Dosing and Administration Guide

DARZALEX *Faspro*™
(daratumumab and hyaluronidase-fihj)
Injection for subcutaneous use | 1,800mg/30,000units

INDICATIONS

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

Select 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

Warnings and Precautions include: Hypersensitivity and Other Administration Reactions, Neutropenia, Thrombocytopenia, Embryo-Fetal Toxicity, Interference with Serological Testing, and Interference with Determination of Complete Response.

Please see Important Safety Information on pages 12-18. Please click here to see the full Prescribing Information for DARZALEX *FASPRO*™ and click here to see the full Prescribing Information for DARZALEX®.

DARZALEX *FASPRO*™ benefits[1,2]

Subcutaneous administration with DARZALEX *FASPRO*™ (daratumumab and hyaluronidase-fihj)

~3 to 5 minute administration by a healthcare provider

Fixed dose; no weight-based calculations

Single-dose vial, no dilution needed

Same dosing schedules as DARZALEX® (daratumumab) for approved indications*

*Split first dose option for DARZALEX® is not applicable to DARZALEX *FASPRO*™.

Formulated with hyaluronidase for subcutaneous administration

Select Important Safety Information

CONTRAINDICATIONS

DARZALEX *FASPRO*™ (daratumumab and hyaluronidase-fihj) 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*™.

Systemic Reactions

In a pooled safety population of 490 patients who received DARZALEX *FASPRO*™ as monotherapy or in combination, 11% of patients experienced a systemic administration-related reaction (Grade 2: 3.9%, Grade 3: 1.4%). Systemic administration-related reactions occurred in 10% of patients with the first injection, 0.2% with the second injection, and cumulatively 0.8% with subsequent injections. The median time to onset was 3.7 hours (range: 9 minutes to 3.5 days). Of the 84 systemic administration-related reactions that occurred in 52 patients, 73 (87%) occurred on the day of DARZALEX *FASPRO*™ administration. Delayed systemic administration-related reactions have occurred in less than 1% of the patients.

~3 to 5 minute administration possible with subcutaneous formulation

DARZALEX *FASPRO*™ is a CD38-targeted monoclonal antibody in a subcutaneous formulation[1]

DARZALEX *FASPRO*™ contains recombinant hyaluronidase, which is a naturally occurring substance that increases permeability of subcutaneous tissue, making it possible for 15 mL of daratumumab to be administered in approximately 3 to 5 minutes.[1]

Recombinant hyaluronidase works locally and transiently to degrade hyaluronan ([HA], a naturally occurring glycosaminoglycan found throughout the body) in the extracellular matrix of the subcutaneous space. It cleaves the linkage between the 2 sugars (N-acetylglucosamine and glucuronic acid) that comprise HA. Recombinant hyaluronidase has a half-life in skin of less than 30 minutes.[1]

- The effects of hyaluronidase are reversible and permeability of the subcutaneous tissue is restored within 24 to 48 hours

DID YOU KNOW?

DARZALEX *FASPRO*™ is administered subcutaneously over ~3 to 5 minutes while DARZALEX® is given intravenously over 7 hours for the first infusion, 4 hours for Week 2, and 3 hours for subsequent infusions (median).

Select Important Safety Information (cont)

Severe reactions included hypoxia, dyspnea, hypertension and tachycardia. 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, pruritis, chills, vomiting, nausea, and hypotension. (Continued on next page)

Please see Important Safety Information on pages 12-18. Please click here to see the full Prescribing Information for DARZALEX *FASPRO*™ and click here to see the full Prescribing Information for DARZALEX®.

DARZALEX *Faspro*™
(daratumumab and hyaluronidase-fihj)
Injection for subcutaneous use | 1,800mg/30,000units

~3 to 5 minute subcutaneous administration starting with the first dose

DARZALEX *FASPRO*™ contains 30,000 units of recombinant hyaluronidase[1]

- Increases permeability of subcutaneous tissue[1]
- Enables 15 mL of daratumumab to be absorbed into the subcutaneous tissue of the abdomen[1]
- Use an appropriate needle gauge. In the clinical trials, 23- to 25-gauge needles were used for the injection[1,3]
- For subcutaneous use only. DARZALEX *FASPRO*™ has different dosage and administration instructions than DARZALEX® (daratumumab). Do not administer intravenously[1,2]

Pre-medication[1]

Pre-medicate patients 1 to 3 hours before each dose with histamine-1 receptor antagonist, acetaminophen, and a corticosteroid.

