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) 11/2021
Indications and Usage (1.2) 1/2021
Dosage and Administration (2.2) 11/2021
Dosage and Administration (2.3) 1/2021
Warnings and Precautions (5.1) 11/2021
Warnings and Precautions (5.2) 1/2021

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 transplantation
• multiple myeloma in combination with lenalidomide and dexamethasone in newly diagnosed patients who are ineligible for autologous stem cell transplantation 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 transplantation
• multiple myeloma in combination with bortezomib and dexamethasone in patients who have received at least one prior therapy
• multiple myeloma in combination with pomalidomide and dexamethasone in patients who have received at least one prior line of therapy including lenalidomide and a proteasome inhibitor
• multiple myeloma in combination with carfilzomib and dexamethasone in patients with relapsed or refractory multiple myeloma who have received one to three prior lines of 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)

DARZALEX FASPRO® (daratumumab and hyaluronidase-fihj) injection

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, hyaluronidase 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 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 (≥20%) in patients with multiple myeloma who received DARZALEX FASPRO monotherapy is upper respiratory tract infection. (6.1)
• The most common adverse reactions (≥20%) in patients with multiple myeloma who received DARZALEX FASPRO-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%) in patients with multiple myeloma who received DARZALEX FASPRO-Rd are fatigue, diarrhea, upper respiratory tract infection, muscle spasms, constipation, pyrexia, pneumonia, and dyspnea. (6.1)
• The most common adverse reactions (≥20%) in patients with multiple myeloma who received DARZALEX FASPRO-Pd are fatigue, pneumonia, upper respiratory tract infection, and diarrhea. (6.1)
• The most common adverse reactions (≥20%) in patients with multiple myeloma who received DARZALEX FASPRO-Kd are upper respiratory tract infection, fatigue, insomnia, hypertension, diarrhea, cough, dyspnea, headache, pyrexia, nausea, and edema peripheral. (6.1)
• The most common adverse reactions (≥20%) in patients with light chain (AL) amyloidosis are upper respiratory tract infection, diarrhea, peripheral edema, constipation, fatigue, peripheral sensory neuropathy, nausea, insomnia, dyspnea, and cough. (6.1)
• The most common (≥40%) hematology laboratory abnormalities with DARZALEX FASPRO are decreased leukocytes, decreased lymphocytes, decreased neutrophils, decreased platelets, and decreased hemoglobin. (8.6)

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: 11/2021
FULL PRESCRIBING INFORMATION: CONTENTS*

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.
- in combination with pomalidomide and dexamethasone in patients who have received at least one prior therapy.
- in combination with carfilzomib and dexamethasone in patients with relapsed or refractory multiple myeloma who have received one to three prior lines of 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.
- in combination with lenalidomide and dexamethasone (4-week cycle) OR
- in combination with pomalidomide and dexamethasone (4-week cycle) OR
- in combination with carfilzomib and dexamethasone (4-week cycle) OR
- as monotherapy.

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 (14.3)). 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 dosage schedule when DARZALEX FASPRO® is administered as monotherapy or as part of a combination therapy.

7 DRUG INTERACTIONS

7.1 Effects of Daratumumab on Laboratory Tests

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*Sections or subsections omitted from the full prescribing information are not listed.
Table 3: DARZALEX FASPRO dosing schedule in combination with bortezomib, thalidomide and dexamethasone (4-week cycle)

<table>
<thead>
<tr>
<th>Treatment phase</th>
<th>Weeks</th>
<th>Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>Induction</td>
<td>Weeks 1 to 8</td>
<td>weekly (total of 8 doses)</td>
</tr>
<tr>
<td></td>
<td>Weeks 9 to 16</td>
<td>every two weeks (total of 4 doses)</td>
</tr>
<tr>
<td>Stop for high dose chemotherapy and ASCT</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Consolidation</td>
<td>Weeks 1 to 8</td>
<td>every two weeks (total of 4 doses)</td>
</tr>
</tbody>
</table>

