## 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**

### ----------INDICATIONS AND USAGE----------

DARZALEX FASPRO is a combination of daratumumab, a CD38-directed cytolytic antibody, and hyaluronidase, an endoglycosidase, 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 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)

### ----------DOSAGE AND ADMINISTRATION----------

**For subcutaneous use only.**

- Pre-medicate with a corticosteroid, acetaminophen and a histamine-1 receptor antagonist. (2.3)
- 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)
- Administer post-medications as recommended. (2.3)

### ----------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)
- 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. (5.2)
- Thrombocytopenia: Monitor complete blood cell counts periodically during treatment. Consider withholding DARZALEX FASPRO to allow recovery of platelets. (5.3)
- 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 (5.4, 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. (5.5, 7.1)

### ----------ADVERSE REACTIONS----------

- The most common adverse reaction (≥20%) with DARZALEX FASPRO monotherapy is: upper respiratory tracts infection. (6.1)
- The most common adverse reactions (≥20%) with 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 (≥20%) with D-Rd are fatigue, diarrhea, upper respiratory tract infection, muscle spasms, constipation, pyrexia, pneumonia and dyspnea. (6.1)
- The most common hematology laboratory abnormalities (≥40%) 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: 05/2020**

## FULL PRESCRIBING INFORMATION: CONTENTS*



*Sections or subsections omitted from the full prescribing information are not listed.


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## FULL PRESCRIBING INFORMATION

## 1 INDICATIONS AND USAGE

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 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.

## 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 (2.3)]*.
- Type and screen patients prior to starting DARZALEX FASPRO.

### 2.2 Recommended Dosage

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, and 3 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

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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 and Dexamethasone (D-Vd)

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

**Table 3: 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.

### Missed DARZALEX FASPRO Doses

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.

## 2.3 Recommended Concomitant Medications

### Pre-medication

Administer the following pre-medications 1-3 hours before each dose of DARZALEX FASPRO:

- Acetaminophen 650 to 1,000 mg orally
- Diphenhydramine 25 to 50 mg (or equivalent) orally or intravenously

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- Corticosteroid (long- or intermediate-acting)

  *Monotherapy*

  Administer methylprednisolone 100 mg (or equivalent) orally or intravenously. Consider reducing the dose of methylprednisolone to 60 mg (or equivalent) following the second dose of DARZALEX FASPRO.

  *In Combination*

  Administer dexamethasone 20 mg (or equivalent) orally or intravenously prior to every DARZALEX FASPRO administration.

  When dexamethasone is the background regimen-specific corticosteroid, the dexamethasone dose that is part of the background regimen will serve as pre-medication on DARZALEX FASPRO administration days *[see Clinical Studies (14)]*.

  Do not administer background regimen-specific corticosteroids (e.g. prednisone) on DARZALEX FASPRO administration days when patients have received dexamethasone (or equivalent) as a pre-medication.

Post-medication

Administer the following post-medications:

*Monotherapy*

Administer methylprednisolone 20 mg (or an equivalent dose of an intermediate- or long-acting corticosteroid) orally for 2 days starting the day after the administration of DARZALEX FASPRO.

*In Combination*

Consider administering oral methylprednisolone at a dose of less than or equal to 20 mg (or an equivalent dose of an intermediate- or long-acting corticosteroid) beginning the day after administration of DARZALEX FASPRO.

If a background regimen-specific corticosteroid (e.g. dexamethasone, prednisone) is administered the day after the administration of DARZALEX FASPRO, additional corticosteroids may not be needed *[see Clinical Studies (14)]*.

If the patient does not experience a major systemic administration-related reaction after the first 3 doses of DARZALEX FASPRO, consider discontinuing the administration of corticosteroids (excluding any background regimen-specific corticosteroid).

For patients with a history of chronic obstructive pulmonary disease, consider prescribing short and long-acting bronchodilators and inhaled corticosteroids. Following the first 4 doses of DARZALEX FASPRO, consider discontinuing these additional post-medications, if the patient does not experience a major systemic administration-related reaction.

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Prophylaxis for Herpes Zoster Reactivation

Initiate antiviral prophylaxis to prevent herpes zoster reactivation within 1 week after starting DARZALEX FASPRO and continue for 3 months following the end of treatment *[see Adverse Reactions (6.1)]*.

## 2.4 Dosage Modifications for Adverse Reactions

No dose reductions of DARZALEX FASPRO are recommended. Consider withholding DARZALEX FASPRO to allow recovery of blood cell counts in the event of myelosuppression *[see Warnings and Precautions (5.2, 5.3)]*.

## 2.5 Preparation and Administration

DARZALEX FASPRO should be administered by a healthcare provider.

To prevent medication errors, check the vial labels to ensure that the drug being prepared and administered is DARZALEX FASPRO for subcutaneous use. **Do not administer DARZALEX FASPRO intravenously**.

DARZALEX FASPRO is ready to use.

Preparation

- Remove the DARZALEX FASPRO vial from refrigerated storage [2°C to 8°C (36°F to 46°F)] and equilibrate to ambient temperature [15°C to 30°C (59°F to 86°F)]. Store the unpunctured vial at ambient temperature and ambient light for a maximum of 24 hours. Keep out of direct sunlight. Do not shake.
- Withdraw 15 mL from the vial into a syringe.
- DARZALEX FASPRO is compatible with polypropylene or polyethylene syringe material; polypropylene, polyethylene, or polyvinyl chloride (PVC) subcutaneous infusion sets; and stainless steel transfer and injection needles. Use the product immediately.
- After the solution of DARZALEX FASPRO is withdrawn into the syringe, replace the transfer needle with a syringe closing cap. Label the syringe appropriately to include the route of administration per institutional standards. Label the syringe with the peel-off label.
- To avoid needle clogging, attach the hypodermic injection needle or subcutaneous infusion set to the syringe immediately prior to injection.
- Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. Do not use if opaque particles, discoloration or other foreign particles are present.

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