~3 to 5 minute injection[1]

Post-medication[1]

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 (ARRs).*

Monitor patients for systemic ARRs, especially following the first and second injections. For anaphylactic reaction or life-threatening (Grade 4) ARRs, immediately and permanently discontinue DARZALEX *FASPRO*™.

*In clinical trials of DARZALEX *FASPRO*™, DARZALEX®, and the Prescribing Information for DARZALEX®, the term "infusion reactions" was used instead of "systemic administration-related reactions."

Select Important Safety Information (cont)

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 *FASPRO*™. 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.

DARZALEX *FASPRO*™ dosing schedule[1]

Ready-to-use, single-use vial includes a fixed dose for shorter preparation and no weight-based calculations

Indicated regimen*	Weeks	Schedule
In combination with lenalidomide (REVLIMID®) (4-week cycle) and dexamethasone, or for monotherapy	1–8	Weekly (total of 8 doses)
	9–24	Every 2 weeks (total of 8 doses)
	25 onward until disease progression	Every 4 weeks
With bortezomib (VELCADE®), melphalan, and prednisone (6-week cycle)	1–6	Weekly (total of 6 doses)
	7–54	Every 3 weeks (total of 16 doses)
	55 onward until disease progression	Every 4 weeks
With bortezomib and dexamethasone (3-week cycle)	1–9	Weekly (total of 9 doses)
	10–24	Every 3 weeks (total of 5 doses)
	25 onward until disease progression	Every 4 weeks

*See dosage and administration section of the full Prescribing Information for more detail.
When DARZALEX *FASPRO*™ is administered as part of a combination therapy, see the prescribing information for dosage recommendations for the other drugs.

Select Important Safety Information (cont)

Local Reactions

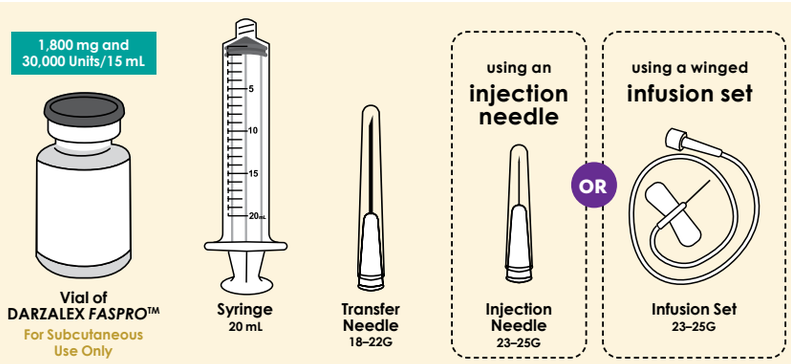
In this pooled safety population, injection-site reactions occurred in 8% of patients, including Grade 2 reactions in 0.6%. The most frequent (>1%) injection-site reaction was injection site erythema. These local reactions occurred a median of 7 minutes (range: 0 minutes to 4.7 days) after starting administration of DARZALEX *FASPRO*™. Monitor for local reactions and consider symptomatic management.

Please see Important Safety Information on pages 12-18. Please click here to see the full Prescribing Information for DARZALEX *FASPRO*™ and click here to see the full Prescribing Information for DARZALEX®.

DARZALEX *Faspro*™
(daratumumab and hyaluronidase-fihj)
Injection for subcutaneous use | 1,800mg/30,000units

Preparation

Before you begin, collect your supplies[3]*



*Please note that the syringe volume and the gauges for the transfer needle and injection needles shown here were used in clinical trials.