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, Cyclophosphamide and Dexamethasone (DARZALEX FASPRO-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)

<table>
<thead>
<tr>
<th>Weeks</th>
<th>Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 to 9</td>
<td>weekly (total of 9 doses)</td>
</tr>
<tr>
<td>10 to 24</td>
<td>every three weeks (total of 5 doses)</td>
</tr>
<tr>
<td>25 onwards</td>
<td>every four weeks</td>
</tr>
</tbody>
</table>

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 (DARZALEX FASPRO-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)

<table>
<thead>
<tr>
<th>Weeks</th>
<th>Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 to 8</td>
<td>weekly (total of 8 doses)</td>
</tr>
<tr>
<td>9 to 24</td>
<td>every two weeks (total of 8 doses)</td>
</tr>
<tr>
<td>25 onwards</td>
<td>every four weeks</td>
</tr>
</tbody>
</table>

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.

2.5 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
- 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)].

In 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.

Prophylaxis for Herpes Zoster Reactivation

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

2.6 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 (5.3, 5.4)].

2.7 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.

Storage

- If the syringe containing DARZALEX FASPRO is not used immediately, store the DARZALEX FASPRO solution for up to 4 hours at ambient temperature and ambient light. Discard after 4 hours, if not used.

Administration

- Inject 15 mL of DARZALEX FASPRO into the subcutaneous tissue of the abdomen approximately 3 inches (7.5 cm) to the right or left of the navel over approximately 3-5 minutes. No data are available on performing the injection at other sites of the body.
- Rotate injection sites for successive injections.
- Never inject DARZALEX FASPRO into areas where the skin is red, bruised, tender, hard or areas where there are scars.
- Pause or slow down delivery rate if the patient experiences pain. In the event pain is not alleviated by pausing or slowing down delivery rate, a second injection site may be chosen on the opposite side of the abdomen to deliver the remainder of the dose.
- During treatment with DARZALEX FASPRO, do not administer other medications for subcutaneous use at the same site as DARZALEX FASPRO.
3 DOSE FORMS AND STRENGTHS
Injection: 1,800 mg daratumumab and 30,000 units hyaluronidase per 15 mL (120 mg and 2,000 units/mL) colorless to yellow and clear to opalescent solution in a single-dose vial.

4 CONTRAINDICATIONS
Darzalex Faspro is contraindicated in patients with a history of severe hypersensitivity to daratumumab, hyaluronidase or any of the components of the formulation [see Warnings and Precautions (5.1) and Adverse Reactions (6.3)].

5 WARNINGS AND PRECAUTIONS
5.1 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 [see Adverse Reactions (6.3)].

Systemic Reactions
In a pooled safety population of 898 patients with multiple myeloma (N=705) or light chain (AL) amyloidosis (N=193) who received Darzalex Faspro as monotherapy or as part of a combination therapy, 9% of patients experienced a systemic administration-related reaction (Grade 2: 3.2%, Grade 3: 1%). Systemic administration-related reactions occurred in 8% of patients with the first injection, 0.3% 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 140 systemic administration-related reactions that occurred on 77 patients, 121 (86%) 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 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, pruritus, chills, vomiting, nausea, and hypotension.

Pre-medicate patients with histamine-1 receptor antagonist, acetaminophen and corticosteroids [see Dosage and Administration (2.5)]. 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 [see Dosage and Administration (2.5)].

Local Reactions
In this pooled safety population, injection-site reactions occurred in 8% of patients, including Grade 2 reactions in 0.7%. The most frequent (>1%) injection-site reaction was injection site erythema. These local reactions are generally mild to moderate in severity. In a pooled safety population, injection-site reactions occurred in 8% of patients, including Grade 2 reactions in 0.7%. The most frequent (>1%) injection-site reaction was injection site erythema. These local reactions are generally mild to moderate in severity.

