit. The contact information can be found at the top of the form.

All adverse events that have not resolved by the end of the treatment must be followed until any of the following occurs:

- The event resolves
- The event stabilizes
- The event returns to baseline, if a baseline value/status is available
- The event can be attributed to agents other than the drug provided via PAA or to factors unrelated to the conduct of the PAA program
- It becomes unlikely that any additional information can be obtained (e.g., patient refusal to provide additional information, lost to follow-up after demonstration of due diligence with follow-up efforts)

Any event requiring hospitalization (or prolongation of hospitalization) that occurs during the course of a patient's treatment must be reported as a serious adverse event.

The cause of death of a patient receiving treatment on a PAA basis whether or not the event is expected or associated with the product used, is considered a serious adverse event.

Janssen will submit all applicable reports to the relevant health authorities according to the local laws and regulations.

c) PREGNANCY [IN PATIENTS AND/OR PARTNERS]

All initial reports of pregnancy in female patients or partners of male patients must be reported to Janssen by the treating physician within 24 hours of his or her knowledge of the pregnancy to the Local Safety Contact, listed on the TV-FRM-04813: Pre-Approval Access (Serious) Adverse Event Form. The contacted person will send a Pregnancy Report Form to the treating physician, for completion and return to Janssen. Abnormal pregnancy outcomes (e.g., spontaneous abortion, fetal death, stillbirth, congenital anomalies, ectopic pregnancy) are considered serious adverse events and must be reported using the Pre-Approval Access (Serious) Adverse Event Form (TV-FRM-04813). Any patient who becomes pregnant during the program must be promptly withdrawn from the program and discontinue further treatment with the product].

Because the effect of the drug on sperm is unknown, all pregnancy-in-partner cases must be reported by the treating physician within 24 hours of him or her becoming aware of the pregnancy to the Local Safety Contact, listed on the Pre-Approval Access (Serious) Adverse Event Form (TV-FRM-04813). The Local Safety Contact will send a Pregnancy Report Form to the treating physician, for completion and return.

(Follow-up information regarding the outcome of the pregnancy and any postnatal sequelae in the infant is required.)

d) CONTACTING THE COMPANY REGARDING SAFETY

The appropriate fax number/e-mail (secure mail) for the reporting of adverse events and special situations is provided at the top of the first page of the Pre-Approval Access (Serious) Adverse Event Form (TV-FRM-04813). (This form can be accessed from GTS-MAc [www.janssenmanagedaccess.com]).

e) REFERENCE SAFETY INFORMATION

If there is no marketing authorization for the product and/or indication in the country where the product is being requested (i.e., unlicensed product and/or unlicensed indication), please refer to the to the latest approved version of the IB and any updates/addenda available within Janssen's GTS-MAc (www.janssenmanagedaccess.com). During the program, the local Janssen representative will inform the treating physician when new updates to the IB become available. This new Reference Safety Information will be made accessible via GTS-MAc.

If there is a marketing authorization for the product and indication in the country where the treatment is being requested (i.e., licensed product and licensed indication), please refer to the approved product label in the country where the treatment is being requested, known as Summary of Product Characteristics (SmPC) and/or United States Prescribing Information (USPI) and/or the local label. These are located on the Health Authority website.

f) PRODUCT QUALITY COMPLAINTS

A Product Quality Complaint (PQC) may have an impact on the safety and efficacy of the product. Timely, accurate, and complete reporting and analysis of PQC information are crucial for the patient's safety, treating physicians, and the manufacturer, and are mandated by regulatory agencies worldwide. The manufacturer has established procedures in conformity with regulatory requirements worldwide to ensure appropriate reporting of PQC information.

All PQCs involving a Janssen product must be reported to the Janssen Managed Access Team via JanssenMAc@its.jnj.com by the participating site personnel within 24 hours after being made aware of the event.

A sample of the suspected product should be maintained under the correct storage conditions for further investigation in case it is requested by Janssen.

Any failure where a product did not achieve expected pharmacological action/therapeutic benefit (i.e., lack of effect) when used in accordance with the Company Core Data Sheet (CCDS) or local label will need to be reported as a Product Quality Complaint (PQC) within 24 hours of site staff awareness.