STEP 1: Inspect and prepare the vial[1]

- Remove the DARZALEX *FASPRO*™ vial from the refrigerator and warm to room temperature. Check the liquid in the vial. Keep out of direct sunlight and do not shake
- To prevent medication errors, it is important to check the vial labels to ensure that the drug being prepared and administered is DARZALEX *FASPRO*™ for subcutaneous injection and not DARZALEX® (daratumumab)
- DARZALEX *FASPRO*™ subcutaneous formulation is not intended for intravenous administration and should be administered via subcutaneous injection only
- Label the syringe appropriately to include the route of administration per institutional standards
- 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

DID YOU KNOW? If you prefer, you may use a winged infusion set to administer DARZALEX *FASPRO*™.[3]

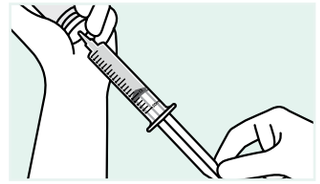
Select Important Safety Information (cont)

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.

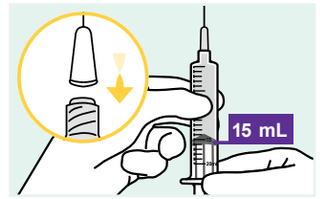
STEP 2: Attach the transfer needle and fill the syringe[1]

Prepare the dosing syringe in controlled and validated aseptic conditions.



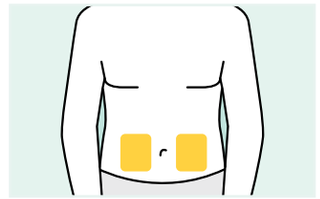
- Using the transfer needle, withdraw the full content of the vial into a 20 mL dosing syringe
- To avoid clogging, attach the needle to the syringe immediately prior to injection

STEP 3: Attach the injection needle and set the dose[3]



- Remove the transfer needle and attach the injection needle to the syringe
- Prime the syringe and set the dose to 15 mL

STEP 4: Choose the injection site on the abdomen[1,3]



- Do not inject into skin on the abdomen that is tender, bruised, red, hard or has scars
- Wipe your chosen injection site with an alcohol swab and allow it to dry
- Rotate injection sites for each successive injection

NEED TO KNOW To prevent medication errors, it is important to check the vial labels to ensure that the drug being prepared and administered is DARZALEX *FASPRO*™ and not DARZALEX®.[1]

Select Important Safety Information (cont)

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.

Please see Important Safety Information on pages 12-18. Please click here to see the full Prescribing Information for DARZALEX *FASPRO*™ and click here to see the full Prescribing Information for DARZALEX®.

DARZALEX *Faspro*™
(daratumumab and hyaluronidase-fihj)
Injection for subcutaneous use | 1,800mg/30,000units

Administration

DARZALEX *FASPRO*™ makes subcutaneous administration possible starting with the first dose

DARZALEX *FASPRO*™ is for single use only and comes in a ready-to-use vial

STEP 1: Insert needle at a 45-degree angle[3]

When you and your patient are comfortable, start the injection.

- Pinch skin at the injection site on the abdomen. It is important to pinch enough skin to inject under the skin and not into the muscle
- Insert needle with a quick, dart-like motion
- Try to limit needle and syringe movement during the injection. If needed, secure the infusion set in place with a bandage

STEP 2: Inject the dose[1]

- **Inject 15 mL DARZALEX *FASPRO*™ into the subcutaneous tissue of the abdomen approximately 3 inches (7.5 cm) to the right or left of the navel**

- Press the plunger with a constant rate of administration for approximately 3 to 5 minutes
- If the patient feels pain, pause or slow down the rate of administration. If the patient still feels pain, consider using a different injection site on the opposite side of the abdomen to deliver the remainder of the dose
- Do not inject DARZALEX *FASPRO*™ at other sites of the body as no data are available
- Injection sites should be rotated for successive injections
- Do not administer other medications for subcutaneous use at the same site
- DARZALEX *FASPRO*™ subcutaneous formulation should never be injected into areas where the skin is red, bruised, tender, hard or areas where there are scars

Select Important Safety Information (cont)

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.

Handling and storage[1]

Prior to administration, remove DARZALEX *FASPRO*™ from refrigerated storage (2°C–8°C [36°F–46°F]) and equilibrate to ambient temperature (15°C–30°C [59°F–86°F]). The unpunctured vial may be stored at ambient temperature and ambient light for a maximum of 24 hours. Keep out of direct sunlight. Do not shake.