5.2 Cardiac Toxicity in Patients with Light Chain (AL) Amyloidosis
Serious or fatal cardiac adverse reactions occurred in patients with light chain (AL) amyloidosis who received Darzalex Faspro in combination with bortezomib, cyclophosphamide and dexamethasone [see Adverse Reactions (6.1)]. Serious cardiac disorders occurred in 18% and fatal cardiac disorders occurred in 10% of patients. Patients with NYHA Class III or IV were at greater risk. Patients with NYHA Class IIIb or IV disease were not studied.

Monitor patients with cardiac involvement of light chain (AL) amyloidosis more frequently for cardiac adverse reactions and administer supportive care as appropriate.

5.3 Neutropenia
Daratumumab may increase neutropenia induced by background therapy [see Adverse Reactions (6.1)]. 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.

5.4 Thrombocytopenia
Daratumumab may increase thrombocytopenia induced by background therapy [see Adverse Reactions (6.1)]. 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.

5.5 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 death 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 [see Use in Specific Populations (8.1, 8.3)]. The combination of Darzalex Faspro with lenalidomide, thalidomide or pomalidomide is contraindicated in pregnant women, because lenalidomide, thalidomide or pomalidomide may cause birth defects and death of the unborn child. Refer to the lenalidomide, thalidomide or pomalidomide prescribing information on use during pregnancy.

5.6 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 [see References (15)]. The determination of a patient’s ABO and Rh blood type are not impacted [see Drug Interactions (7.1)].

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 [see Dosage and Administration (2.1)].

5.7 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 [see Drug Interactions (7.1)]. This interference can impact the determination of complete response and of disease progression in some Darzalex Faspro-treated patients with IgG kappa myeloma protein.

6 ADVERSE REACTIONS
The following clinically significant adverse reactions are described elsewhere in the labeling:

• Hypersensitivity and Other Administration Reactions [see Warnings and Precautions (5.1)].
• Cardiac Toxicity in Patients with Light Chain (AL) Amyloidosis [see Warnings and Precautions (5.2)].
• Neutropenia [see Warnings and Precautions (5.3)].
• Thrombocytopenia [see Warnings and Precautions (5.4)].

6.1 Clinical Trials Experience
Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Newly Diagnosed Multiple Myeloma
In Combination with Bortezomib, Melphalan and Prednisone
The safety of Darzalex Faspro with bortezomib, melphalan and prednisone was evaluated in a single-arm cohort of PLEIADES [see Clinical Studies (14.1)]. Patients received Darzalex Faspro 1,800 mg/30,000 units administered subcutaneously once weekly from weeks 1 to 6, once every 3 weeks from weeks 7 to 54 and once every 4 weeks starting with week 55 until disease progression or unacceptable toxicity (N=67) in combination with bortezomib, melphalan and prednisone. Among these patients, 93% were exposed for 6 months or longer and 19% were exposed for greater than one year.

Serious adverse reactions occurred in 39% of patients who received Darzalex Faspro. Serious adverse reactions in ≥5% of patients included pneumonia and pyrexia. Fatal adverse reactions occurred in 3% of patients. Permanent discontinuation of Darzalex Faspro due to an adverse reaction occurred in 4.5% of patients. The adverse reaction resulting in permanent discontinuation of Darzalex Faspro in more than 1 patient was neutropenic sepsis.

Doseage interruptions (defined as dose delays or skipped doses) due to an adverse reaction occurred in 51% of patients who received Darzalex Faspro. Adverse reactions requiring dosage interruptions in ≥5% of patients included thrombocytopenia, neutropenia, anemia, and pneumonia.

The most common adverse reactions (≥20%) were upper respiratory tract infection, constipation, nausea, fatigue, pyrexia, peripheral sensory neuropathy, diarrhea, cough, insomnia, vomiting, and back pain.

