TECVAYLI®
(teclistamab-cqyv) Injection for subcutaneous use
10 mg/mL and 90 mg/mL

MajesTEC-3 Edition

A Guide to TECVAYLI® (teclistamab-cqyv) for Clinical Pharmacists

Approved in 2L+ in combination with DARZALEX *FASPRO*® (daratumumab and hyaluronidase-fihj) in adult patients with RRMM who have received at least 1 prior line of therapy, including a PI and an immunomodulatory agent.[1]

INDICATIONS AND USAGE

TECVAYLI® (teclistamab-cqyv) is a bispecific B-cell maturation antigen (BCMA)-directed CD3 T-cell engager indicated for the treatment of adult patients with relapsed or refractory multiple myeloma:

- in combination with daratumumab and hyaluronidase-fihj in patients who have received at least one prior line of therapy, including a proteasome inhibitor and an immunomodulatory agent.
- as monotherapy, in patients who have received at least four prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent and an anti-CD38 monoclonal antibody.

IMPORTANT SAFETY INFORMATION

WARNING: CYTOKINE RELEASE SYNDROME and NEUROLOGIC TOXICITY including IMMUNE EFFECTOR CELL-ASSOCIATED NEUROTOXICITY SYNDROME

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 risk of CRS. Withhold TECVAYLI until CRS resolves or permanently discontinue based on severity.

Neurologic toxicity, including Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS) and serious, life-threatening, or fatal reactions, can occur in patients receiving TECVAYLI. 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.

TECVAYLI is available only through a restricted program called the TECVAYLI and TALVEY® Risk Evaluation and Mitigation Strategy (REMS).

2L+, second line and beyond; BCMA, B-cell maturation antigen; CD3, cluster of differentiation 3; CD38, cluster of differentiation 38; PI, proteasome inhibitor; RRMM, relapsed or refractory multiple myeloma.

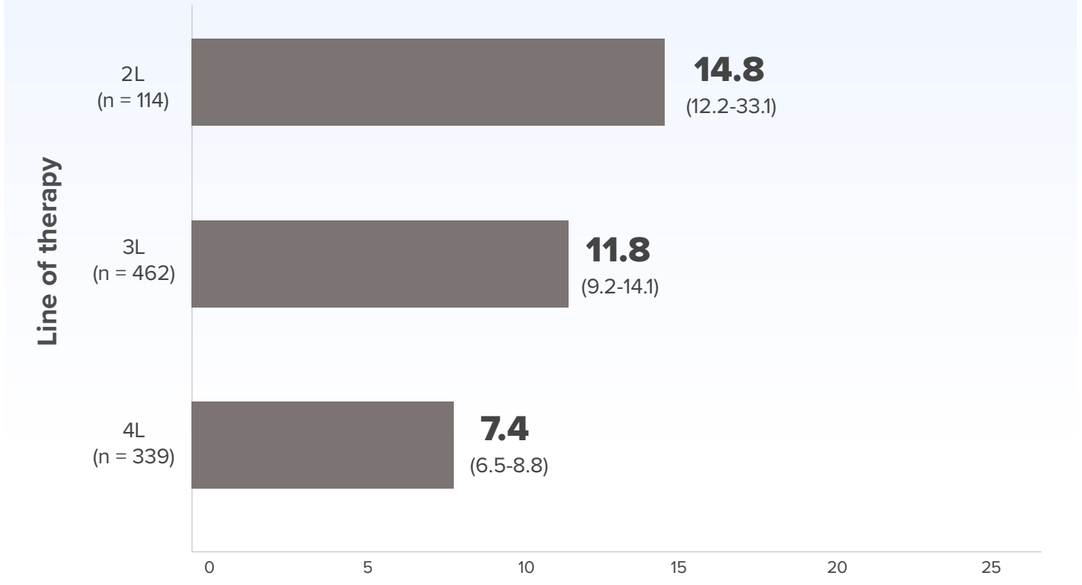
Please read full Important Safety Information on pages 10-11 and full Prescribing Information, including Boxed WARNING, for TECVAYLI.

Treatment Insights

Efficacy diminishes with each line of therapy in the RRMM setting[2]

The following analysis is based on individual patient-level data from 915 patients identified as lenalidomide-refractory with 1-3 prior LOT, and ECOG PS <2, who were exposed to a PI and a lenalidomide, from 9 daratumumab clinical trials including 4764 patients.[2]

Median PFS by Line of Therapy



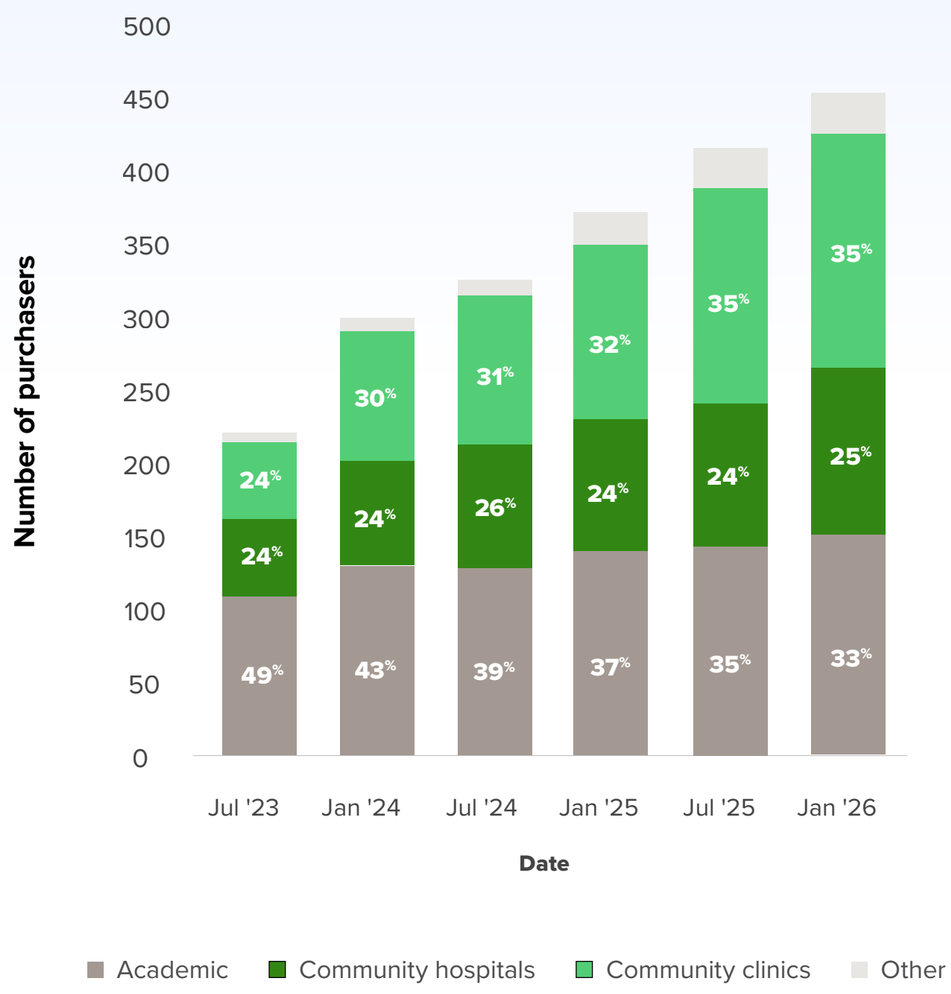
Median PFS of 10 months (95% CI: 8.8-11.1) in the overall population (N=915)

Declining PFS drives urgency to consider different treatment strategies

2L, second line; 3L, third line; 4L, fourth line; CI, confidence interval; ECOG PS, Eastern Cooperative Oncology Group Performance Status; LOT, line of therapy; MM, multiple myeloma; PFS, progression-free survival; PI, proteosome inhibitor; RRMM, relapsed or refractory multiple myeloma.

Adoption of a bispecific for RRMM continues to grow across sites of care[3]

Purchasers of a Leading Bispecific in RRMM by Practice Type



MajesTEC-3 Trial

TECVAYLI and DARZALEX *FASPRO* (daratumumab and hyaluronidase-fihj): An all-immunotherapy combination[1,4]

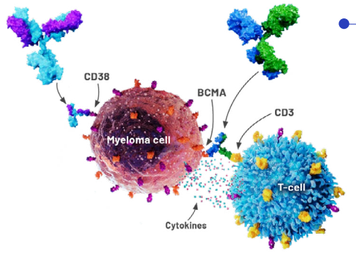
Mechanism of Action

Daratumumab enables the CD38-mediated microenvironment by decreasing immunosuppressive CD38+T_{regs} and B_{regs}, in addition to its direct on-tumor effects

+

The binding of **TECVAYLI** to both BCMA and CD3 leads to the **activation of T-cells** and the release of various proinflammatory cytokines, resulting in the lysis of MM cells

DARZALEX *FASPRO*
Anti-CD38 mAb



TECVAYLI
BCMA × CD3 BsAb

Daratumumab binds to CD38 on the surface of MM cells, as well as on certain other types of cells, such as RBCs

TECVAYLI binds to BCMA on the surface of MM cells and some healthy B-lineage cells, **as well as to CD3** on the surface of T-cells

DARZALEX *FASPRO*, when used in combination with TECVAYLI, enables and enhances the immune-mediated lysis of MM cells.

BCMA, B-cell maturation antigen; B_{regs}, regulatory B-cells; BsAb, bispecific antibody; CD3, cluster of differentiation 3; CD38 cluster of differentiation 38; mAb, monoclonal antibody; MM, multiple myeloma; RBCs, red blood cells; T_{regs}, regulatory T-cells.

IMPORTANT SAFETY INFORMATION (cont.)

WARNINGS AND PRECAUTIONS

Cytokine Release Syndrome - TECVAYLI can cause cytokine release syndrome (CRS), including life-threatening or fatal reactions.

In the clinical trials (monotherapy and combination therapy; N=448), CRS occurred in 64% of patients who received TECVAYLI at the recommended dosage, with Grade 1 CRS occurring in 46% of patients, Grade 2 in 18%, and Grade 3 in 0.2%. Recurrent CRS occurred in 27% of patients. Most patients experienced CRS during the initial step-up dosing schedule (step-up dose 1 [37%], step-up dose 2 [32%], or the initial treatment dose [20%]). CRS first occurred following subsequent doses of TECVAYLI in 2.5% of patients. The median time to onset of CRS was 2 (range: 1 to 9) days after the most recent dose and the median duration of CRS was 2 (range: 1 to 22) days.

