

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use DARZALEX FASPRO safely and effectively. See full prescribing information for DARZALEX FASPRO.

DARZALEX FASPRO® (daratumumab and hyaluronidase-fihj) injection, for subcutaneous use
Initial U.S. Approval: 2020

RECENT MAJOR CHANGES

Indications and Usage (1.1, 1.2)	01/2021
Dosage and Administration (2.2, 2.3)	01/2021
Warnings and Precautions (5.1, 5.2)	01/2021

INDICATIONS AND USAGE

DARZALEX FASPRO is a combination of daratumumab, a CD38-directed cytolytic antibody, and hyaluronidase, an endoglycosidase, indicated for the treatment of adult patients with:

- multiple myeloma in combination with bortezomib, melphalan and prednisone in newly diagnosed patients who are ineligible for autologous stem cell transplant
- multiple myeloma 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
- multiple myeloma in combination with bortezomib, thalidomide, and dexamethasone in newly diagnosed patients who are eligible for autologous stem cell transplant
- multiple myeloma in combination with bortezomib and dexamethasone in patients who have received at least one prior therapy
- multiple myeloma as monotherapy, in patients who have received at least three prior lines of therapy including a proteasome inhibitor (PI) and an immunomodulatory agent or who are double-refractory to a PI and an immunomodulatory agent.
- light chain (AL) amyloidosis in combination with bortezomib, cyclophosphamide and dexamethasone in newly diagnosed patients. This indication is approved under accelerated approval based on response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s). (1.2)

Limitations of Use:

- DARZALEX FASPRO is not indicated and is not recommended for the treatment of patients with light chain (AL) amyloidosis who have NYHA Class IIIB or Class IV cardiac disease or Mayo Stage IIIB outside of controlled clinical trials (1.2)

DOSAGE AND ADMINISTRATION

For subcutaneous use only.

- Pre-medicate with a corticosteroid, acetaminophen and a histamine-1 receptor antagonist. (2.5)
- The recommended dosage of DARZALEX FASPRO is (1,800 mg daratumumab and 30,000 units hyaluronidase) administered subcutaneously into the abdomen over approximately 3 to 5 minutes according to recommended schedule. (2.2, 2.3)
- Administer post-medications as recommended. (2.5)

DOSAGE FORMS AND STRENGTHS

- Injection:** 1,800 mg daratumumab and 30,000 units hyaluronidase per 15 mL (120 mg and 2,000 units/mL) solution in a single-dose vial (3)

CONTRAINDICATIONS

Patients with a history of severe hypersensitivity to daratumumab or any of the components of the formulation. (4)

WARNINGS AND PRECAUTIONS

- Hypersensitivity and Other Administration Reactions:** Permanently discontinue DARZALEX FASPRO for life-threatening reactions. (5.1)
- Cardiac Toxicity in Patients with Light Chain (AL) Amyloidosis:** Monitor patients with cardiac involvement more frequently for cardiac adverse reactions and administer supportive care as appropriate. (5.2)
- Neutropenia:** Monitor complete blood cell counts periodically during treatment. Monitor patients with neutropenia for signs of infection. Consider withholding DARZALEX FASPRO to allow recovery of neutrophils. (5.3)
- Thrombocytopenia:** Monitor complete blood cell counts periodically during treatment. Consider withholding DARZALEX FASPRO to allow recovery of platelets. (5.4)
- Embryo-Fetal Toxicity:** Can cause fetal harm. Advise pregnant women of the potential risk to a fetus and advise females of reproductive potential to use effective contraception (5.5, 8.1, 8.3).
- Interference with cross-matching and red blood cell antibody screening:** Type and screen patients prior to starting treatment. Inform blood banks that a patient has received DARZALEX FASPRO. (5.6, 7.1)

ADVERSE REACTIONS

- The most common adverse reaction ($\geq 20\%$) in patients with multiple myeloma who received DARZALEX FASPRO monotherapy is upper respiratory tracts infection. (6.1)
- The most common adverse reactions ($\geq 20\%$) in patients with multiple myeloma who received D-VMP are upper respiratory tract infection, constipation, nausea, fatigue, pyrexia, peripheral sensory neuropathy, diarrhea, cough, insomnia, vomiting, and back pain. (6.1)
- The most common adverse reactions ($\geq 20\%$) in patients with multiple myeloma who received D-Rd are fatigue, diarrhea, upper respiratory tract infection, muscle spasms, constipation, pyrexia, pneumonia and dyspnea. (6.1)
- The most common adverse reactions ($\geq 20\%$) in patients with light chain (AL) amyloidosis who received DARZALEX FASPRO as monotherapy are upper respiratory tract infection, diarrhea, peripheral edema, constipation, fatigue, peripheral sensory neuropathy, nausea, insomnia, dyspnea, and cough. (6.1)
- The most common ($\geq 40\%$) hematology laboratory abnormalities with DARZALEX FASPRO are decreased leukocytes, decreased lymphocytes, decreased neutrophils, decreased platelets, and decreased hemoglobin. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Janssen Biotech, Inc. at 1-800-526-7736 (1-800-JANSSEN) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 01/2021

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

1.1 Multiple Myeloma

DARZALEX FASPRO is indicated for the treatment of adult patients with multiple myeloma:

- 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 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 proteasome inhibitor (PI) and an immunomodulatory agent or who are double-refractory to a PI and an immunomodulatory agent.

1.2 Light Chain Amyloidosis

DARZALEX FASPRO in combination with bortezomib, cyclophosphamide and dexamethasone is indicated for the treatment of adult patients with newly diagnosed light chain (AL) amyloidosis.