Liquid product (1,800 mg) comes in a single-use, sterile vial; inspect the vial contents and expiration.

If the syringe containing DARZALEX *FASPRO*™ is not used immediately, store the DARZALEX *FASPRO*™ solution (in syringe) for up to 4 hours at ambient temperature and ambient light.

Select Important Safety Information (cont)

The combination of DARZALEX *FASPRO*™ with lenalidomide is contraindicated in pregnant women, because lenalidomide may cause birth defects and death of the unborn child. Refer to the lenalidomide 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 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.

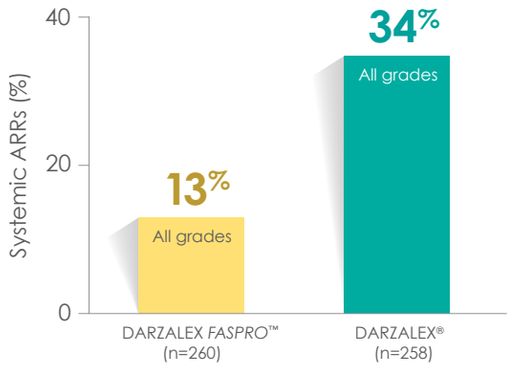
Please see Important Safety Information on pages 12-18. Please click here to see the full Prescribing Information for DARZALEX *FASPRO*™ and click here to see the full Prescribing Information for DARZALEX®.

DARZALEX *Faspro*™
(daratumumab and hyaluronidase-fihj)
Injection for subcutaneous use | 1,800mg/30,000units

Fewer systemic administration-related reactions (ARRs)

Nearly **3x reduction in systemic ARRs** with DARZALEX *FASPRO*™ vs DARZALEX® (daratumumab) observed in the COLUMBA trial[1]

Systemic ARRs[1,4]



Systemic ARRs

Most systemic ARRs were **Grade 1 or 2** and occurred with the first injection.

The most common systemic ARRs (DARZALEX *FASPRO*™ vs DARZALEX®) were chills (5% vs 12%), pyrexia (5% vs 3%), and dyspnea (1% vs 7%).[4]

Grade 3 systemic ARRs occurred in 2% of patients using DARZALEX *FASPRO*™ vs 5% of those on DARZALEX®.

No Grade 4 systemic ARRs were reported.

Both systemic ARRs, including severe or life-threatening reactions, and local injection-site reactions can occur with DARZALEX *FASPRO*™.[1]

In a pooled safety population of 490 patients, the rate of systemic ARRs was 11% for DARZALEX *FASPRO*™[1]

- The median time to onset of systemic ARRs following an injection of DARZALEX *FASPRO*™ was 3.7 hours (range: 9 minutes to 3.5 days). The majority of systemic ARRs occurred on the day of treatment. Delayed systemic ARRs, those occurring after the day of administration, have occurred in less than 1% of patients
- The incidence of any grade systemic ARRs was 10% with the first injection of DARZALEX *FASPRO*™ at Week 1, 0.2% with the second injection at Week 2, and cumulatively 0.8% with subsequent injections

Local reactions[1]

- In this pooled safety population, injection-site reactions occurred in 8% of patients, including Grade 2 reactions in 0.6%. The most frequent (>1%) injection-site reaction was injection site erythema
- These local reactions occurred a median of 7 minutes (range: 0 minutes to 4.7 days) after starting administration of DARZALEX *FASPRO*™. Monitor for local reactions and consider symptomatic management

*Systemic ARRs causing severe reactions included hypoxia, dyspnea, hypertension, and tachycardia. Other signs and symptoms of systemic ARRs 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, and hypotension.[1]

NEED TO KNOW

The most common adverse reactions with combination therapy (≥20% for any combination) include fatigue, nausea, diarrhea, dyspnea, insomnia, pyrexia, cough, muscle spasms, back pain, vomiting, upper respiratory tract infection, peripheral sensory neuropathy, constipation, and pneumonia[1]