Clinical signs and symptoms of CRS included, but were not limited to, fever, hypoxia, chills, hypotension, sinus tachycardia, headache, and elevated liver enzymes (aspartate aminotransferase and alanine aminotransferase elevation).

Initiate therapy according to TECVAYLI step-up dosing schedule to reduce risk of CRS. Administer pretreatment medications to reduce risk of CRS and monitor patients following administration of TECVAYLI accordingly.

At the first sign of CRS, immediately evaluate the patient for hospitalization. Administer supportive care based on severity and consider further management per current practice guidelines. Withhold until CRS resolves or permanently discontinue TECVAYLI based on severity.

TECVAYLI is available only through a restricted program under a REMS.

MajesTEC-3: Study design and patient characteristics[1]

The efficacy of TECVAYLI in combination with DARZALEX *FASPRO* vs DPd or DVd was evaluated in 587 patients with RRMM in a randomized, open-label study. Patients had received 1-3 prior lines of therapy, including a PI and lenalidomide.

Major efficacy outcome measure*: PFS

Key secondary endpoints: OS, ORR, ≥CR, MRD negativity 10^{-5}

Baseline disease characteristics:
- Median prior lines of therapy: 2 (range 1-3)
- 38% of patients had received 1 prior line of therapy
- 100% of patients were previously exposed to lenalidomide and 84% were refractory
- 99.8% of patients were previously exposed to a PI
- 74% of patients previously received autologous stem cell transplantation
- 5% of patients received a prior anti-CD38 monoclonal antibody†

*Assessment based on IMWG 2018 criteria by IRC.
†There is limited data with TECVAYLI + DARZALEX *FASPRO* in patients who have received or are refractory to prior anti-CD38 monoclonal antibody therapy.

Baseline Patient Characteristics

Patient characteristics	N = 587
Age (median)	64 years (range 25-88)
≥75 years of age	10%
Male	55%
White	65%
Black or African American	6%
Asian	22%
ISS Stage I at screening	63%
ISS Stage II at screening	29%
ISS Stage III at screening	8%
High-risk cytogenetics (presence of del [17p], t[4;14], and t[14;16])	35%
Extramedullary disease	5%

CR, complete response; DPd, daratumumab, pomalidomide, and dexamethasone; DVd; daratumumab, bortezomib, and dexamethasone; IMWG, International Myeloma Working Group; IRC, Independent Review Committee; ISS, International Staging System; MRD, minimal residual disease; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PI, protease inhibitor; RRMM, relapsed or refractory multiple myeloma.

Please read full Important Safety Information on pages 10-11 and full Prescribing Information, including Boxed WARNING, for TECVAYLI.
Please see Important Safety Information on pages 24 to 25 and click here to read full Prescribing Information for DARZALEX *FASPRO*.

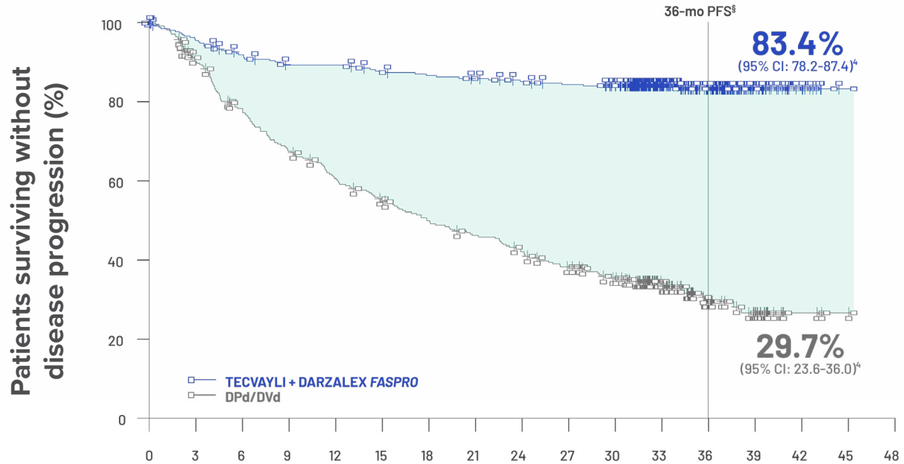
TECVAYLI® (teclistamab-cqyv) Injection for subcutaneous use
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TECVAYLI and DARZALEX *FASPRO* (daratumumab and hyaluronidase-fihj) demonstrated superior PFS vs DPd/DVd (HR=0.17*; *P*<0.0001†)[1,3,5]

At a median follow-up of 34.5 months‡

83% reduction in the risk of progression or death with TECVAYLI and DARZALEX *FASPRO* (HR = 0.17* [95% CI: 0.12-0.23]; *P*<0.0001†)

PFS* (Major Efficacy Outcome Measure)



No. at Risk

TEC-DARA SC	291	262	249	240	240	233	230	227	222	218	214	142	89	34	9	0	0
DPd/DVd	296	254	218	188	167	149	135	124	112	99	87	52	26	14	3	1	0

Median PFS was not reached in the TECVAYLI and DARZALEX *FASPRO* arm (95% CI: NE-NE) vs 18.1 months (95% CI: 14.6-22.8) in the DPd/DVd arm.

*Stratified Cox proportional hazard model. For all stratified analyses, stratification was based on ISS staging (I vs II or III) and number of prior lines of therapy (1 vs 2 or 3), as randomized.
†Stratified log-rank test.
‡Based on the ITT population.
§Kaplan-Meier estimate.

CI, confidence interval; DPd, daratumumab, pomalidomide, and dexamethasone; DVd; daratumumab, bortezomib, and dexamethasone; HR, hazard ratio; NE, not estimable; PFS, progression-free survival; ITT, intention-to-treat.

IMPORTANT SAFETY INFORMATION (cont.)

WARNINGS AND PRECAUTIONS (cont.)

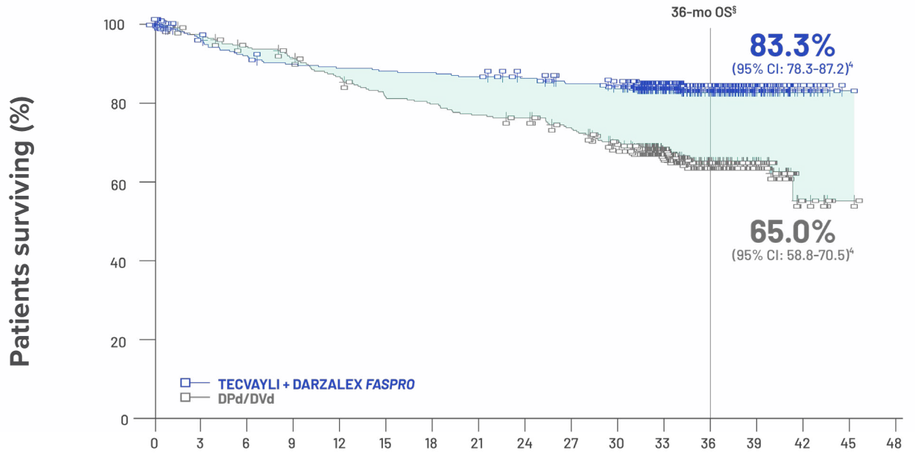
Neurologic Toxicity including Immune Effector Cell-Associated Neurotoxicity Syndrome - TECVAYLI can cause serious, life-threatening, or fatal neurologic toxicity, including immune effector cell-associated neurotoxicity syndrome (ICANS).

TECVAYLI + DARZALEX *FASPRO* demonstrated statistically significant OS compared to DPd/DVd[1,5]

At a median follow-up of 34.5 months‡

54% reduction in the risk of death with TECVAYLI and DARZALEX *FASPRO* (HR = 0.45* [95% CI: 0.32-0.65]; *P*<0.0001†)

OS§ (Secondary Endpoint)



No. at Risk

TEC-DARA SC	291	272	259	252	249	247	246	243	239	232	227	160	100	40	9	0	0
DPd/DVd	296	285	274	265	250	235	229	221	218	208	190	127	66	33	5	1	0

Median OS was not reached in either the TECVAYLI and DARZALEX *FASPRO* arm (95% CI: NE-NE) or the DPd/DVd arm (95% CI: 41.4 months to NE).

OS, overall survival.

IMPORTANT SAFETY INFORMATION (cont.)

WARNINGS AND PRECAUTIONS (cont.)

Neurologic Toxicity including Immune Effector Cell-Associated Neurotoxicity Syndrome (cont.)

In the clinical trials (monotherapy and combination therapy trials; N=448), neurologic toxicity occurred in 60% of patients who received TECVAYLI at the recommended dosage, with Grade 3 or 4 neurologic toxicity in 6%. Neurologic toxicities reported in ≥5% of patients included headache (27%), sensory neuropathy (16%), motor dysfunction (15%), insomnia (12%), encephalopathy (11%), and dizziness (8%). Fatal neurologic toxicity occurred in 0.4% of patients, including Guillain-Barré syndrome and status epilepticus (one patient each).

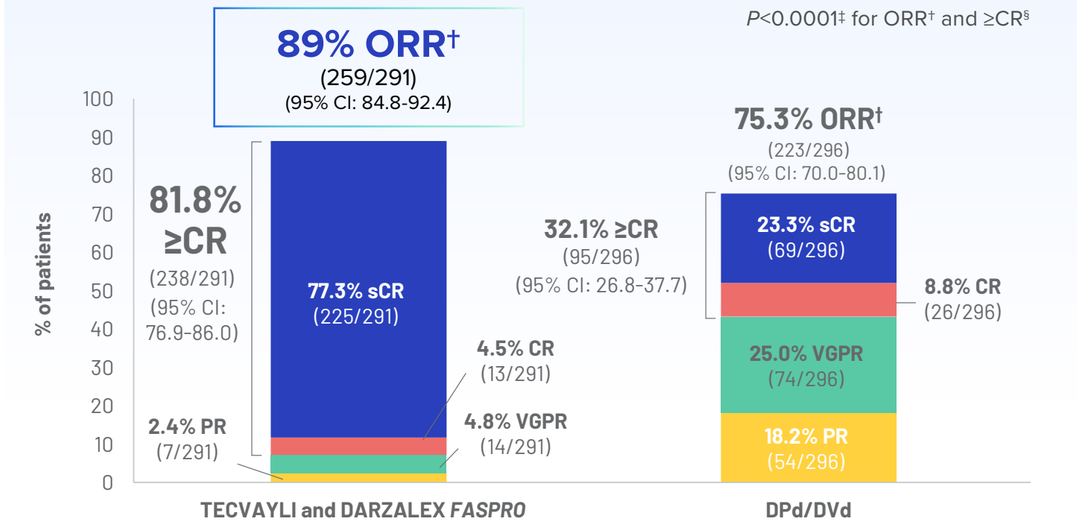
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TECVAYLI and DARZALEX *FASPRO* (daratumumab and hyaluronidase-fihj), with an ORR of 89%[1,5*]

At a median follow-up of 34.5 of months*

Response Rates: ≥CR & ORR (Key Secondary Endpoints)



The TECVAYLI and DARZALEX *FASPRO* group had ~82% of patients achieving CR or better.