- All reports of disease progression, when the product is being used as intended per the CCDS, should not be forwarded as "Lack of Effect" unless evidenced by statements such as or similar to "the product did not work/perform as expected."
- All reports of the drug not working during the titration period or in situations where the dose is modified per expected clinical practice, should not be forwarded as "Lack of effect" unless the reporter EXPLICITY attributes it to a quality issue.
- All reports of drug not working with any of the following conditions, should not be forwarded as "Lack of Effect"
    - The complaint involves improper dosing due to human error
    - Where the product was used off label

8. Abbreviations

ADL activities of daily living
ASTCT American Society for Transplantation and Cellular Therapy
BCMA B cell maturation antigen
BiPAP Bilevel positive airway pressure
CPAP Continuous positive airway pressure
CR complete response
CRS cytokine release syndrome
CSF cerebrospinal fluid
CTCAE Common Terminology Criteria for Adverse Events
ECG electrocardiogram
EEG electroencephalogram
FLC free light chain
FSH follicle-stimulating hormone
GTS-MAc Janssen's Global Tracking System for Managed Access
HBc hepatitis B core antibody
HBs hepatitis B surface antibody
HBsAg hepatitis B surface antigen
HIV human immunodeficiency virus
ICAN immune effector cell-associated neurotoxicity syndrome
ICE immune effector cell-associated encephalopathy
ICP intracranial pressure
IMiD immunomodulatory imide drug
IMWG International Myeloma Working Group
IP Investigational Product
IPPI Investigational Product Preparation Instructions
irAE immune-related adverse events
IV intravenous(ly)
NCI National Cancer Institute
NPP Named Patient Program
PAA pre-approval access
$PaCO_2$ partial pressure of arterial carbon dioxide
PI proteasome inhibitor
PR partial response
RRMM relapsed/ refractory multiple myeloma
SAE serious adverse event
sARR systemic administration-related reaction
SC subcutaneous(ly)
SPEP serum M-protein quantitation by electrophoresis
T cell T lymphocyte
TLS tumor lysis syndrome
ULN upper limit of normal

9. Appendices

APPENDIX 1: Physician declaration.

I confirm that I accept full legal liability and responsibility for the use of teclistamab for this patient under my care and that I have the appropriate qualifications and expertise for administering teclistamab.

1. I have requested supply of teclistamab for the patient on a named patient basis for the treatment of multiple myeloma. I have informed the patient about the use and benefit/risk profile of teclistamab, that it is provided on a named patient basis and is not yet commercially available in my country for the treatment of multiple myeloma according to local laws. I confirm that the supply of teclistamab will only be used for this patient for the purpose for which it was ordered and labelled.
2. I confirm that my patient is not eligible for a clinical trial or other Compassionate Use/Pre-Approval Access program.
3. I confirm that permission for this patient to start in the Compassionate Use/Pre-Approval Access has been confirmed in accordance with the criteria in the Treatment Guideline or Protocol (as appropriate) and informed consent is obtained prior to commencing treatment with teclistamab. In case when re-consent is needed, I confirm an updated informed consent form has been obtained.
4. I will ensure any unused or expired product will be destroyed according to local procedures.
5. I have informed the patient that the personal information provided to Janssen will not contain information, which allows Janssen to identify the patient, that such information will be used to conduct the program and could be used for additional research purposes and publication related to the program and pharmaceutical compound. I also confirm that such use is covered in the Informed Consent as referred to in paragraph 3. I have further informed the patient that the manufacturer of the medicinal product or the appropriate regulatory/competent authority will be notified of any safety information as required per local legislation.
6. I confirm that I will complete contact information on clinical label.
7. I have informed the patient how I can be contacted in case of an urgent medical question, (Serious) Adverse Event, pregnancy or another special situation.
8. I have read and understood the Treatment Guideline or Protocol (as appropriate) provided which includes safety information, prescribing, storage and administration requirements for the teclistamab.
9. I confirm that I have all applicable approvals available prior to teclistamab being supplied and shipped.
10. I understand that (Serious) Adverse Events, pregnancies, and other special situations should be reported according to the instructions provided in the Treatment Guideline or Protocol (as appropriate). I will respond to any query from Janssen related to the reported (Serious) Adverse Events, pregnancies and special situations.
11. I understand and agree to comply with all the requirements as they are described in the Treatment Guideline or Protocol (as appropriate). I will notify the company of any deviation from the Treatment Guideline or Protocol (as appropriate).
12. I understand the timing and process of closeout as described in the Treatment Guideline or Protocol (as appropriate). I understand that, in principle, the program ends for enrolled patients when patients can safely be transitioned to an available source of teclistamab, at the time teclistamab becomes commercially available to the patient in the country and/or reimbursement is granted per local regulations, or the patient can be transitioned to alternative therapies.
13. I understand that Janssen reserves the right to discontinue the program at any time if such discontinuation is necessary based upon – but not limited to - considerations of patient safety or upon receipt of data suggesting lack of sufficient efficacy, regulatory decision, drug manufacturing or supply issues or discontinuation of teclistamab development.
14. I understand that Janssen will not provide any compensation for this program or my participation in it. I understand that Janssen will provide teclistamab only for the purpose of providing Compassionate Use/Pre-Approval Access, and that no other support - material, financial or otherwise - will be provided.
15. I understand that Janssen or its delegate reserves the right to audit this program for any reason with prior notice, which may include audit of product supplies provided to you under this program.
16. I confirm all delegates will be trained to prepare and administer the product as per provided instructions.
17. I understand I shall not publish, disseminate, or otherwise disclose or make available any information regarding the Product or the treatment of the patient without prior written consent/approval from Janssen