Table 6 summarizes the adverse reactions in patients who received Darzalex Faspro in PLEIADES.
### Table 6: Adverse Reactions (≥10%) in Patients Who Received DARZALEX FASPRO with Bortezomib, Melphalan and Prednisone (DARZALEX FASPRO-VMP) in PLEIADES

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>DARZALEX FASPRO with Bortezomib, Melphalan and Prednisone (N=67)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Infections</strong></td>
<td>All Grades (%)</td>
</tr>
<tr>
<td>Upper respiratory tract infection</td>
<td>39</td>
</tr>
<tr>
<td>Bronchitis</td>
<td>16</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>15</td>
</tr>
<tr>
<td><strong>Gastrointestinal disorders</strong></td>
<td></td>
</tr>
<tr>
<td>Constipation</td>
<td>36</td>
</tr>
<tr>
<td>Nausea</td>
<td>7</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>33</td>
</tr>
<tr>
<td>Vomiting</td>
<td>21</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>18</td>
</tr>
<tr>
<td><strong>General disorders and administration site conditions</strong></td>
<td></td>
</tr>
<tr>
<td>Fatigue</td>
<td>36</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>34</td>
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<tr>
<td>Edema peripheral</td>
<td>13</td>
</tr>
<tr>
<td><strong>Nervous system disorders</strong></td>
<td></td>
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<tr>
<td>Peripheral sensory neuropathy</td>
<td>13</td>
</tr>
<tr>
<td><strong>Respiratory, thoracic and mediastinal disorders</strong></td>
<td></td>
</tr>
<tr>
<td>Cough</td>
<td>24</td>
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<td><strong>Psychiatric disorders</strong></td>
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<tr>
<td>Insomnia</td>
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<td><strong>Musculoskeletal and connective tissue disorders</strong></td>
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</tr>
<tr>
<td>Back pain</td>
<td>21</td>
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<tr>
<td>Musculoskeletal chest pain</td>
<td>12</td>
</tr>
<tr>
<td><strong>Metabolism and nutrition disorders</strong></td>
<td></td>
</tr>
<tr>
<td>Decreased appetite</td>
<td>15</td>
</tr>
<tr>
<td><strong>Skin and subcutaneous tissue disorders</strong></td>
<td></td>
</tr>
<tr>
<td>Rash</td>
<td>13</td>
</tr>
<tr>
<td>Pruritus</td>
<td>12</td>
</tr>
<tr>
<td><strong>Vascular disorders</strong></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>12</td>
</tr>
<tr>
<td>Hypotension</td>
<td>10</td>
</tr>
</tbody>
</table>
| a Upper respiratory tract infection includes nasopharyngitis, respiratory syncytial virus infection, respiratory tract infection, rhinitis, tonsillitis, upper respiratory tract infection, and viral pharyngitis.
| b Pneumonia includes lower respiratory tract infection, lung infection, pneumocystis proqvenica pneumonia, pneumonia, and pneumonia bacterial.
| c Abdominal pain includes abdominal pain, and abdominal pain upper.
| d Fatigue includes asthenia, and fatigue.
| e Edema peripheral includes edema, edema peripheral, and peripheral swelling.
| f Cough includes cough, and productive cough.
| g Only grade 3 adverse reactions occurred.


Table 7 summarizes the laboratory abnormalities in patients who received DARZALEX FASPRO in PLEIADES.