*Based on intent-to-treat analysis set.
†ORR: sCR+CR+VGPR+PR.
‡Stratified Cochran-Mantel-Haenszel Chi-Squared test.
§≥CR: sCR+CR.

CI, confidence interval; CR, complete response; DPd, daratumumab, pomalidomide, and dexamethasone; DVd; daratumumab, bortezomib, and dexamethasone; ORR, overall response rate; PR, partial response; sCR, stringent complete response; VGPR, very good partial response.

IMPORTANT SAFETY INFORMATION (cont.)

WARNINGS AND PRECAUTIONS (cont.)

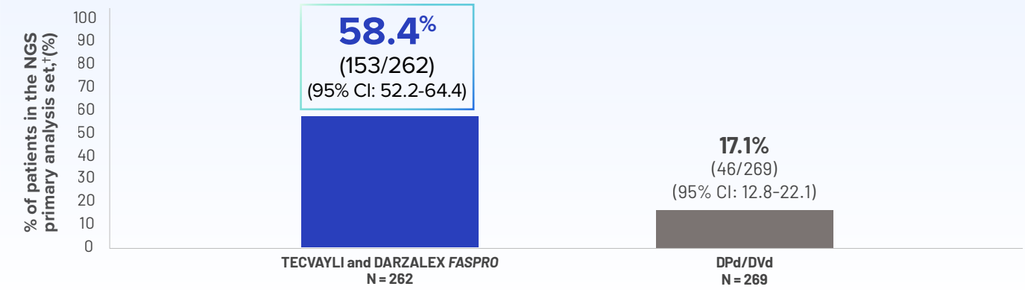
Neurologic Toxicity including Immune Effector Cell-Associated Neurotoxicity Syndrome (cont.)

In MajesTEC-1, ICANS was reported in 6% of patients who received TECVAYLI as monotherapy at the recommended dosage. Recurrent ICANS occurred in 1.8% of patients. Most patients experienced ICANS following step-up dose 1 (1.2%), step-up dose 2 (0.6%), or the initial treatment dose (1.8%). Less than 3% of patients developed first occurrence of ICANS following subsequent TECVAYLI doses. The median time to onset of ICANS was 4 (range: 2 to 8) days after the most recent dose with a median duration of 3 (range: 1 to 20) days. The most frequent clinical manifestations of ICANS reported were confusional state and dysgraphia.

The percentage of patients with MRD (10^{-5}) was 3x higher with the TECVAYLI and DARZALEX *FASPRO* group compared with DPd/DVd[1,5]

At a median follow-up of 34.5 of months*

MRD Negativity (10^{-5}) Rate† (Key Secondary Endpoint)



TECVAYLI and DARZALEX *FASPRO* demonstrated a MRD negativity rate of ~58% (95% CI: 52.2-64.4) vs 17.1% in DPd/DVd (95% CI, 12.8-22.1); *P*<0.0001.

MRD Negativity (10^{-5}) in Patients With ≥CR†

TECVAYLI + DARZALEX *FASPRO*	DPd/DVd
70.8%	53.3%
(n = 153/216; 95% CI: 64.3-76.8)	(n = 46/86; 95% CI: 42.4-64.3)

*Based on MRD NGS primary analysis set, defined as all randomized patients enrolled at sites where next generation sequencing an NGS assay was available.
†Based on a threshold of 10^{-5} using an NGS assay (clonoSEQ).
‡Fisher's exact test.

MRD, minimal residual disease; NGS, next-generation sequencing.

IMPORTANT SAFETY INFORMATION (cont.)

WARNINGS AND PRECAUTIONS (cont.)

Neurologic Toxicity including Immune Effector Cell-Associated Neurotoxicity Syndrome (cont.)

In MajesTEC-3, ICANS was reported in 1.1% of patients who received the recommended TECVAYLI dosage in combination with daratumumab and hyaluronidase-fihj, including Grade 4 ICANS in 1 patient. All events of ICANS occurred during the step-up dosing schedule. The median time to onset of ICANS was 2 (range: 1 to 3) days after the most recent dose and the median duration of ICANS was 2 (range: 1 to 2) days. The clinical manifestations of ICANS reported were amnesia, encephalopathy and delirium.

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IMPORTANT SAFETY INFORMATION FOR TECVAYLI

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WARNING: CYTOKINE RELEASE SYNDROME and NEUROLOGIC TOXICITY including IMMUNE EFFECTOR CELL-ASSOCIATED NEUROTOXICITY SYNDROME

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 risk of CRS. Withhold TECVAYLI until CRS resolves or permanently discontinue based on severity.

Neurologic toxicity, including Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS) and serious, life-threatening, or fatal reactions, can occur in patients receiving TECVAYLI. 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.

TECVAYLI is available only through a restricted program called the TECVAYLI and TALVEY® Risk Evaluation and Mitigation Strategy (REMS).

WARNINGS AND PRECAUTIONS

Cytokine Release Syndrome - TECVAYLI can cause cytokine release syndrome (CRS), including life-threatening or fatal reactions.

In the clinical trials (monotherapy and combination therapy; N=448), CRS occurred in 64% of patients who received TECVAYLI at the recommended dosage, with Grade 1 CRS occurring in 46% of patients, Grade 2 in 18%, and Grade 3 in 0.2%. Recurrent CRS occurred in 27% of patients. Most patients experienced CRS during the initial step-up dosing schedule (step-up dose 1 [37%], step-up dose 2 [32%], or the initial treatment dose [20%]). CRS first occurred following subsequent doses of TECVAYLI in 2.5% of patients. The median time to onset of CRS was 2 (range: 1 to 9) days after the most recent dose and the median duration of CRS was 2 (range: 1 to 22) days.

Clinical signs and symptoms of CRS included, but were not limited to, fever, hypoxia, chills, hypotension, sinus tachycardia, headache, and elevated liver enzymes (aspartate aminotransferase and alanine aminotransferase elevation).

Initiate therapy according to TECVAYLI step-up dosing schedule to reduce risk of CRS. Administer pretreatment medications to reduce risk of CRS and monitor patients following administration of TECVAYLI accordingly.

At the first sign of CRS, immediately evaluate the patient for hospitalization. Administer supportive care based on severity and consider further management per current practice guidelines. Withhold until CRS resolves or permanently discontinue TECVAYLI based on severity.

TECVAYLI is available only through a restricted program under a REMS.

Neurologic Toxicity including Immune Effector Cell-Associated Neurotoxicity Syndrome - TECVAYLI can cause serious, life-threatening, or fatal neurologic toxicity, including immune effector cell-associated neurotoxicity syndrome (ICANS).

In the clinical trials (monotherapy and combination therapy trials; N=448), neurologic toxicity occurred in 60% of patients who received TECVAYLI at the recommended dosage, with Grade 3 or 4 neurologic toxicity in 6%. Neurologic toxicities reported in ≥5% of patients included headache (27%), sensory neuropathy (16%), motor dysfunction (15%), insomnia (12%), encephalopathy (11%), and dizziness (8%). Fatal neurologic toxicity occurred in 0.4% of patients, including Guillain-Barré syndrome and status epilepticus (one patient each).

In MajesTEC-1, ICANS was reported in 6% of patients who received TECVAYLI as monotherapy at the recommended dosage. Recurrent ICANS occurred in 1.8% of patients. Most patients experienced ICANS following step-up dose 1 (1.2%), step-up dose 2 (0.6%), or the initial treatment dose (1.8%). Less than 3% of patients developed first occurrence of ICANS following subsequent TECVAYLI doses. The median time to onset of ICANS was 4 (range: 2 to 8) days after the most recent dose with a median duration of 3 (range: 1 to 20) days. The most frequent clinical manifestations of ICANS reported were confusional state and dysgraphia.

In MajesTEC-3, ICANS was reported in 1.1% of patients who received the recommended TECVAYLI dosage in combination with daratumumab and hyaluronidase-fihj, including Grade 4 ICANS in 1 patient. All events of ICANS occurred during the step-up dosing schedule. The median time to onset of ICANS was 2 (range: 1 to 3) days after the most recent dose and the median duration of ICANS was 2 (range: 1 to 2) days. The clinical manifestations of ICANS reported were amnesia, encephalopathy and delirium.

The onset of ICANS can be concurrent with CRS, following resolution of CRS, or in the absence of CRS.

Monitor patients for signs and symptoms of neurologic toxicity, including ICANS during TECVAYLI treatment. At the first sign of neurologic toxicity, including ICANS, immediately evaluate patient and provide supportive therapy based on severity. Withhold until neurologic toxicity resolves or permanently discontinue TECVAYLI based on severity per recommendations and consider further management per current practice guidelines.

Due to the potential for neurologic toxicity, patients receiving TECVAYLI are at risk of depressed level of consciousness.

WARNINGS AND PRECAUTIONS (cont.)

Advise patients to refrain from driving or operating heavy or potentially dangerous machinery during and for 48 hours after completion of TECVAYLI step-up dosing schedule and in the event of new onset of any neurologic toxicity symptoms until neurologic toxicity resolves.

TECVAYLI is available only through a restricted program under a REMS.

TECVAYLI and TALVEY REMS - TECVAYLI is available only through a restricted program under a REMS called the TECVAYLI and TALVEY REMS because of the risks of CRS and neurologic toxicity, including ICANS.