APPENDIX 2: Contraceptive [and Barrier] Guidance and Collection of Pregnancy Information

Patients must follow contraceptive measures as outlined in Section 4. Pregnancy information will be collected and reported as noted in Section 7.

Women of child-bearing potential/contraception

Pregnancy status for females of child-bearing potential should be verified prior to starting treatment with teclistamab.

Women of child-bearing potential should use effective contraception during treatment and for 3 months after the final dose of teclistamab. Male patients with a female partner of child-bearing potential should use effective contraception during treatment and for three months after the last dose of teclistamab.

Pregnancy

There are no available data on the use of teclistamab in pregnant women or animal data to assess the risk of teclistamab in pregnancy. Human IgG is known to cross the placenta after the first trimester of pregnancy. Therefore, teclistamab, a humanised IgG4-based antibody, has the potential to be transmitted from the mother to the developing foetus. Teclistamab is not recommended for women who are pregnant. Teclistamab is associated with hypogammaglobulinaemia, therefore, assessment of immunoglobulin levels in newborns of mothers treated with teclistamab should be considered.

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 teclistamab, advise patients not to breastfeed during treatment with teclistamab and for at least three months after the last dose.

Fertility

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

Definitions

Woman of Childbearing Potential
A woman is considered fertile following menarche and until becoming postmenopausal unless permanently sterile (see below).

Woman Not of Childbearing Potential
- **premenarchal**
  A premenarchal state is one in which menarche has not yet occurred.
- **postmenopausal**
  A postmenopausal state is defined as no menses for 12 months without an alternative medical cause. A high FSH level (>40 IU/L or mIU/mL) in the postmenopausal range may be used to confirm a postmenopausal state in women not using hormonal contraception or hormonal replacement therapy, however in the absence of 12 months of amenorrhea, a single FSH measurement is insufficient. If there is a question about menopausal status in women on HRT, the woman will be required to use one of the non-estrogen-containing hormonal highly effective contraceptive methods if she wishes to continue HRT during the program.
- **permanently sterile (for the purpose of this program)**
  Permanent sterilization methods include hysterectomy, bilateral salpingectomy, and bilateral oophorectomy.

  If reproductive status is questionable, additional evaluation should be considered.
  Contraceptive (birth control) use by men or women should be consistent with local regulations regarding the acceptable methods of contraception for those participating in pre-approval access programs.

Examples of Contraceptives[a]

HIGHLY EFFECTIVE METHODS *(Failure rate of <1% per year when used consistently and correctly.)*

USER INDEPENDENT – Highly Effective Methods
- Implantable progestogen-only hormone contraception associated with inhibition of ovulation[b]
- Intrauterine device
- Intrauterine hormone-releasing system
- Bilateral tubal ligation/occlusion
- Vasectomized partner.

(Vasectomized partner is a highly effective contraceptive method provided that the partner is the sole sexual partner of the woman of childbearing potential and the absence of sperm has been confirmed. If not, additional highly effective method(s) of contraception should be used. Spermatogenesis cycle is approximately 74 days.)