### Table 7: Select Hematology Laboratory Abnormalities Worsening from Baseline in Patients Who Received DARZALEX FASPRO with Bortezomib, Melphalan and Prednisone (DARZALEX FASPRO-VMP) in PLEIADES

<table>
<thead>
<tr>
<th>Laboratory Abnormality</th>
<th>DARZALEX FASPRO with Bortezomib, Melphalan and Prednisone (N=67)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decreased leukocytes</td>
<td>96</td>
</tr>
<tr>
<td>Decreased lymphocytes</td>
<td>93</td>
</tr>
<tr>
<td>Decreased platelets</td>
<td>93</td>
</tr>
<tr>
<td>Decreased neutrophils</td>
<td>88</td>
</tr>
<tr>
<td>Decreased hemoglobin</td>
<td>48</td>
</tr>
</tbody>
</table>

### Table 8: Adverse Reactions (≥10%) in Patients Who Received DARZALEX FASPRO with Lenalidomide and Dexamethasone (DARZALEX FASPRO-Rd) in PLEIADES

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>DARZALEX FASPRO with Lenalidomide and Dexamethasone (N=65)</th>
</tr>
</thead>
<tbody>
<tr>
<td>General disorders and administration site conditions</td>
<td>All Grades (%)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>52</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>23</td>
</tr>
<tr>
<td>Edema peripheral</td>
<td>18</td>
</tr>
<tr>
<td>Gastrointestinal disorders</td>
<td></td>
</tr>
<tr>
<td>Diarrhea</td>
<td>45</td>
</tr>
<tr>
<td>Nausea</td>
<td>36</td>
</tr>
<tr>
<td>Vomiting</td>
<td>21</td>
</tr>
<tr>
<td>Infections</td>
<td></td>
</tr>
<tr>
<td>Upper respiratory tract infection</td>
<td>43</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>23</td>
</tr>
<tr>
<td>Bronchitis</td>
<td>14</td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>11</td>
</tr>
<tr>
<td>Musculoskeletal and connective tissue disorders</td>
<td></td>
</tr>
<tr>
<td>Muscle spasm</td>
<td>31</td>
</tr>
<tr>
<td>Back pain</td>
<td>14</td>
</tr>
<tr>
<td>Respiratory, thoracic and mediastinal disorders</td>
<td></td>
</tr>
<tr>
<td>Dyspnea</td>
<td>22</td>
</tr>
<tr>
<td>Cough</td>
<td>14</td>
</tr>
<tr>
<td>Musculoskeletal and connective tissue disorders</td>
<td></td>
</tr>
<tr>
<td>Hyperglycemia</td>
<td>12</td>
</tr>
<tr>
<td>Hypocalcemia</td>
<td>11</td>
</tr>
</tbody>
</table>

Fatigue includes asthenia, and fatigue. Upper respiratory tract infection includes nasopharyngitis, pharyngitis, respiratory tract infection viral, rhinitis, sinusitis, upper respiratory tract infection, and upper respiratory tract infection bacterial. Pneumonia includes lower respiratory tract infection, lung infection, and pneumonia. Bronchitis includes bronchitis, and bronchitis viral. Dyspnea includes dyspnea, and dyspnea exertional. Only grade 3 adverse reactions occurred. Clinically relevant adverse reactions in <10% of patients who received DARZALEX FASPRO with lenalidomide and dexamethasone included: Musculoskeletal and connective tissue disorders: arthralgia, musculoskeletal chest pain. Nervous system disorders: dizziness, headache, paresthesia.
DARZALEX FASPRO® (daratumumab and hyaluronidase-fihj) injection

- Skin and subcutaneous tissue disorders: rash, pruritus
- Gastrointestinal disorders: abdominal pain
- Infections: influenza, sepsis, herpes zoster
- Metabolism and nutrition disorders: decreased appetite
- Cardiac disorders: atrial fibrillation
- General disorders and administration site conditions: chills, infusion reaction, injection site reaction
- Vascular disorders: hypertension, hypotension

Table 9 summarizes the laboratory abnormalities in patients who received DARZALEX FASPRO in APOLLO.