Hepatotoxicity - TECVAYLI can cause hepatotoxicity, including fatalities. There was one fatal case of hepatic failure in MajesTEC-1. In patients who received TECVAYLI at the recommended dosage in the clinical trials (monotherapy and combination therapy trials; N=448) elevated aspartate aminotransferase (AST) occurred in 47% of patients, with Grade 3 or 4 elevations in 2.9%. Elevated alanine aminotransferase (ALT) occurred in 48% of patients, with Grade 3 or 4 elevations in 3.8%. Elevated total bilirubin occurred in 10% of patients with Grade 3 or 4 elevations in 0.7%. Liver enzyme elevation can occur with or without concurrent CRS.

Monitor liver enzymes and bilirubin at baseline and during treatment as clinically indicated. Withhold TECVAYLI or consider permanent discontinuation of TECVAYLI based on severity.

Infections - TECVAYLI can cause severe, life-threatening, or fatal infections.

In MajesTEC-1 (N=165), in patients who received the recommended TECVAYLI dosage, serious infections, including opportunistic infections, occurred in 30% of patients, Grade 3 or 4 infections in 35% of patients, and fatal infections in 4.2% of patients.

In MajesTEC-3 (N=283), in patients who received TECVAYLI in combination with daratumumab and hyaluronidase-fihj at the recommended dosage, serious infections, including opportunistic infections, occurred in 54% of patients, Grade 3 or Grade 4 infections in 54% of patients, and fatal infections in 4.6% of patients.

Monitor patients for signs and symptoms of infection prior to and during treatment with TECVAYLI and treat appropriately. Administer prophylactic antimicrobials according to current practice guidelines.

Withhold TECVAYLI or consider permanent discontinuation of TECVAYLI based on severity.

Monitor immunoglobulin levels prior to and during treatment with TECVAYLI and administer subcutaneous or intravenous immunoglobulin (IVIG) to maintain the serum levels >400 mg/dL.

Neutropenia - TECVAYLI can cause neutropenia and febrile neutropenia. In patients who received TECVAYLI at the recommended dosage in the clinical trials (monotherapy and combination therapy trials; N=448), decreased neutrophils occurred in 88% of patients, with Grade 3 or 4 decreased neutrophils in 70%. Febrile neutropenia occurred in 6% of patients.

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

Monitor patients with neutropenia for signs of infection.

Withhold TECVAYLI based on severity.

Hypersensitivity and Other Administration Reactions - TECVAYLI can cause both systemic administration-related and local injection-site reactions.

Systemic Reactions - In patients who received the recommended TECVAYLI dosage in the clinical trials (monotherapy and combination therapy trials; N=448), 2.5% of patients experienced systemic-administration reactions, which included recurrent pyrexia and rash.

Local Reactions - In patients who received TECVAYLI at the recommended dosage in the clinical trials (monotherapy and combination therapy trials; N=448), injection-site reactions occurred in 37% of patients, with Grade 1 injection-site reactions in 29% and Grade 2 in 9%.

Withhold TECVAYLI or consider permanent discontinuation of TECVAYLI based on severity.

Embryo-Fetal Toxicity - Based on its mechanism of action, TECVAYLI may cause fetal harm when administered to a pregnant patient. Advise pregnant patients of the potential risk to the fetus. Advise females of reproductive potential to use effective contraception during treatment with TECVAYLI and for 5 months after the last dose.

ADVERSE REACTIONS

The most common adverse reactions (≥20%) in patients who received TECVAYLI monotherapy were pyrexia, CRS, musculoskeletal pain, injection site reaction, fatigue, upper respiratory tract infection, nausea, headache, pneumonia, and diarrhea. The most common adverse reactions (≥20%) in patients who received TECVAYLI in combination with daratumumab and hyaluronidase-fihj were hypogammaglobulinemia, upper respiratory tract infection, CRS, cough, diarrhea, musculoskeletal pain, COVID-19, pneumonia, injection site reaction, fatigue, pyrexia, headache, nausea, gastroenteritis, and weight decreased.

The most common Grade 3 to 4 laboratory abnormalities (≥20%) with TECVAYLI (as monotherapy or in combination with daratumumab and hyaluronidase-fihj) were decreased lymphocytes, decreased neutrophils, decreased white blood cells, decreased hemoglobin, and decreased platelets.

Please read full Prescribing Information, including Boxed WARNING, for TECVAYLI.

cp-322629v4

MajesTEC-3: Safety summary[1]

Among patients who received TECVAYLI in combination with DARZALEX *FASPRO* (daratumumab and hyaluronidase-fihj), the median exposure was 32 (range: 0.03 to 43) months. Among patients who received DPd or DVd, the median exposure was 16 (range: 0.03 to 45) months.

Serious adverse reactions occurred in 71% of patients who received TECVAYLI in combination with DARZALEX *FASPRO* compared with 62% in DPd/DVd. Serious adverse reactions reported in ≥3% of patients included pneumonia (33%), upper respiratory tract infection (15%), cytokine release syndrome (10%), COVID-19 (7%), sepsis (6%), second primary malignancy (5%), pyrexia (4.9%), febrile neutropenia (4.6%), and gastroenteritis (4.2%).

Fatal adverse reactions occurred in 2.5% of patients who received TECVAYLI in combination with DARZALEX *FASPRO* compared with 3.8% in DPd/DVd. Specific fatal reactions for TECVAYLI with DARZALEX *FASPRO* included sepsis (0.7%), pneumonia (0.4%), sudden death (0.4%), myocardial infarction (0.4%), enterovirus myocarditis (0.4%), and hemophagocytic lymphohistiocytosis (0.4%).

Adverse reactions leading to discontinuation of TECVAYLI in more than 1 patient were pneumonia (1.1%), diarrhea (0.7%), fatigue (0.7%), second primary malignancy (0.7%), upper respiratory tract infection (0.7%), and cough (0.7%).

Dosage interruptions of TECVAYLI due to an adverse reaction occurred in 94% of patients. Adverse reactions which required dosage interruption of TECVAYLI in ≥5% of patients included neutropenia (53%), upper respiratory tract infection (48%), COVID-19 (34%), pneumonia (34%), thrombocytopenia (14%), cytokine release syndrome (13%), gastroenteritis (10%), cough (10%), pyrexia (8%), diarrhea (7%), sepsis (6%), and fatigue (5%).

The most common adverse reactions (≥20%) were hypogammaglobulinemia, upper respiratory tract infection, cytokine release syndrome, cough, diarrhea, musculoskeletal pain, COVID-19, pneumonia, injection site reaction, fatigue, pyrexia, headache, nausea, gastroenteritis, and weight decreased.

The most common Grade 3 to 4 laboratory abnormalities (≥20%) were decreased lymphocytes, decreased neutrophils, decreased white blood cells, and decreased platelets.

Clinically relevant adverse reactions in <10% of patients who received TECVAYLI in combination with DARZALEX *FASPRO* included sepsis, encephalopathy, CMV infection, febrile neutropenia, and ICANS.

Please see Table 13 in the full Prescribing Information for a summary of select laboratory abnormalities (≥30%) that worsened from baseline in patients with multiple myeloma who received TECVAYLI in combination with DARZALEX *FASPRO* in MajesTEC-3.

CMV, cytomegalovirus; COVID-19, coronavirus disease 2019; CRS, cytokine release syndrome; DPd, daratumumab, pomalidomide, and dexamethasone; DVd; daratumumab, bortezomib, and dexamethasone; ICANS, immune effector cell-associated neurotoxicity syndrome.

MajesTEC-3: Safety summary (cont.)[1]

Adverse reactions (≥10%) in patients with relapsed or refractory multiple myeloma who received TECVAYLI in combination with DARZALEX *FASPRO* (daratumumab and hyaluronidase-fihj) in MajesTEC-3

Adverse Reactions	TECVAYLI in combination with DARZALEX *FASPRO* (N=283)		DPd or DVd (N=290)	
	n (%)		n (%)	
	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4
Immune system disorders				
Hypogammaglobulinemia*	84	6	60	1.4
CRS	60	0	0	0
Infections and infestations				
URTI†	79	17	62	13
COVID-19‡	45	6	33	2.1
Pneumonia§‖	42	33	35	28
Gastroenteritis‡	20	4.9	8	0.7
UTI‡	17	2.8	13	1
Herpes virus infection‡	11	2.1	6	0.3
Respiratory, thoracic, and mediastinal disorders				
Cough‡	53	0.7	24	0
Dyspnea‡	13	1.8	20	2.1
Gastrointestinal disorders				
Diarrhea‡	52	3.9	31	2.4
Nausea	23	0	12	0.3
Vomiting	17	0	7	0
Abdominal pain‡	16	0.7	13	0
Constipation	14	0	20	0.3
Musculoskeletal and connective tissue disorders				
Musculoskeletal pain‡	50	1.4	47	4.5
General disorders and administration site conditions				
Injection site reaction‡¶	41	0	4.5	0
Fatigue‡	39	3.9	40	4.1
Pyrexia	37	1.4	19	0.3
Edema‡	13	0.4	22	0.3
Nervous system disorders				
Headache	26	1.4	12	0.3
Sensory neuropathy#	17	0.7	25	0.3
Motor dysfunction**	14	0	30	1
Investigations				
Weight decreased	20	2.8	7	1.4
Metabolism and nutrition disorders				
Decreased appetite	19	1.1	7	0
Cardiac disorders				
Cardiac arrhythmia‡	11	1.1	8	2.1
Neoplasms				
Second primary malignancy‡	11	4.6	9	4.8
Vascular disorders				
Hypertension‡	11	4.6	6	2.4

ARs were graded according to NCI-CTCAE Version 5.0, with the exception of ICANS and CRS, which were graded by ASTCT 2019 consensus grading system; ARs that were considered symptoms of CRS or ICANS were not included.