USER DEPENDENT – Highly Effective Methods

- Combined (estrogen- and progestogen-containing) hormonal contraception associated with inhibition of ovulation[b]
  - Oral
  - Intravaginal
  - Transdermal
  - Injectable
- Progestogen-only hormone contraception associated with inhibition of ovulation[b]
  - Oral
  - Injectable
- Sexual abstinence

(Sexual abstinence is considered a highly effective method only if defined as refraining from heterosexual intercourse during the entire period of risk associated with teclistamab treatment. The reliability of sexual abstinence needs to be evaluated in relation to the duration of the program and the preferred and usual lifestyle of the patient.)

NOT HIGHLY EFFECTIVE METHODS *(Failure rate of >1% per year)*
USER DEPENDENT and NOT considered to be (highly) effective methods.

- Progestogen-only oral hormonal contraception where inhibition of ovulation is not the primary mode of action
- Male or female condom with or without spermicide[c]
- Cap, diaphragm, or sponge with spermicide
- A combination of male condom with either cap, diaphragm, or sponge with spermicide (double-barrier methods)[c]
- Periodic abstinence (calendar, symptothermal, post-ovulation methods)
- Withdrawal (coitus-interruptus)
- Spermicides alone
- Lactational amenorrhea method

[a]Typical use failure rates may differ from those when used consistently and correctly. Use should be consistent with local regulations regarding the use of contraceptive methods for patients in pre-approval access programs.
[b]Teclistamab may interact with hormonal contraception, which may reduce the efficacy of the contraceptive method. In addition, consider if the hormonal contraception may interact with teclistamab.
[c]Male condom and female condom should not be used together (due to risk of failure with friction).

APPENDIX 3: Conversion table for Glucocorticoid Dose

Steroid	Approximate Equivalent Dose to Dexamethasone 8 mg	Approximate Equivalent Dose to Dexamethasone 16 mg	Approximate Equivalent Dose to Dexamethasone 20 mg	Approximate Equivalent Dose to Dexamethasone 40 mg
Methylprednisolone	45 mg	90 mg	110 mg	220 mg
Prednisone/Prednisolone	55 mg	110 mg	140 mg	280 mg

APPENDIX 4: Clinically significant cardiac disease

Clinically significant cardiac disease includes:

a) New York Heart Association stage III or IV congestive heart failure
b) Myocardial infarction or coronary artery bypass graft ≤6 months prior to starting on teclistamab
c) History of clinically significant ventricular arrhythmia or unexplained syncope, not believed to be vasovagal in nature or due to dehydration
d) History of severe non-ischemic cardiomyopathy

APPENDIX 5: Allowed exceptions for active malignancies other than multiple myeloma at program start

The only allowed exceptions are:

a. Non-muscle invasive bladder cancer treated within the last 24 months that is considered completely cured
b. Skin cancer (non-melanoma or melanoma) treated within the last 24 months that is considered

completely cured.

c. Noninvasive cervical cancer treated within the last 24 months that is considered completely cured
d. Localized prostate cancer (N0M0):
    1) With a Gleason score of ≤6, treated within the last 24 months, or untreated and under surveillance
    2) With a Gleason score of 3+4 that has been treated >6 months prior to starting on teclistamab and considered to have a very low risk of recurrence, or
e. History of localized prostate cancer and receiving androgen deprivation therapy and considered to have a very low risk of recurrence.
f. Breast cancer: adequately treated lobular carcinoma in situ or ductal carcinoma in situ, or history of localized breast cancer and receiving antihormonal agents and considered to have a very low risk of recurrence
g. Other malignancy that is considered cured with minimal risk of recurrence

APPENDIX 6: ASTCT Grading System for CRS

Grade	Toxicity
Grade 1	Fever[a] (Temperature ≥38°C)
Grade 2	Fever[a] (Temperature ≥38°C) with either: • Hypotension not requiring vasopressors. • And/or[c] hypoxia requiring low-flow nasal cannula[b] or blow-by.
Grade 3	Fever[a] (Temperature ≥38°C) with either: • Hypotension requiring a vasopressor with or without vasopressin, • And/or[c] hypoxia requiring high-flow nasal cannula,[b] facemask, nonrebreather mask, or Venturi mask.
Grade 4	Fever[a] (Temperature ≥38°C) with either: • hypotension requiring multiple vasopressors (excluding vasopressin), • And/or[c] hypoxia requiring positive pressure (eg, CPAP, BiPAP, intubation and mechanical ventilation).
Grade 5	Death

[a]Fever not attributable to any other cause. In patients who have CRS then receive antipyretics or anticytokine therapy such as tocilizumab or steroids, fever is no longer required to grade subsequent CRS severity. In this case, CRS grading is driven by hypotension and/or hypoxia.
[b]Low-flow nasal cannula is defined as oxygen delivered at ≤6 L/minute or blow-by oxygen delivery. High-flow nasal cannula is defined as oxygen delivered at >6 L/minute.
[c]CRS grade is determined by the more severe event: hypotension or hypoxia not attributable to any other cause.