Safety generally consistent with DARZALEX®

Adverse reactions reported in ≥10% of patients and select laboratory abnormalities worsening from baseline in patients receiving either DARZALEX *FASPRO*™ or DARZALEX®[1]

	DARZALEX *FASPRO*™ (n=260)		DARZALEX® (n=258)	
Adverse reactions	All grades (%)	Grade ≥3 (%)	All grades (%)	Grade ≥3 (%)
Upper respiratory tract infection[a]	24	1[g]	22	1[g]
Pneumonia[b]	8	5	10	6[h]
Diarrhea	15	1[g]	11	0.4[g]
Nausea	8	0.4[g]	11	0.4[g]
Fatigue[c]	15	1[g]	16	2[g]
Systemic ARRs[d]	13	2[g]	34	5[g]
Pyrexia	13	0	13	1[g]
Chills	6	0.4[g]	12	1[g]
Back pain	10	2[g]	12	3[g]
Cough[e]	9	1[g]	14	0
Dyspnea[f]	6	1[g]	11	1[g]

[a]Upper respiratory tract infection includes acute sinusitis, nasopharyngitis, pharyngitis, respiratory syncytial virus infection, respiratory tract infection, rhinitis, rhinovirus infection, sinusitis, and upper respiratory tract infection.
[b]Pneumonia includes lower respiratory tract infection, lung infection, pneumocystis jirovecii pneumonia, and pneumonia.
[c]Fatigue includes asthenia and fatigue.
[d]Systemic ARRs includes terms determined by investigators to be related to infusion. In clinical trials of DARZALEX *FASPRO*™, DARZALEX®, and the Prescribing Information for DARZALEX®, the term "infusion reactions" was used instead of "systemic ARRs."
[e]Cough includes cough and productive cough.
[f]Dyspnea includes dyspnea and dyspnea exertional.
[g]Only Grade 3 adverse reactions occurred.
[h]Grade 5 adverse reactions occurred.

- Serious adverse reactions occurred in 26% of patients who received DARZALEX *FASPRO*™ vs 29% who received DARZALEX®. Fatal adverse reactions occurred in 5% of patients receiving DARZALEX *FASPRO*™. Fatal adverse reactions occurring in more than 1 patient were general physical health deterioration, septic shock, and respiratory failure. Fatal adverse reactions occurred in 7% of patients receiving DARZALEX®[1,4]

	DARZALEX *FASPRO*™ (n=260)[a]		DARZALEX® (n=258)[a]	
Laboratory abnormalities	All grades (%)	Grade 3–4 (%)	All grades (%)	Grade 3–4 (%)
Leukopenia	65	19	57	14
Lymphopenia	59	36	56	36
Neutropenia	55	19	43	11
Thrombocytopenia	43	16	45	14
Anemia	42	14	39	16

[a]Denominator is based on the safety population treated with DARZALEX *FASPRO*™ (n=260) or with DARZALEX® (n=258).

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DARZALEX *Faspro*™
(daratumumab and hyaluronidase-fihj)
Injection for subcutaneous use | 1,800mg/30,000units

Important Safety Information for DARZALEX *FASPRO*™

CONTRAINDICATIONS

DARZALEX *FASPRO*™ (daratumumab and hyaluronidase-fihj) 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*™.

Systemic Reactions

In a pooled safety population of 490 patients who received DARZALEX *FASPRO*™ as monotherapy or in combination, 11% of patients experienced a systemic administration-related reaction (Grade 2: 3.9%, Grade 3: 1.4%). Systemic administration-related reactions occurred in 10% of patients with the first injection, 0.2% with the second injection, and cumulatively 0.8% with subsequent injections. The median time to onset was 3.7 hours (range: 9 minutes to 3.5 days). Of the 84 systemic administration-related reactions that occurred in 52 patients, 73 (87%) occurred on the day of DARZALEX *FASPRO*™ administration. Delayed systemic administration-related reactions have occurred in less than 1% of the patients.

Severe reactions included hypoxia, dyspnea, hypertension and tachycardia. 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, pruritis, chills, vomiting, nausea, and hypotension.

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 *FASPRO*™. 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.