*Hypogammaglobulinemia includes hypogammaglobulinemia, hypoglobulinemia; and/or patients with laboratory IgG levels below 400 mg/dL following treatment with TECVAYLI.
†Upper respiratory tract infection includes bronchitis, bronchiolitis, pharyngitis, rhinitis, sinusitis, sinobronchitis, tracheitis, and tracheobronchitis, and other related terms.
‡Includes other related terms.
§Pneumonia includes atypical pneumonia, bacterial pneumonia, fungal pneumonia, viral pneumonia, and other related terms.
‖Includes the following fatal ARs: TECVAYLI and DARZALEX *FASPRO*: Pneumonia (n=1); DPd/DVd: Pneumonia (n=2).
¶Includes injection site reactions related to TECVAYLI, DARZALEX *FASPRO*, or bortezomib.
#Sensory neuropathy includes dysaesthesia, hyperaesthesia, hypoaesthesia, paraesthesia, neuralgia, peripheral neuropathy, polyneuropathy, sciatica, and other related terms.
**Motor dysfunction includes balance disorder, dysarthria, dysphonia, gait disturbance, muscle contracture, muscle spasms, muscle spasticity, muscle twitching, muscular weakness, myopathy, peripheral motor neuropathy, tremor, and other related terms.

AR, adverse reaction; ASTCT, American Society of Transplantation and Cellular Therapy; IgG, immunoglubulin G; NCI-CTCAE, National Cancer Institute Common Terminology Criteria for Adverse Events; URTI, upper respiratory tract infection; UTI, urinary tract infection.

Please read full Important Safety Information on pages 10-11 and full Prescribing Information, including Boxed WARNING, for TECVAYLI.

TECVAYLI® (teclistamab-cqyv) Injection for subcutaneous use 10 mg/mL and 90 mg/mL

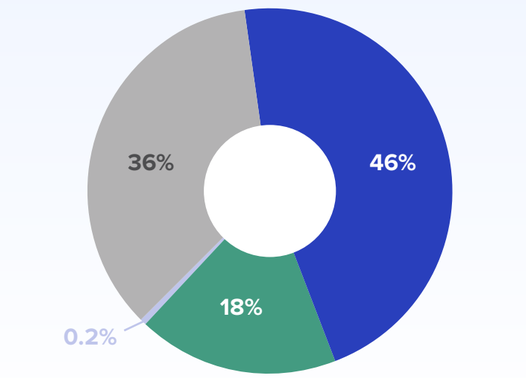
CRS & Neurotoxicity

Across 448 patients in 2 clinical trials,* most CRS events were Grades 1 and 2[1]

CRS, including life-threatening or fatal reactions, may occur in patients receiving TECVAYLI.

CRS of any grade was reported in 64% of patients receiving TECVAYLI at the recommended dosage.

Incidence of CRS



Median time to onset

2 DAYS

After most recent dose (range: 1-9 days)

Median duration

2 DAYS

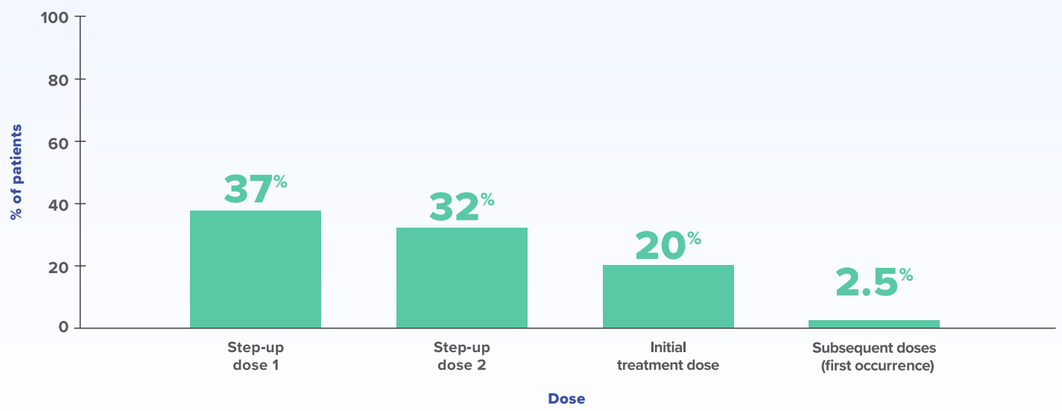
(range: 1-22 days)

*In monotherapy and combination therapy trials; N = 448.

Most CRS events occurred during the step-up dosing period.

Recurrent CRS occurred in 27% of patients.

CRS Experienced After Specific Dose of TECVAYLI



CRS, cytokine release syndrome.

At the first sign of CRS, immediately evaluate patient for hospitalization. Administer supportive care based on severity and consider further management per current practice guidelines. Withhold or permanently discontinue TECVAYLI based on severity.

TECVAYLI is available only through a restricted program under a REMS.

Signs and symptoms of CRS may include

- Fever
- Hypoxia
- Chills
- Hypotension
- Sinus tachycardia
- Headache
- Elevated liver enzymes (aspartate aminotransferase and alanine aminotransferase)

Advise patients to immediately contact their healthcare provider if they experience any signs or symptoms of CRS. Advise patients that they will be hospitalized for 48 hours after administration of both step-up dose 1 and step-up dose 2, and to remain within proximity of a healthcare facility to be monitored daily for 48 hours after the first treatment dose within the TECVAYLI step-up dosing schedule.

Manage CRS according to the recommendations in Table 4 in the full Prescribing Information and consider further management per current practice guidelines.

REMS, Risk Evaluation and Mitigation Strategy.

IMPORTANT SAFETY INFORMATION (cont.)

WARNINGS AND PRECAUTIONS (cont.)

Neurologic Toxicity including Immune Effector Cell-Associated Neurotoxicity Syndrome (cont.)

The onset of ICANS can be concurrent with CRS, following resolution of CRS, or in the absence of CRS. Monitor patients for signs and symptoms of neurologic toxicity, including ICANS during TECVAYLI treatment. At the first sign of neurologic toxicity, including ICANS, immediately evaluate patient and provide supportive therapy based on severity. Withhold until neurologic toxicity resolves or permanently discontinue TECVAYLI based on severity per recommendations and consider further management per current practice guidelines.

Due to the potential for neurologic toxicity, patients receiving TECVAYLI are at risk of depressed level of consciousness. Advise patients to refrain from driving or operating heavy or potentially dangerous machinery during and for 48 hours after completion of TECVAYLI step-up dosing schedule and in the event of new onset of any neurologic toxicity symptoms until neurologic toxicity resolves.

Please read full Important Safety Information on pages 10-11 and full Prescribing Information, including Boxed WARNING, for TECVAYLI.

TECVAYLI® (teclistamab-cqyv) Injection for subcutaneous use
10 mg/mL and 90 mg/mL

Across 448 patients in 2 clinical trials,* most neurologic toxicities were Grades 1 and 2[1]

TECVAYLI can cause serious, life-threatening, or fatal neurologic toxicity, including ICANS.

Neurologic toxicity occurred in 60% of patients who received TECVAYLI at the recommended dosage.

- Grade 3 or 4 neurologic toxicity occurred in 6% of patients
- Neurologic toxicities reported in ≥5% of patients included headache (27%), sensory neuropathy (16%), motor dysfunction (15%), insomnia (12%), encephalopathy (11%), and dizziness (8%). Fatal neurologic toxicity occurred in 0.4% of patients, including Guillain-Barré syndrome and status epilepticus (1 patient each)
- Fatal neurologic toxicity occurred in 0.4% of patients, including Guillain-Barré syndrome and status epilepticus (1 patient each)

Manage neurologic toxicities and ICANS according to the recommendations in Tables 5-6 in the full Prescribing Information and consider further management per current practice guidelines.

*In monotherapy and combination therapy trials; N = 448.

ICANS, immune effector cell-associated neurotoxicity syndrome.

In the MajesTEC-3 trial (N = 283), 1.1% of patients receiving TECVAYLI + DARZALEX *FASPRO* (daratumumab and hyaluronidase-fihj) at the recommended dosage experienced ICANS.

- Grade 4 event occurred in 1 patient
- All events of ICANS occurred during the step-up dosing schedule
- The reported clinical manifestations of ICANS were amnesia, encephalopathy, and delirium

Median time to onset	Median duration
2 DAYS	2 DAYS
After most recent dose (range: 1-3 days)	(range: 1-2 days)

IMPORTANT SAFETY INFORMATION (cont.)

WARNINGS AND PRECAUTIONS (cont.)

TECVAYLI is available only through a restricted program under a REMS.

TECVAYLI and TALVEY REMS - TECVAYLI is available only through a restricted program under a REMS called the TECVAYLI and TALVEY REMS because of the risks of CRS and neurologic toxicity, including ICANS.

Hepatotoxicity - TECVAYLI can cause hepatotoxicity, including fatalities. There was one fatal case of hepatic failure in MajesTEC-1. In patients who received TECVAYLI at the recommended dosage in the clinical trials (monotherapy and combination therapy trials; N=448) elevated aspartate aminotransferase (AST) occurred in 47% of patients, with Grade 3 or 4 elevations in 2.9%. Elevated alanine aminotransferase (ALT) occurred in 48% of patients, with Grade 3 or 4 elevations in 3.8%. Elevated total bilirubin occurred in 10% of patients with Grade 3 or 4 elevations in 0.7%. Liver enzyme elevation can occur with or without concurrent CRS.

Monitor liver enzymes and bilirubin at baseline and during treatment as clinically indicated. Withhold TECVAYLI or consider permanent discontinuation of TECVAYLI based on severity.

Infections - TECVAYLI can cause severe, life-threatening, or fatal infections.

In MajesTEC-1 (N=165), in patients who received the recommended TECVAYLI dosage, serious infections, including opportunistic infections, occurred in 30% of patients, Grade 3 or 4 infections in 35% of patients, and fatal infections in 4.2% of patients.

The onset of ICANS can be concurrent with CRS, following resolution of CRS, or in the absence of CRS.

Due to the potential for neurologic toxicity, patients receiving TECVAYLI are at risk of depressed level of consciousness. Advise patients to refrain from driving or operating heavy or potentially dangerous machinery during and for 48 hours after completing TECVAYLI step-up dosing schedule and in the event of new onset of any neurologic toxicity symptoms until neurologic toxicity resolves.

Monitor patients for signs and symptoms of neurologic toxicity during treatment. At first sign of neurologic toxicity, including ICANS, immediately evaluate patient and provide supportive therapy based on severity. Withhold until neurologic toxicity resolves or permanently discontinue TECVAYLI based on severity per recommendations and consider further management per current practice guidelines.