Table 9: Select Hematology Laboratory Abnormalities Worsening from Baseline in Patients Who Received DARZALEX FASPRO with Lenalidomide and Dexamethasone (DARZALEX FASPRO-Pd) in PLEIADES

<table>
<thead>
<tr>
<th>Laboratory Abnormality</th>
<th>All Grades (%)</th>
<th>Grades 3-4 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decreased leukocytes</td>
<td>94</td>
<td>34</td>
</tr>
<tr>
<td>Decreased lymphocytes</td>
<td>82</td>
<td>58</td>
</tr>
<tr>
<td>Decreased platelets</td>
<td>88</td>
<td>9</td>
</tr>
<tr>
<td>Decreased neutrophils</td>
<td>89</td>
<td>52</td>
</tr>
<tr>
<td>Decreased hemoglobin</td>
<td>45</td>
<td>8</td>
</tr>
</tbody>
</table>

* Denominator is based on the safety population treated with DARZALEX FASPRO-Pd (N=149).

In Combination with Pomalidomide and Dexamethasone

The safety of DARZALEX FASPRO with pomalidomide and dexamethasone compared to pomalidomide and dexamethasone (Pd) in patients who had received at least one prior line of therapy with lenalidomide and a proteasome inhibitor (PI) was evaluated in APOLLO [see Clinical Studies (14.2)]. Patients received DARZALEX FASPRO 1,800 mg/30,000 units administered subcutaneously once weekly from weeks 1 to 8, once every 2 weeks from weeks 9 to 24 and once every 4 weeks starting with week 25 until disease progression or unacceptable toxicity in combination with pomalidomide and dexamethasone (n=149) or pomalidomide and dexamethasone (n=150). Among patients receiving DARZALEX FASPRO-Pd, 71% were exposed for 6 months or longer and 50% were exposed for greater than one year.

Serious adverse reactions occurred in 50% of patients who received DARZALEX FASPRO-Pd. The most frequent serious adverse reactions in >5% of patients who received DARZALEX FASPRO-Pd were pneumonia (15%) and lower respiratory tract infection (12%). Fatal adverse reactions occurred in 7% of patients who received DARZALEX FASPRO-Pd.

Permanent treatment discontinuation due to an adverse reaction occurred in 2% of patients who received DARZALEX FASPRO-Pd.

The most common adverse reactions (≥10%) were fatigue, pneumonia, upper respiratory, thoracic and mediastinal disorders, and headache. Among patients receiving DARZALEX FASPRO-Pd, 71% were exposed for 6 months or longer and 27% were exposed for greater than one year.

Dosage interruptions due to an adverse reaction occurred in 46% of patients who received DARZALEX FASPRO.

The most common adverse reactions (≥20%) were rash, pruritus, oropharyngeal pain, and fatigue.

In Combination with Carfilzomib and Dexamethasone

The safety of DARZALEX FASPRO with carfilzomib and dexamethasone was evaluated in a single-arm cohort of PLEIADES [see Clinical Studies (14.2)]. Patients received DARZALEX FASPRO 1,800 mg/30,000 units administered subcutaneously once weekly from Weeks 1 to 8, once every 2 weeks from Weeks 9 to 24 and once every 4 weeks starting with Week 25 until disease progression or unacceptable toxicity (N=66) in combination with carfilzomib and dexamethasone.

Serious adverse reactions occurred in 27% of patients who received DARZALEX FASPRO in combination with carfilzomib and dexamethasone.

Permanently discontinued DARZALEX FASPRO due to an adverse reaction occurred in 6% of patients who received DARZALEX FASPRO.

Dose interruptions due to an adverse reaction occurred in 46% of patients who received DARZALEX FASPRO.

The most common adverse reactions (≥20%) were upper respiratory tract infection, fatigue, insomnia, hypertension, diarrhea, cough, dyspnea, headache, pyrexia, nausea and edema peripheral.