Source: Lee D, Santomasso B, Locke F, et al. ASTCT Consensus grading for cytokine release syndrome and neurologic toxicity associated with immune effector cells. Biol Blood Marrow Transplant. 2019;25:625-638

APPENDIX 7: Immune Effector Cell-associated Encephalopathy (ICE) Tool

Category	Points
Orientation: orientation to year, month, city, hospital	4 points
Naming: ability to name 3 objects (eg, point to clock, pen, button)	3 points
Following commands: ability to follow simple commands (eg, “Show me 2 fingers” or “Close your eyes and stick out your tongue”)	1 point
Writing: ability to write a standard sentence (eg, “Our national bird is the bald eagle.”)	1 point
Attention: ability to count backward from 100 by 10	1 point

Scoring is as follows (see also Appendix 8 for additional details regarding ICANS severity grading):

a. 10; no impairment
b. 7 to 9; Grade 1 ICANS
c. 3 to 6; Grade 2 ICANS
d. 0 to 2; Grade 3 ICANS
e. 0 due to patient unarousable and unable to perform ICE assessment; Grade 4 ICANS.

Source: Lee D, Santomasso B, Locke F, et al. ASTCT Consensus grading for cytokine release syndrome and neurologic toxicity associated with immune effector cells. Biol Blood Marrow Transplant. 2019;25:625-638

APPENDIX 8: ASTCT ICANS Consensus Grading for Adults

Neurotoxicity Domain	Grade 1	Grade 2	Grade 3	Grade 4
ICE score[a]	7-9	3-6	0-2	0 (patient is unarousable and unable to perform ICE testing)
Depressed level of consciousness[b]	Awakens spontaneously	Awakens to voice	Awakens only to tactile stimulus	Patient is unarousable or requires vigorous or repetitive tactile stimuli to arouse Stupor or coma
Seizures	N/A	N/A	Any clinical seizure focal or general that resolves rapidly; or non-convulsive seizures on EEG that resolve with intervention	Life-threatening, prolonged seizures (>5 min) or repetitive clinical or electrical seizures without return to baseline in between
Motor findings[c]	N/A	N/A	N/A	Deep focal motor weakness such as hemiparesis or paraparesis
Raised ICP/IOP/cerebral edema	N/A	N/A	Focal/local edema on neuroimaging[d]	Diffuse cerebral edema on neuroimaging; decerebrate or decorticate posturing; or cranial nerve VI palsy; or papilledema; or Cushing's Triad

ICANS grade is determined by the most severe event (ICE score, level of consciousness, seizure, motor findings, raised ICP/cerebral edema) not attributable to any other cause; for example, a patient with an ICE score of 3 who has a generalized seizure is classified as grade 3 ICANS.

N/A indicates not applicable.

[a]A patient with an ICE score of 0 may be classified as grade 3 ICANS if awake with global aphasia, but a patient with an ICE score of 0 may be classified as grade 4 ICANS if unarousable.

[b]Depressed level of consciousness should be attributable to no other cause (eg, no sedating medication).

[c]Tremors and myoclonus associated with immune effector cell therapies may be graded according to CTCAE v5.0, but they do not influence ICANS grading.

[d]Intracranial hemorrhage with or without associated edema is not considered a neurotoxicity feature and is excluded from ICANS grading. It may be graded according to CTCAE v5.0.

APPENDIX 9: Recommendations for COVID-19 Vaccination

Administration of non-live vaccines approved or authorized for emergency use (e.g., COVID-19) by local health authorities are allowed before or during this program.

It is recommended that patients receive prophylactic COVID-19 vaccination when locally available, at the discretion of physician judgement or institutional practice, and in compliance with this treatment guideline and local labels for the vaccine. Below is general guidance for consideration.