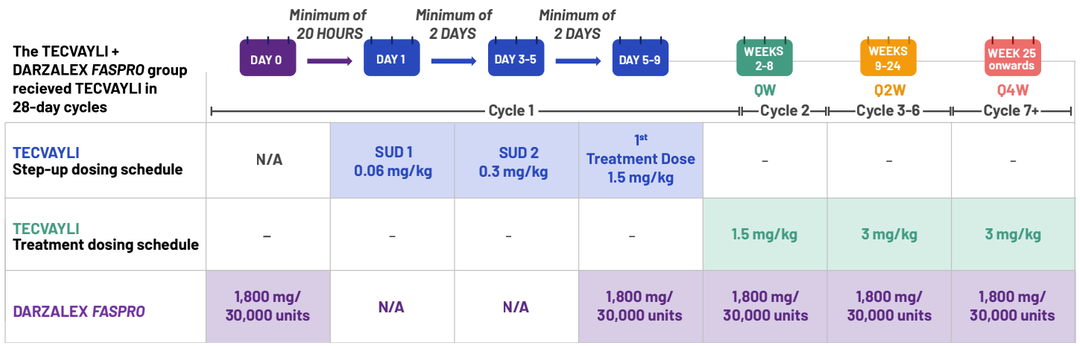
CRS, cytokine release syndrome.

Please read full Important Safety Information on pages 10-11 and full Prescribing Information, including Boxed WARNING, for TECVAYLI.

TECVAYLI® (teclistamab-cqyv) Injection for subcutaneous use
10 mg/mL and 90 mg/mL

MajesTEC-3 Dosing

TECVAYLI + DARZALEX *FASPRO* (daratumumab and hyaluronidase-fihj) offers Q4W dosing from Week 25 onward



See Table 3 in the full Prescribing Information for recommendations on restarting TECVAYLI after dose delays.

Step-up dosing schedule

- The step-up dosing schedule is a component of the recommended TECVAYLI dosage but is not applicable for the DARZALEX *FASPRO* dosing
- Step-up dose 1 must be administered 20 hours or more after DARZALEX *FASPRO*
- Step-up dose 2 may be given between 2 to 4 days after step-up dose 1 and, if ARs occur, may be given up to 7 days after step-up dose 1 to allow for resolution of ARs
- The first treatment dose (1.5 mg/kg) may be given between 2 to 4 days after step-up dose 2 and, if ARs occur, may be given up to 7 days after step-up dose 2 to allow for resolution of ARs
- Administer TECVAYLI at least 3 hours after DARZALEX *FASPRO* for the first treatment dose

Treatment dosing schedule

After step-up dosing, patients will receive weekly, bi-weekly, and every-4-week treatment doses.

- Administer TECVAYLI at least 15 minutes after DARZALEX *FASPRO* for all subsequent treatment doses
- Maintain a minimum of 5 days between 1.5 mg/kg QW
- Maintain a minimum of 12 days between 3 mg/kg Q2W
- Maintain a minimum of 25 days between 3 mg/kg Q4W

For dosage and administration instructions for DARZALEX *FASPRO*, refer to its full Prescribing Information for the recommended dosage when used as a monotherapy.

AR, adverse reaction; QW, every week; Q2W, every two weeks; Q4W, every four weeks; SUD, step-up dosing.

IMPORTANT SAFETY INFORMATION (cont.)

WARNINGS AND PRECAUTIONS (cont.)

Infections (cont.)

In MajesTEC-3 (N=283), in patients who received TECVAYLI in combination with daratumumab and hyaluronidase-fihj at the recommended dosage, serious infections, including opportunistic infections, occurred in 54% of patients, Grade 3 or Grade 4 infections in 54% of patients, and fatal infections in 4.6% of patients.

Monitor patients for signs and symptoms of infection prior to and during treatment with TECVAYLI and treat appropriately. Administer prophylactic antimicrobials according to current practice guidelines.

Withhold TECVAYLI or consider permanent discontinuation of TECVAYLI based on severity.

Important dosing information

- TECVAYLI and DARZALEX *FASPRO* are administered via subcutaneous injection
- Administer TECVAYLI subcutaneously according to the step-up dosing schedule in Table 1 in the full Prescribing Information to reduce the incidence and severity of CRS

Due to the risk of CRS and neurologic toxicity, including ICANS, patients should be hospitalized for 48 hours after administration of both step-up dose 1 and step-up dose 2. Instruct patients to remain within proximity of a healthcare facility and monitor them daily for 48 hours after the first treatment dose within the TECAVYLI step-up dosing schedule.

- Administer pretreatment medications with TECVAYLI as recommended
- TECVAYLI and DARZALEX *FASPRO* should be administered until disease progression or unacceptable toxicity
- The dosage of TECVAYLI is based on actual body weight. Please refer to Tables 8-11 in the full Prescribing Information to determine the dosage based on predetermined weight ranges
- For pre-medication and post-medication requirements for management of administration-related reactions and other considerations for DARZALEX *FASPRO*, see the Prescribing Information for DARZALEX *FASPRO*

SELECT IMPORTANT SAFETY INFORMATION FOR DARZALEX *FASPRO*®

Both systemic administration-related reactions, including severe or life-threatening reactions, and local injection-site reactions can occur with DARZALEX *FASPRO*®. Fatal reactions have been reported with daratumumab-containing products, including DARZALEX *FASPRO*®.

Please see Important Safety Information on pages 24-25 and click here to read full Prescribing Information for DARZALEX *FASPRO*®.

CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome.

IMPORTANT SAFETY INFORMATION (cont.)

WARNINGS AND PRECAUTIONS (cont.)

Infections (cont.)

Monitor immunoglobulin levels prior to and during treatment with TECVAYLI and administer subcutaneous or intravenous immunoglobulin (IVIG) to maintain the serum levels >400 mg/dL.

Neutropenia - TECVAYLI can cause neutropenia and febrile neutropenia. In patients who received TECVAYLI at the recommended dosage in the clinical trials (monotherapy and combination therapy trials; N=448), decreased neutrophils occurred in 88% of patients, with Grade 3 or 4 decreased neutrophils in 70%. Febrile neutropenia occurred in 6% of patients.

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

Monitor patients with neutropenia for signs of infection.

Withhold TECVAYLI based on severity.

Please read full Important Safety Information on pages 10-11 and full Prescribing Information, including Boxed WARNING, for TECVAYLI.

TECVAYLI® (teclistamab-cqyv) Injection for subcutaneous use
10 mg/mL and 90 mg/mL

Dosing Information (cont.)

Pretreatment medications[1]

Prior to starting treatment with TECVAYLI

Consider initiation of antiviral prophylaxis to prevent herpes zoster reactivation per guidelines.

1 to 3 hours before each dose of the TECVAYLI step-up dosing schedule (step-up doses 1 and 2, and the first treatment dose)

Administer the following pretreatment medications of the TECVAYLI step-up dosing schedule to reduce the risk of CRS.

- Corticosteroid (oral or intravenous dexamethasone 16 mg)
- Histamine-1 (H1) receptor antagonist (oral or intravenous diphenhydramine 50 mg or equivalent)
- Antipyretics (oral or intravenous acetaminophen 650 mg to 1,000 mg)

Prior to administration of subsequent treatment doses

The following patients may need pretreatent medications administered before subsequent doses of TECVAYLI:

- Patients who repeat doses within the step-up dosing schedule following a dose delay
- Patients who experienced CRS following the prior dose of TECVAYLI

Review recommended TECVAYLI dosage modifications for other adverse reactions as outlined in Table 7 in the full Prescribing Information.

CRS, cytokine release syndrome.

IMPORTANT SAFETY INFORMATION (cont.)
WARNINGS AND PRECAUTIONS (cont.)

Hypersensitivity and Other Administration Reactions - TECVAYLI can cause both systemic administration-related and local injection-site reactions.

Systemic Reactions - In patients who received the recommended TECVAYLI dosage in the clinical trials (monotherapy and combination therapy trials; N=448), 2.5% of patients experienced systemic-administration reactions, which included recurrent pyrexia and rash.

Local Reactions - In patients who received TECVAYLI at the recommended dosage in the clinical trials (monotherapy and combination therapy trials; N=448), injection-site reactions occurred in 37% of patients, with Grade 1 injection-site reactions in 29% and Grade 2 in 9%.

Dosage modifications for ARs[1]

Dosage reductions of TECVAYLI are not recommended.

Refer to DARZALEX *FASPRO* (daratumumab and hyaluronidase-fihj) Prescribing Information for information about dosage modifications for DARZALEX *FASPRO*.

Dosage delays may be required to manage toxicities related to TECVAYLI.

See Tables 4-6 for recommended actions for ARs of CRS, neurologic toxicity (excluding ICANS), and ICANS. See Table 7 for recommended actions for other adverse reactions following administration of TECVAYLI.

Permanent discontinuation of TECVAYLI due to adverse reactions occurred in 6% of patients.

- ARs leading to discontinuation of TECVAYLI in more than 1 patient were pneumonia (1.1%), diarrhea (0.7%), fatigue (0.7%), second primary malignancy (0.7%), upper respiratory tract infection (0.7%), and cough (0.7%)

MajesTEC-3 Analysis (N=283)

Percentage of patients who permanently discontinued TECVAYLI due to adverse reactions.



Review recommendations for restarting TECVAYLI after dosage delays as outlined in Table 3 in the full Prescribing Information.

AR, adverse reaction.

IMPORTANT SAFETY INFORMATION (cont.)
WARNINGS AND PRECAUTIONS (cont.)

Hypersensitivity and Other Administration Reactions (cont.)

Withhold TECVAYLI or consider permanent discontinuation of TECVAYLI based on severity.

Embryo-Fetal Toxicity - Based on its mechanism of action, TECVAYLI may cause fetal harm when administered to a pregnant patient. Advise pregnant patients of the potential risk to the fetus. Advise females of reproductive potential to use effective contraception during treatment with TECVAYLI and for 5 months after the last dose.

Please read full Important Safety Information on pages 10-11 and full Prescribing Information, including Boxed WARNING, for TECVAYLI.