Table 10: Adverse Reactions Reported in ≥10% of Patients and With at Least a 5% Greater Frequency in the DARZALEX FASPRO-Pd Arm in APOLLO

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>DARZALEX FASPRO-Pd (N=149)</th>
<th>DARZALEX FASPRO-Pd (N=150)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All Grades (%)</td>
<td>Grades ≥3 (%)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>46</td>
<td>13</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>19</td>
<td>0</td>
</tr>
<tr>
<td>Edema peripheral</td>
<td>15</td>
<td>0</td>
</tr>
<tr>
<td>Infections</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pneumonia</td>
<td>38</td>
<td>23</td>
</tr>
<tr>
<td>Upper respiratory infection</td>
<td>36</td>
<td>1</td>
</tr>
<tr>
<td>Gastrointestinal disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diarrhea</td>
<td>22</td>
<td>5</td>
</tr>
<tr>
<td>Respiratory, thoracic and mediastinal disorders</td>
<td>13</td>
<td>0</td>
</tr>
</tbody>
</table>

Key: Pd=pomalidomide-dexamethasone

Table 11: Select Hematology Laboratory Abnormalities Worsening from Baseline in Patients Who Received DARZALEX FASPRO-Pd or Pd in APOLLO

<table>
<thead>
<tr>
<th>Laboratory Abnormality</th>
<th>DARZALEX FASPRO-Pd (N=149)</th>
<th>DARZALEX FASPRO-Pd (N=150)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decreased neutrophils</td>
<td>97</td>
<td>84</td>
</tr>
<tr>
<td>Decreased leukocytes</td>
<td>95</td>
<td>64</td>
</tr>
<tr>
<td>Decreased lymphocytes</td>
<td>93</td>
<td>59</td>
</tr>
<tr>
<td>Decreased platelets</td>
<td>75</td>
<td>19</td>
</tr>
<tr>
<td>Decreased hemoglobin</td>
<td>51</td>
<td>16</td>
</tr>
</tbody>
</table>

Key: Pd=pomalidomide-dexamethasone

Table 12: Adverse Reactions in <10% of Patients Who Received DARZALEX FASPRO with Pomalidomide and Dexamethasone include:

- Metabolism and nutrition disorders: hypocalcemia, hypokalemia, decreased appetite, dehydration
- Nervous system disorders: peripheral sensory neuropathy, syncope, headache, paresthesia, dizziness
- Musculoskeletal and connective tissue disorders: muscle spasms, musculoskeletal chest pain, arthralgia
- Psychiatric disorders: insomnia
- Gastrointestinal disorders: nausea, abdominal pain, vomiting
- Skin and subcutaneous tissue disorders: rash, pruritus
- Cardiac disorders: atrial fibrillation
- General disorders and administration site conditions: infusion reactions, chills, injection site reaction
- Infections: urinary tract infection, influenza, hepatitis B reactivation, herpes zoster, sepsis
- Vascular disorders: hypertension, hypotension
Table 12: Adverse Reactions (≥10%) in Patients Who Received DARZALEX FASPRO with Carfilzomib and Dexamethasone (DARZALEX FASPRO-Kd) in PLEIADES

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>DARZALEX FASPRO-Kd (N=66)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infections and infestations</td>
<td></td>
</tr>
<tr>
<td>Upper respiratory tract infection</td>
<td>52</td>
</tr>
<tr>
<td>Bronchitis</td>
<td>12</td>
</tr>
<tr>
<td>General disorders and administration site conditions</td>
<td></td>
</tr>
<tr>
<td>Fatigue</td>
<td>2</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>2</td>
</tr>
<tr>
<td>Edema peripheral</td>
<td>0</td>
</tr>
<tr>
<td>Insomnia</td>
<td>6</td>
</tr>
<tr>
<td>Vascular disorders</td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>32</td>
</tr>
<tr>
<td>Gastrointestinal disorders</td>
<td></td>
</tr>
<tr>
<td>Diarrhea</td>
<td>29</td>
</tr>
<tr>
<td>Nausea</td>
<td>21</td>
</tr>
<tr>
<td>Vomiting</td>
<td>15</td>
</tr>
<tr>
<td>Respiratory, thoracic and mediastinal disorders</td>
<td></td>
</tr>
<tr>
<td>Cough</td>
<td>24</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>23</td>
</tr>
<tr>
<td>Nervous system disorders</td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>23</td>
</tr>
<tr>
<td>Peripheral sensory neuropathy</td>
<td>11</td>
</tr>
<tr>
<td>Musculoskeletal and connective tissue disorders</td>
<td></td>
</tr>
<tr>
<td>Back pain</td>
<td>17</td>
</tr>
<tr>
<td>Musculoskeletal chest pain</td>
<td>11</td>
</tr>
</tbody>
</table>