Many vaccines against COVID-19 are being developed with different technologies and platforms and may have safety and efficacy profiles that are not fully characterized even after preliminary health authority approval. However, the benefit-risk ratio of receiving a COVID-19 vaccine among patients with multiple myeloma treated with teclistamab is considered to be positive and should be considered for administration when not otherwise contraindicated for use in the vaccine label.

Per treatment guideline, live attenuated vaccines must be completed ≥4 weeks prior to start of teclistamab treatment or initiated ≥30 days after last dose of teclistamab. There are no specific timing restrictions for inactivated vaccines, which include vaccines which use alternative technology like mRNA or replication-incompetent viral vectors. Enrolment into an interventional clinical trial for an experimental vaccine is prohibited during program. AEs and SAEs associated with the COVID-19 vaccine must be collected and reported in accordance with the pharmacovigilance practice.

No data are currently available to suggest that COVID-19 vaccines pose specific or additional safety risk beyond other vaccines for cancer patients undergoing treatment. Theoretically, a diminished immune response may occur in immunocompromised patients, and therefore these patients may have reduced vaccine effectiveness.

For guidance on vaccination, please refer to:
National Comprehensive Cancer Network. Preliminary recommendations of the NCCN COVID-19 Vaccination Advisory Committee Version 1.0 1/22/2021. NCCN https://www.nccn.org/covid-19/pdf/COVID-19_Vaccination_Guidance_V1.0.pdf (2021),*
Garassino, M. C. et al. The ESMO call to action on COVID-19 vaccinations and patients with cancer: Vaccinate. Monitor. Educate. Ann. Oncol. https://doi.org/10.1016/j.annonc.2021.01.068 (2021), and
Desai et al. COVID-19 vaccine guidance for patients with cancer participating in oncology clinical trials Nature Reviews Vol18; 313 https://doi.org/10.1038/s41571-021-00487-z.For additional information for reference or guidance, several organizations and journals have published recommendations for COVID-19 vaccine administration in cancer patients, including the following:
European Society for Blood and Marrow Transplantation: https://www.ebmt.org/covid-19-and-bmt
ASTCT: https://www.hematology.org/covid-19/ash-astct-covid-19-vaccination-for-hct-and-car-t-cell-recipients
National Comprehensive Cancer Network: https://www.nccn.org/covid-19/pdf/COVID-19_Vaccination_Guidance_V2.0.pdf https://www.nccn.org/docs/default-source/covid-19/2021_covid-19_vaccination_guidance_v3-0.pdf?sfvrsn=b483da2b_60
Centers for Disease Control and Prevention: https://www.cdc.gov/vaccines/covid-19/info-by-product/clinical-considerations.html

9. Version History

Document and Revision History

V1.0 (Original/initial) Teclistamab_64007957MMY4001_ Named Patient Program (NPP)_Solicited TG_v1.0_08Mar2022

V2.0 Teclistamab_64007957MMY4001_ Named Patient Program (NPP)_Solicited TG_v2.0_15Jul2022

- Introduction: “relapsed or refractory” changed into “relapsed and refractory”
- Inclusion criteria:
  - Removal of question about ECOG (according to previous numbering) (#5)
  - Update of questions (according to updated numbering): #1 (Deletion of “willing to provide consent to participate”), #2 (“relapsed and refractory MM’ instead of “RRMM”, #4 (concerning exhausted treatment), #6 (“have obtained written consent” instead of “will obtain written consent”
  - Addition of question #3 (according to updated numbering): previously exposure to at least 1 proteasome inhibitor, at least 1 immunomodulatory agent, and an anti-CD38 monoclonal antibody
  - Addition of question #10 (according to updated numbering): concerning wash-out period from previous treatments (Wash-out period for ASCT added)
- Exclusion criteria
  - Removal of question #1 (according to previous numbering)
  - Minor rewording of questions (according to updated numbering): #1, #2, #3, #7, #13, #14, #15
  - Update of questions (according to updated numbering): #5 (allow concurrent malignancy, controlled PLC and AL Amyloidosis), #11 (platelet value)
- Benefit/Risk Profile updated
- Dosage and administration: addition of table 2b
- Updated wording in Appendix 1, physician declaration and appendix 2, Contraceptive [and Barrier] Guidance and Collection of Pregnancy Information
- Minor errors corrected

V2.1 Teclistamab_64007957MMY4001_ Named Patient Program (NPP)_Solicited TG_v2.1_5Aug2022

- corrected typo on table 2a (600 ug for 60 ug)