This indication is approved under accelerated approval based on response rate [see *Clinical Studies (14.1)*]. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

Limitations of Use

DARZALEX FASPRO is not indicated and is not recommended for the treatment of patients with light chain (AL) amyloidosis who have NYHA Class IIIB or Class IV cardiac disease or Mayo Stage IIIB outside of controlled clinical trials [see *Warnings and Precautions (5.2)*].

2 DOSAGE AND ADMINISTRATION

2.1 Important Dosing Information

- **DARZALEX FASPRO is for subcutaneous use only.**
- Administer medications before and after administration of DARZALEX FASPRO to minimize administration-related reactions [see *Dosage and Administration (2.5)*].
- Type and screen patients prior to starting DARZALEX FASPRO.

2.2 Recommended Dosage for Multiple Myeloma

The recommended dose of DARZALEX FASPRO is 1,800 mg/30,000 units (1,800 mg daratumumab and 30,000 units hyaluronidase) administered subcutaneously over approximately 3-5 minutes. Tables 1, 2, 3, and 4 provide the recommended dosing schedule when DARZALEX FASPRO is administered as monotherapy or as part of a combination therapy.

Monotherapy and In Combination with Lenalidomide and Dexamethasone (D-Rd)

Use the dosing schedule provided in Table 1 when DARZALEX FASPRO is administered:

- in combination with lenalidomide and dexamethasone (4-week cycle) OR
- as monotherapy.

Table 1: DARZALEX FASPRO dosing schedule in combination with lenalidomide and dexamethasone (4-week cycle) and for monotherapy

Weeks	Schedule
Weeks 1 to 8	weekly (total of 8 doses)
Weeks 9 to 24 ^a	every two weeks (total of 8 doses)
Week 25 onwards until disease progression ^b	every four weeks

^a First dose of the every-2-week dosing schedule is given at Week 9

^b First dose of the every-4-week dosing schedule is given at Week 25

When DARZALEX FASPRO is administered as part of a combination therapy, *see Clinical Studies (14.2)* and the prescribing information for dosage recommendations for the other drugs.

In Combination with Bortezomib, Melphalan and Prednisone (D-VMP)

Use the dosing schedule provided in Table 2 when DARZALEX FASPRO is administered in combination with bortezomib, melphalan and prednisone (6-week cycle).

Table 2: DARZALEX FASPRO dosing schedule in combination with bortezomib, melphalan and prednisone (6-week cycle)

Weeks	Schedule
Weeks 1 to 6	weekly (total of 6 doses)
Weeks 7 to 54 ^a	every three weeks (total of 16 doses)
Week 55 onwards until disease progression ^b	every four weeks

^a First dose of the every-3-week dosing schedule is given at Week 7

^b First dose of the every-4-week dosing schedule is given at Week 55

When DARZALEX FASPRO is administered as part of a combination therapy, *see Clinical Studies (14.1)* and the prescribing information for dosage recommendations for the other drugs.

In Combination with Bortezomib, Thalidomide, and Dexamethasone (D-VTd)

Use the dosing schedule in Table 3 when DARZALEX FASPRO is administered in combination with bortezomib, thalidomide, and dexamethasone (4-week cycle).

Table 3: DARZALEX FASPRO dosing schedule in combination with bortezomib, thalidomide and dexamethasone (4-week cycle)

Treatment phase	Weeks	Schedule
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Induction	Weeks 1 to 8	weekly (total of 8 doses)
	Weeks 9 to 16 ^a	every two weeks (total of 4 doses)
Stop for high dose chemotherapy and ASCT		
Consolidation	Weeks 1 to 8 ^b	every two weeks (total of 4 doses)

^a First dose of the every-2-week dosing schedule is given at Week 9

^b First dose of the every-2-week dosing schedule is given at Week 1 upon re-initiation of treatment following ASCT

When DARZALEX FASPRO is administered as part of a combination therapy, see the prescribing information for dosage recommendations for the other drugs.

In Combination with Bortezomib and Dexamethasone (D-Vd)

Use the dosing schedule in Table 4 when DARZALEX FASPRO is administered in combination with bortezomib and dexamethasone (3-week cycle).

Table 4: DARZALEX FASPRO dosing schedule in combination with bortezomib and dexamethasone (3-week cycle)

Weeks	Schedule
Weeks 1 to 9	weekly (total of 9 doses)
Weeks 10 to 24 ^a	every three weeks (total of 5 doses)
Week 25 onwards until disease progression ^b	every four weeks

^a First dose of the every-3-week dosing schedule is given at Week 10

^b First dose of the every-4-week dosing schedule is given at Week 25

When DARZALEX FASPRO is administered as part of a combination therapy, see the prescribing information for dosage recommendations for the other drugs.

2.3 Recommended Dosage for Light Chain Amyloidosis

In Combination with Bortezomib, Cyclophosphamide and Dexamethasone (D-VCd)

Use the dosing schedule provided in Table 5 when DARZALEX FASPRO is administered in combination with bortezomib, cyclophosphamide and dexamethasone (4-week cycle).

Table 5: DARZALEX FASPRO dosing schedule in combination with bortezomib, cyclophosphamide and dexamethasone (4-week cycle)

Weeks	Schedule
Weeks 1 to 8	weekly (total of 8 doses)
Weeks 9 to 24 ^a	every two weeks (total of 8 doses)
Week 25 onwards until disease progression or a maximum of 2 years ^b	every four weeks

^a First dose of the every-2-week dosing schedule is given at Week 9

^b First dose of the every-4-week dosing schedule is given at Week 25

When DARZALEX FASPRO is administered as part of a combination therapy, see *Clinical Studies (14.2)* and the prescribing information for dosage recommendations for the other drugs.

2.4 Administration

If a dose of DARZALEX FASPRO is missed, administer the dose as soon as possible and adjust the dosing schedule to maintain the dosing interval.

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