TECVAYLI® (teclistamab-cqyv) Injection for subcutaneous use
10 mg/mL and 90 mg/mL

Prepare and administer TECVAYLI in accordance with the full USPI[1]

Preparation and administration

- TECVAYLI is intended for subcutaneous use by a healthcare provider only
- TECVAYLI should be administered by a healthcare provider with adequate medical personnel and appropriate medical equipment to manage severe reactions, including CRS and ICANS
- Do not combine TECVAYLI vials of different concentrations to achieve treatment dose
- Use aseptic technique to prepare and administer TECVAYLI

Preparation of TECVAYLI

1. Remove the appropriate strength TECVAYLI vial from refrigerated storage [2 °C to 8 °C (36 °F to 46 °F)].
2. Once removed from refrigerated storage, equilibrate TECVAYLI to ambient temperature [15 °C to 30 °C (59 °F to 86 °F)] for at least 15 minutes. Do not warm TECVAYLI in any other way.
3. Once equilibrated, gently swirl the vial for approximately 10 seconds to mix. Do not shake.
4. Withdraw the required injection volume of TECVAYLI from the vial(s) into an appropriately sized syringe using a transfer needle.
5. Replace the transfer needle with an appropriately sized needle for injection.

Each injection volume should not exceed 2 mL. Divide doses requiring greater than 2 mL equally into multiple syringes.

Use TECVAYLI with stainless steel injection needles and polypropylene or polycarbonate syringe material.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. Do not use if the solution is discolored or cloudy, or if foreign particles are present.

Administration of TECVAYLI and disposal

- 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 (eg, 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
- Any unused product or waste material should be disposed in accordance with local requirements

CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome; USPI, United States Prescribing Information.

TECVAYLI dosage strengths

TECVAYLI injection is a sterile, preservative-free, clear to slightly opalescent, colorless to light yellow solution supplied as follows:



One 30 mg/3 mL (10 mg/mL) single-dose vial in a carton (NDC: 57894-449-01)



One 153 mg/1.7 mL (90 mg/mL) single-dose vial in a carton (NDC: 57894-450-01)

TECVAYLI storage and handling

If the prepared dosing syringe(s) of TECVAYLI is not used immediately, store syringe(s) at 2 °C to 8 °C (36 °F to 46 °F) or at ambient temperature 15 °C to 30 °C (59 °F to 86 °F) for a maximum of 20 hours. Discard syringe(s) after 20 hours, if not used.

Store refrigerated at 2 °C to 8 °C (36 °F to 46 °F) in the original carton to protect from light. Do not freeze.

NDC, National Drug Code.

IMPORTANT SAFETY INFORMATION (cont.)

WARNINGS AND PRECAUTIONS (cont.)

ADVERSE REACTIONS

The most common adverse reactions (≥20%) in patients who received TECVAYLI monotherapy were pyrexia, CRS, musculoskeletal pain, injection site reaction, fatigue, upper respiratory tract infection, nausea, headache, pneumonia, and diarrhea. The most common adverse reactions (≥20%) in patients who received TECVAYLI in combination with daratumumab and hyaluronidase-fihj were hypogammaglobulinemia, upper respiratory tract infection, CRS, cough, diarrhea, musculoskeletal pain, COVID-19, pneumonia, injection site reaction, fatigue, pyrexia, headache, nausea, gastroenteritis, and weight decreased.

The most common Grade 3 to 4 laboratory abnormalities (≥20%) with TECVAYLI (as monotherapy or in combination with daratumumab and hyaluronidase-fihj) were decreased lymphocytes, decreased neutrophils, decreased white blood cells, decreased hemoglobin, and decreased platelets.

Please read full Important Safety Information on pages 10-11 and full Prescribing Information, including Boxed WARNING, for TECVAYLI.

TECVAYLI® (teclistamab-cqyv) Injection for subcutaneous use
10 mg/mL and 90 mg/mL

IMPORTANT SAFETY INFORMATION for DARZALEX *FASPRO*

INDICATIONS

DARZALEX *FASPRO*® (daratumumab and hyaluronidase-fihj) is indicated for the treatment of adult patients with multiple myeloma:

- In combination with bortezomib, lenalidomide, and dexamethasone for induction and consolidation in newly diagnosed patients who are eligible for autologous stem cell transplant
- In combination with bortezomib, lenalidomide, and dexamethasone in newly diagnosed patients who are ineligible for autologous stem cell transplant
- In combination with bortezomib, melphalan, and prednisone in newly diagnosed patients who are ineligible for autologous stem cell transplant
- In combination with lenalidomide and dexamethasone in newly diagnosed patients who are ineligible for autologous stem cell transplant and in patients with relapsed or refractory multiple myeloma who have received at least one prior therapy
- In combination with bortezomib, thalidomide, and dexamethasone in newly diagnosed patients who are eligible for autologous stem cell transplant
- In combination with pomalidomide and dexamethasone in patients who have received at least one prior line of therapy including lenalidomide and a proteasome inhibitor (PI)
- In combination with carfilzomib and dexamethasone in patients with relapsed or refractory multiple myeloma who have received one to three prior lines of therapy
- In combination with bortezomib and dexamethasone in patients who have received at least one prior therapy
- As monotherapy in patients who have received at least three prior lines of therapy including a PI and an immunomodulatory agent or who are double refractory to a PI and an immunomodulatory agent

DARZALEX *FASPRO*® as monotherapy is indicated for the treatment of adult patients with high-risk smoldering multiple myeloma.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

DARZALEX *FASPRO*® is contraindicated in patients with a history of severe hypersensitivity to daratumumab, hyaluronidase, or any of the components of the formulation.

WARNINGS AND PRECAUTIONS

Hypersensitivity and Other Administration Reactions

Both systemic administration-related reactions, including severe or life-threatening reactions, and local injection-site reactions can occur with DARZALEX *FASPRO*®. Fatal reactions have been reported with daratumumab-containing products, including DARZALEX *FASPRO*®.

Systemic Reactions

In a pooled safety population of 1446 patients with multiple myeloma (N=1235) or light chain (AL) amyloidosis (N=193) who received DARZALEX *FASPRO*® as monotherapy or as part of a combination therapy, 7% of patients experienced a systemic administration-related reaction (Grade 2: 3%, Grade 3: 0.8%, Grade 4: 0.1%). In patients with high-risk smoldering multiple myeloma (N=193), systemic administration-related reactions occurred in 17% of patients in AQUILA (Grade 2: 7%, Grade 3: 1%).

In all patients (N=1639), systemic administration-related reactions occurred in 7% of patients with the first injection, 0.5% with the second injection, and cumulatively 1% with subsequent injections. The median time to onset was 3.2 hours (range: 4 minutes to 3.5 days). Of the 283 systemic administration-related reactions that occurred in 135 patients, 240 (85%) occurred on the day of DARZALEX *FASPRO*® administration. Delayed systemic administration-related reactions have occurred in 1% of the patients.

Severe reactions included hypoxia, dyspnea, hypertension, tachycardia, and ocular adverse reactions, including choroidal effusion, acute myopia, and acute angle closure glaucoma. Other signs and symptoms of systemic administration-related reactions may include respiratory symptoms, such as bronchospasm, nasal congestion, cough, throat irritation, allergic rhinitis, and wheezing, as well as anaphylactic reaction, pyrexia, chest pain, pruritus, chills, vomiting, nausea, hypotension, and blurred vision.

Pre-medicate patients with histamine-1 receptor antagonist, acetaminophen, and corticosteroids. Monitor patients for systemic administration-related reactions, especially following the first and second injections. For anaphylactic reaction or life-threatening (Grade 4) administration-related reactions, immediately and permanently discontinue DARZALEX F*ASPRO*®. Consider administering corticosteroids and other medications after the administration of DARZALEX *FASPRO*® depending on dosing regimen and medical history to minimize the risk of delayed (defined as occurring the day after administration) systemic administration-related reactions.

Ocular adverse reactions, including acute myopia and narrowing of the anterior chamber angle due to ciliochoroidal effusions with potential for increased intraocular pressure or glaucoma, have occurred with daratumumab-containing products. If ocular symptoms occur, interrupt DARZALEX *FASPRO*® and seek immediate ophthalmologic evaluation prior to restarting DARZALEX *FASPRO*®.

Local Reactions

In this pooled safety population of 1446 patients with multiple myeloma (N=1253) or light chain amyloidosis (N=193), injection-site reactions occurred in 8% of patients, including Grade 2 reactions in 1.1%. The most frequent (>1%) injection-site reactions were injection site erythema and injection site rash.

WARNINGS AND PRECAUTIONS (cont.)

In patients with high-risk smoldering multiple myeloma (N=193), injection-site reactions occurred in 28% of patients, including Grade 2 reactions in 3%. These local reactions occurred a median of 6 minutes (range: 0 minutes to 6.5 days) after starting administration of DARZALEX *FASPRO*®. Monitor for local reactions and consider symptomatic management.

Infections

DARZALEX *FASPRO*® can cause serious, life-threatening, or fatal infections. In patients who received DARZALEX *FASPRO*® in a pooled safety population including patients with smoldering multiple myeloma and light chain (AL) amyloidosis (N=1639), serious infections, including opportunistic infections, occurred in 24% of patients, Grade 3 or 4 infections occurred in 22%, and fatal infections occurred in 2.5%. The most common type of serious infection reported was pneumonia (8.5%).

Monitor patients for signs and symptoms of infection prior to and during treatment with DARZALEX *FASPRO*® and treat appropriately. Administer prophylactic antimicrobials according to guidelines.

Neutropenia

Daratumumab may increase neutropenia induced by background therapy. Monitor complete blood cell counts periodically during treatment according to manufacturer's prescribing information for background therapies. Monitor patients with neutropenia for signs of infection. Consider withholding DARZALEX *FASPRO*® until recovery of neutrophils. In lower body weight patients receiving DARZALEX *FASPRO*®, higher rates of Grade 3-4 neutropenia were observed.

Thrombocytopenia

Daratumumab may increase thrombocytopenia induced by background therapy. Monitor complete blood cell counts periodically during treatment according to manufacturer's prescribing information for background therapies. Consider withholding DARZALEX *FASPRO*® until recovery of platelets.

Embryo-Fetal Toxicity

Based on the mechanism of action, DARZALEX *FASPRO*® can cause fetal harm when administered to a pregnant woman. DARZALEX *FASPRO*® may cause depletion of fetal immune cells and decreased bone density. Advise pregnant women of the potential risk to a fetus. Advise females with reproductive potential to use effective contraception during treatment with DARZALEX *FASPRO*® and for 3 months after the last dose.