Local Reactions

In this pooled safety population, injection-site reactions occurred in 8% of patients, including Grade 2 reactions in 0.6%. The most frequent (>1%) injection-site reaction was injection site erythema. These local reactions occurred a median of 7 minutes (range: 0 minutes to 4.7 days) after starting administration of DARZALEX *FASPRO*™. Monitor for local reactions and consider symptomatic management.

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 is contraindicated in pregnant women, because lenalidomide may cause birth defects and death of the unborn child. Refer to the lenalidomide prescribing information on use during pregnancy.

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Important Safety Information for DARZALEX *FASPRO*™ (cont)

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 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

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, insomnia, pyrexia, cough, muscle spasms, back pain, vomiting, upper respiratory tract infection, peripheral sensory neuropathy, constipation, and pneumonia.

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 see the full Prescribing Information.

cp-143279v1

Indications and Important Safety Information for DARZALEX®

INDICATIONS

DARZALEX® (daratumumab) is a CD38-directed cytolytic antibody indicated for the treatment of adult patients with 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
- in combination with bortezomib, melphalan and prednisone in newly diagnosed patients who are ineligible for autologous stem cell transplant
- 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
- in combination with pomalidomide and dexamethasone in patients who have received at least two prior therapies including lenalidomide and a proteasome inhibitor
- 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

CONTRAINDICATIONS

DARZALEX® (daratumumab) is contraindicated in patients with a history of severe hypersensitivity (eg, anaphylactic reactions) to daratumumab or any of the components of the formulation.

WARNINGS AND PRECAUTIONS

Infusion Reactions – DARZALEX® can cause severe and/or serious infusion reactions, including anaphylactic reactions. In clinical trials, approximately half of all patients experienced an infusion reaction. Most infusion reactions occurred during the first infusion and were Grade 1-2. Infusion reactions can also occur with subsequent infusions. Nearly all reactions occurred during infusion or within 4 hours of completing DARZALEX®. Prior to the introduction of post-infusion medication in clinical trials, infusion reactions occurred up to 48 hours after infusion. Severe reactions have occurred, including bronchospasm, hypoxia, dyspnea, hypertension, laryngeal edema, and pulmonary edema. Signs and symptoms may include respiratory symptoms,

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DARZALEX *Faspro*™
(daratumumab and hyaluronidase-fihj)
Injection for subcutaneous use | 1,800mg/30,000units

Important Safety Information for DARZALEX® (cont)

such as nasal congestion, cough, throat irritation, as well as chills, vomiting, and nausea. Less common symptoms were wheezing, allergic rhinitis, pyrexia, chest discomfort, pruritus, and hypotension.

Pre-medicate patients with antihistamines, antipyretics, and corticosteroids. Frequently monitor patients during the entire infusion. Interrupt infusion for reactions of any severity and institute medical management as needed. Permanently discontinue therapy if an anaphylactic reaction or life-threatening (Grade 4) reaction occurs and institute appropriate emergency care. For patients with Grade 1, 2, or 3 reactions, reduce the infusion rate when re-starting the infusion.

To reduce the risk of delayed infusion reactions, administer oral corticosteroids to all patients following DARZALEX® infusions. Patients with a history of chronic obstructive pulmonary disease may require additional post-infusion medications to manage respiratory complications. Consider prescribing short- and long-acting bronchodilators and inhaled corticosteroids for patients with chronic obstructive pulmonary disease.

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 infusion. 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®. Type and screen patients prior to starting DARZALEX®.

Neutropenia and Thrombocytopenia – DARZALEX® may increase neutropenia and/or thrombocytopenia induced by background therapy. Monitor complete blood cell counts periodically during treatment according to the manufacturer's prescribing information for background therapies. Monitor patients with neutropenia for signs of infection. DARZALEX® dose delay may be required to allow recovery of neutrophils and/or platelets. No dose reduction of DARZALEX® is recommended. Consider supportive care with growth factors for neutropenia or transfusions for thrombocytopenia.

Interference With Determination of Complete Response – Daratumumab is a human 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 patients with IgG kappa myeloma protein.