The combination of DARZALEX *FASPRO*® with lenalidomide, thalidomide, or pomalidomide is contraindicated in pregnant women because lenalidomide, thalidomide, and pomalidomide may cause birth defects and death of the unborn child. Refer to the lenalidomide, thalidomide, or pomalidomide prescribing information on use during pregnancy.

Interference With Serological Testing

Daratumumab binds to CD38 on red blood cells (RBCs) and results in a positive indirect antiglobulin test (indirect Coombs test). Daratumumab-mediated positive indirect antiglobulin test may persist for up to 6 months after the last daratumumab administration. Daratumumab bound to RBCs masks detection of antibodies to minor antigens in the patient's serum. The determination of a patient's ABO and Rh blood type are not impacted.

Notify blood transfusion centers of this interference with serological testing and inform blood banks that a patient has received DARZALEX *FASPRO*®. Type and screen patients prior to starting DARZALEX *FASPRO*®.

Interference With Determination of Complete Response

Daratumumab is a human immunoglobulin G (IgG) kappa monoclonal antibody that can be detected on both the serum protein electrophoresis (SPE) and immunofixation (IFE) assays used for the clinical monitoring of endogenous M-protein. This interference can impact the determination of complete response and of disease progression in some DARZALEX *FASPRO*®-treated patients with IgG kappa myeloma protein.

ADVERSE REACTIONS

In multiple myeloma, the most common adverse reaction (≥20%) with DARZALEX *FASPRO*® monotherapy is upper respiratory tract infection. The most common adverse reactions with combination therapy (≥20% for any combination) include fatigue, nausea, diarrhea, dyspnea, sleep disorder, headache, rash, renal impairment, motor dysfunction, pyrexia, cough, muscle spasms, back pain, vomiting, hypertension, musculoskeletal pain, decreased appetite, urinary tract infection, abdominal pain, upper respiratory tract infection, peripheral neuropathy, peripheral sensory neuropathy, constipation, pneumonia, edema, dizziness, bruising, and COVID-19.

The most common adverse reactions (≥20%) in patients with high-risk smoldering multiple myeloma who received DARZALEX *FASPRO*® monotherapy are upper respiratory tract infection, musculoskeletal pain, fatigue, diarrhea, rash, sleep disorder, sensory neuropathy, and injection site reactions.

The most common hematology laboratory abnormalities (≥40%) with DARZALEX *FASPRO*® are decreased leukocytes, decreased lymphocytes, decreased neutrophils, decreased platelets, and decreased hemoglobin.

Please click here to read full Prescribing Information for DARZALEX *FASPRO*®.

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Operationalizing Bispecifics

The following section provides information taken from resources and professional experience. It is intended to help you achieve RRMM bispecific operational readiness in your facility.

This information, sample milestones, and suggestions to help you achieve operational readiness in your facility are recommendations, but they are not mandatory items for operationalizing bispecific treatment for RRMM. It is recommended that you review this information and adapt it to your own facility.

RRMM, relapsed or refractory multiple myeloma.

Ensuring operational readiness to administer therapy requires several steps unique to bispecifics

The **operational champion** is a designated healthcare provider who facilitates the implementation of RRMM bispecifics.[6] Responsibilities may include coordinating multidisciplinary team requirements and training, overseeing SOP development, and owning the REMS process. *Oftentimes, the responsibilities of an **operational champion** coincide with that of pharmacy staff.*

Identify an operational champion to facilitate key activities for a multidisciplinary team.



Complete REMS

Establish AR Protocols

Align With Partner Sites

Additional activities for establishing outpatient treatment are similar to other RRMM therapies:

- Staff training
- Patient education
- Drug procurement
- Billing and coding

AR, adverse reaction; REMS, Risk Evaluation and Mitigation Strategies; SOP, standard operating procedure.

Complete REMS[7-9]

Thoroughly review the specific REMS requirements for each bispecific antibody therapy, as they may vary.

Pharmacies and healthcare settings must be certified to dispense bispecific antibodies that have a REMS requirement. **REMS enrollment for bispecifics can be completed in 4 steps.**

1. Designate an authorized representative for the pharmacy and healthcare setting
2. Have the authorized representative review the Pharmacy and Healthcare Setting Training Program
3. Have the authorized representative complete the Pharmacy and Healthcare Setting Enrollment Form and submit it to the REMS
4. Train all relevant staff involved in dispensing bispecifics with REMS requirements using the Pharmacy and Healthcare Setting Training Program

Providers must be certified to prescribe bispecifics that have a REMS requirement. **Become a certified prescriber of bispecifics in 3 steps.**

1. Review the Prescriber Training Program and AR Management Guide
2. Complete the REMS Knowledge Assessment and submit it to the REMS program
3. Complete the Prescriber Enrollment Form and submit it to the REMS program

AR, adverse reaction; REMS, Risk Evaluation and Mitigation Strategies.

Define adverse reaction protocols for team preparedness[10,11]

Ensure that providers are familiar with product AR profiles.

Risks include

- CRS
- Neurologic toxicity, including ICANS
- Additional ARs, both hematologic and non-hematologic

Tailor your monitoring and management protocols

- Define patient monitoring protocols
- Develop a centralized repository of treatment protocols and algorithms for toxicity management
- Establish an on-call physician to help manage CRS and neurotoxicity, including ICANS

SUD Considerations

- Define prophylaxis and pretreatment protocols for ARs
- Confirm the availability of supportive therapies in the event of ARs

Deploy stakeholder education

- Train staff on protocols and establish a plan for periodic refresher training
- Educate patients and care partners on AR monitoring and what to do in case of an emergency

SUD Considerations

Deploy bispecifics training to broader care team and specialists (eg, ED, hospitalists, neurologists) who may be involved in step-up dosing administration, monitoring, and AR management.

Considerations for Protocol Development

- Leverage and adjust your center's existing protocols for treatments with similar AR profiles
- Use a treatment center locator to identify and contact peer sites and gain insight into their protocols
- Utilize published resources and online support as a starting point for protocols

See page 16 to view some of the protocol resources available.

CRS, cytokine release syndrome; ED, emergency department; ICANS, immune effector cell-associated neurotoxicity syndrome; SUD, step-up dosing.

Determine where the patient will receive bispecific therapy in each treatment phase[11]

	Diagnosis & treatment choice	SUD	Treatment dosing
1 Center	1 care center for diagnosis, SUD, and treatment dosing		
2 Centers	Facility A refers patient for SUD (T)	Facility B provides SUD (T)	Patient returns to Facility A for treatment dosing
Multi-center	Facility A refers patient for SUD (T)	Facility B provides SUD (T)	Patient goes to Facility C for treatment dosing

It is crucial to assess your organization's infrastructure and ability to support patients through both SUD and treatment dosing.

(T) = transition site of care; SUD, step-up dosing.

When a patient stays at your care center from start to finish, define the patient-specific plan for SUD and ensure patient readiness.

Treatment Plan Considerations

- Coordinate with the healthcare team and the patient to develop a plan for hospitalization and schedule SUD
- Define the individual patient plan for monitoring after each SUD
- Educate patient and caregiver on the therapy, including AR monitoring, plans of action, and logistical support
- Ensure that the care team is prepared in the event of ARs
- Monitor the patient for ARs for 48 hours following administration of each SUD

If referring your patient to a center that provides SUD, align with collaborating sites of care to help ensure a seamless treatment experience[11,12]

1 Identify the appropriate center that provides SUD

This may be an existing collaborating site. Treatment locators can help you find nearby certified physicians who have indicated they administer SUD

2 Define responsibilities for each care center

- Conduct BI/PA & benefit transfers
- Develop treatment plan
- Inform patient of estimated costs/ financials
- Review treatment plan with patient*
- Schedule patient
- Connect patient with a Care Navigator
- Follow-up care/ rehospitalization
- Provide patient with wallet cards
- Provide social work support
- Provide care partner support and education

3 Align on transfer processes

- What information needs to be transferred and who is responsible for transferring it?
- Are the EHR systems compatible? How will receipt of information be confirmed?
- Who will ensure scheduling of dose at the next site to ensure continuity of care?
- How will peer-to-peer conversations be initiated when transferring patients?

Consider creating a standardized agreement for collaboration among institutions.

*Ensure the patient understands potential toxicities and complications of treatment.

AR, adverse reaction; BI/PA, benefits investigation/prior authorization; EHR, electronic health record; SUD, step-up dosing.

Protocol resources may help prepare your team to operationalize bispecifics

Select Protocol Resources*

IMWG Consensus Guidelines and Recommendations for Optimal Use of T-cell-Engaging Bispecific Antibodies in Multiple Myeloma

NCODA Immunotherapy Hub Example SOPs and Documents

Select Recommendations for Managing Adverse Reactions*

American Oncology Network

Management recommendations for CRS/ICANS

Consensus for CRS and neurotoxicity, including ICANS

Management recommendations for CRS/ICANS

Mayo Stratification for Myeloma and Risk-Adapted Therapy

Management recommendations for CRS/ICANS

Consensus recommendations from an expert panel

Monitoring, prophylaxis, and treatment of infections in patients with RRMM receiving bispecific antibody therapy

*The links to resources above may contain data, conclusions, and recommendations that do not conform to the FDA-approved labeling for bispecific therapies from Johnson & Johnson. The opinions expressed in the links above do not necessarily reflect those of Johnson & Johnson. Bispecific therapies from Johnson & Johnson should be used only as specified in the Prescribing Information.

CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome; IMWG, International Myeloma Working Group; NCODA, Network for Collaborative Oncology Development & Advancement; RRMM, relapsed or refractory multiple myeloma; SOP, standard operating procedure.

Manufacturers may have resources to help accelerate operational readiness for your facility, staff, and patients

Facility Readiness

- EHR order set guides
- Bispecific operations guides
- Operational checklists
- Product-specific billing and coding flashcards
- Product-specific access and reimbursement guides

Provider & Care Team Readiness

- Product-specific treatment management guides
- Product-specific clinical pharmacist guides
- Treatment center locators

Patient & Care Partner Readiness

- Patient teaching tools
- Product-specific starting treatment guides
- Product-specific patient starter kits
- Product-specific patient brochures
- Product-specific caregiver brochures

Visit BispecificsGuide.com for information on preparing your organization across the 3 states of operational readiness.

Connect with a local Johnson & Johnson representative for more information

EHR, electronic health record.

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