Adverse Reactions – The most frequently reported adverse reactions (incidence ≥20%) were: infusion reactions, neutropenia, thrombocytopenia, fatigue, asthenia, nausea, diarrhea, constipation, decreased appetite, vomiting, muscle spasms, arthralgia, back pain, pyrexia, chills, dizziness, insomnia, cough, dyspnea, peripheral edema, peripheral sensory neuropathy, bronchitis, pneumonia, and upper respiratory tract infection.

DARZALEX® in combination with lenalidomide and dexamethasone (DRd): The most frequent (≥20%) adverse reactions for newly diagnosed or relapsed/refractory patients were, respectively, infusion reactions (41%, 48%), diarrhea (57%, 43%), nausea (32%, 24%), fatigue (40%, 35%), pyrexia (23%, 20%), upper respiratory tract infection (52%, 65%), muscle spasms (29%, 26%), dyspnea (32%, 21%), and cough (30%, 30%). In newly diagnosed patients, constipation (41%), peripheral edema (41%), back pain (34%), asthenia (32%), bronchitis (29%), pneumonia (26%), peripheral sensory neuropathy (24%), and decreased appetite (22%) were also reported. In newly diagnosed patients, serious adverse reactions (≥2% compared to Rd) were pneumonia (15%), bronchitis (4%), and dehydration (2%), and treatment-emergent Grade 3-4 hematology laboratory abnormalities (≥20%) were neutropenia (56%), lymphopenia (52%), and leukopenia (35%). In relapsed/refractory patients, serious adverse reactions (≥2% compared to Rd) were pneumonia (12%), upper respiratory tract infection (7%), influenza (3%), and pyrexia (3%), and treatment-emergent Grade 3-4 hematology laboratory abnormalities (≥20%) were neutropenia (53%) and lymphopenia (52%).

DARZALEX® in combination with bortezomib, melphalan, and prednisone (DVMP): The most frequently reported adverse reactions (≥20%) were upper respiratory tract infection (48%), infusion reactions (28%), and peripheral edema (21%). Serious adverse reactions (≥2% compared to the VMP arm) were pneumonia (11%), upper respiratory tract infection (5%), and pulmonary edema (2%). Treatment-emergent Grade 3-4 hematology laboratory abnormalities (≥20%) were lymphopenia (58%), neutropenia (44%), and thrombocytopenia (38%).

Continued on next page

DARZALEX®
(daratumumab)
injection for intravenous infusion
100 mg/5 mL, 400 mg/20 mL

Important Safety Information for DARZALEX® (cont)

DARZALEX® in combination with bortezomib and dexamethasone (DVd): The most frequently reported adverse reactions (≥20%) were peripheral sensory neuropathy (47%), infusion reactions (45%), upper respiratory tract infection (44%), diarrhea (32%), cough (27%), peripheral edema (22%), and dyspnea (21%). The overall incidence of serious adverse reactions was 42%. Serious adverse reactions (≥2% compared to Vd) were upper respiratory tract infection (5%), diarrhea (2%), and atrial fibrillation (2%). Treatment-emergent Grade 3-4 hematology laboratory abnormalities (≥20%) were lymphopenia (48%) and thrombocytopenia (47%).

DARZALEX® in combination with bortezomib, thalidomide, and dexamethasone (DVTd): The most frequent adverse reactions (≥20%) were infusion reactions (35%), nausea (30%), upper respiratory tract infection (27%), pyrexia (26%), and bronchitis (20%). Serious adverse reactions (≥2% compared to the VTd arm) were bronchitis (DVTd 2% vs VTd <1%) and pneumonia (DVTd 6% vs VTd 4%). Treatment-emergent Grade 3-4 hematology laboratory abnormalities (≥20%) were lymphopenia (59%), neutropenia (33%), and leukopenia (24%).

DARZALEX® in combination with pomalidomide and dexamethasone (DPd): The most frequent adverse reactions (>20%) were fatigue (50%), infusion reactions (50%), upper respiratory tract infection (50%), cough (43%), diarrhea (38%), constipation (33%), dyspnea (33%), nausea (30%), muscle spasms (26%), back pain (25%), pyrexia (25%), insomnia (23%), arthralgia (22%), dizziness (21%), and vomiting (21%). The overall incidence of serious adverse reactions was 49%. Serious adverse reactions reported in ≥5% of patients included pneumonia (7%). Treatment-emergent Grade 3-4 hematology laboratory abnormalities (≥20%) were neutropenia (82%), lymphopenia (71%), and anemia (30%).

DARZALEX® as monotherapy: The most frequently reported adverse reactions (≥20%) were infusion reactions (48%), fatigue (39%), nausea (27%), back pain (23%), pyrexia (21%), cough (21%), and upper respiratory tract infection (20%). The overall incidence of serious adverse reactions was 33%. The most frequent serious adverse reactions were pneumonia (6%), general physical health deterioration (3%), and pyrexia (3%). Treatment-emergent Grade 3-4 hematology laboratory abnormalities (≥20%) were lymphopenia (40%) and neutropenia (20%).

Please click here to see the full Prescribing Information.

cp-60862v3

Janssen CarePath

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Janssen CarePath is your one source for access, affordability, and treatment support for your patients.

Janssen CarePath helps verify insurance coverage for your patients, provides reimbursement information, helps find financial assistance options for eligible patients, and provides ongoing support to help patients start and stay on DARZALEX *FASPRO*™.

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DARZALEX *Faspro*™
(daratumumab and hyaluronidase-fihj)
Injection for subcutaneous use | 1,800mg/30,000units

DARZALEX *FASPRO*™ – a subcutaneous formulation for use across 5 indications spanning a wide range of multiple myeloma patients[1]

Five approved indications

- Multiple regimens approved across a wide range of patients, including DRd and DVMP for patients who are newly diagnosed and transplant ineligible, DRd and DVd after ≥1 prior therapy, and monotherapy after ≥3 prior lines of therapy[1]*

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

Faster administration

- ~3–5 minute injection is substantially faster than DARZALEX® (daratumumab)[1,2]

Dosing features

- Ready-to-use, fixed-dose vial requires no preparation, reconstitution, or weight-based calculations[1]
- Same dosing schedules as DARZALEX® for approved indications[1,2†]

†Split first dose option for DARZALEX® is not applicable to DARZALEX *FASPRO*™.

Fewer systemic administration-related reactions (ARRs)

- Nearly 3x reduction in systemic ARRs vs DARZALEX® (13% vs 34%)[1,4]
- Both systemic ARRs, including severe or life-threatening reactions, and local injection-site reactions can occur with DARZALEX *FASPRO*™. See Important Safety Information on pages 12-14 for more details[1]

DRd=DARZALEX *FASPRO*™ (D) + lenalidomide (R) + dexamethasone (d); DVd=DARZALEX *FASPRO*™ (D) + bortezomib (V) + dexamethasone (d); DVMP=DARZALEX *FASPRO*™ (D) + bortezomib (V) + melphalan (M) + prednisone (P).

Select Important Safety Information (cont)

CONTRAINDICATIONS

DARZALEX *FASPRO*™ (daratumumab and hyaluronidase-fihj) is contraindicated in patients with a history of severe hypersensitivity to daratumumab, hyaluronidase or any of the components of the formulation.

WARNINGS AND PRECAUTIONS

Warnings and Precautions include: Hypersensitivity and Other Administration Reactions, Neutropenia, Thrombocytopenia, Embryo-Fetal Toxicity, Interference with Serological Testing, and Interference with Determination of Complete Response.

Please see Important Safety Information on pages 12-18. Please click here to see the full Prescribing Information for DARZALEX *FASPRO*™ and click here to see the full Prescribing Information for DARZALEX®.

References: 1. DARZALEX *FASPRO*™ [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc. **2.** DARZALEX® [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc. **3.** Data on file. Janssen Biotech, Inc. **4.** Mateos M-V, Nahi H, Legiec W, et al. Subcutaneous versus intravenous daratumumab in patients with relapsed or refractory multiple myeloma (COLUMBA): a multicentre, open-label, non-inferiority, randomised, phase 3 trial. *Lancet Haematol*. 2020. doi: 10.1016/S2352-3026(20)30070-3. [Epub ahead of print].

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Injection for subcutaneous use | 1,800mg/30,000units