Table 13: Select Laboratory Abnormalities (≥30%) Worsening from Baseline in Patients Who Received DARZALEX FASPRO-Kd in PLEIADES

Table 14: Adverse Reactions (≥10%) in Patients Who Received DARZALEX FASPRO or Intravenous Daratumumab in COLUMBA

Table 15: Laboratory Abnormalities (≥30%) worsening from baseline in patients who received DARZALEX FASPRO-Kd (N=66).

**Monotherapy**

The safety of DARZALEX FASPRO as monotherapy was evaluated in COLUMBA (see Clinical Trials [14.2]). Patients received DARZALEX FASPRO 1,800 mg/30,000 units administered subcutaneously or daratumumab 18 mg/kg administered intravenously, each administered once weekly from weeks 1 to 8, once every 2 weeks from weeks 9 to 24 and once every 4 weeks starting with week 25 until disease progression or unacceptable toxicity. Among patients receiving DARZALEX FASPRO, 37% were exposed for 6 months or longer and 1% were exposed for greater than one year.

Serious adverse reactions occurred in 26% of patients who received DARZALEX FASPRO. Fatal adverse reactions occurred in 5% of patients. Fatal adverse reactions occurring in more than 1 patient were general physical health deterioration, septic shock, and respiratory failure.

Permanent discontinuation due to an adverse reaction occurred in 10% of patients who received DARZALEX FASPRO. Adverse reactions resulting in permanent discontinuation of DARZALEX FASPRO in more than 2 patients were thrombocytopenia and hypercalcemia.

Dosage interruptions due to an adverse reaction occurred in 26% of patients who received DARZALEX FASPRO. Adverse reactions requiring dosage interruption in >5% of patients included thrombocytopenia.

The most common adverse reaction (≥20%) was upper respiratory tract infection. Table 14 summarizes the adverse reactions in COLUMBA.

**Clinical Trial**

The most common adverse reaction (≥20%) was upper respiratory tract infection. Table 14 summarizes the adverse reactions in COLUMBA.
Clinically relevant adverse reactions in <10% of patients who received DARZALEX FASPRO included:

- General disorders and administration site conditions: injection site reaction, peripheral edema
- Musculoskeletal and connective tissue disorders: arthralgia, musculoskeletal chest pain, muscle spasms
- Gastrointestinal disorders: constipation, vomiting, abdominal pain
- Metabolism and nutrition disorders: decreased appetite, hyperglycemia, hypocalcemia, dehydration
- Psychiatric disorders: insomnia
- Vascular disorders: hypertension, hypotension
- Nervous system disorders: dizziness, peripheral sensory neuropathy, paresthesia
- Infections: bronchitis, influenza, urinary tract infection, herpes zoster, sepsis, hepatitis B virus reactivation
- Skin and subcutaneous tissue disorders: pruritus, rash
- Cardiac disorders: atrial fibrillation
- Respiratory, thoracic and mediastinal disorders: pulmonary edema

Table 15 summarizes the laboratory abnormalities in COLUMBA.

<table>
<thead>
<tr>
<th>Laboratory Abnormality</th>
<th>DARZALEX FASPRO®</th>
<th>Intravenous Daratumumab</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All Grades (%)</td>
<td>Grades 3-4 (%)</td>
</tr>
<tr>
<td>Decreased leukocytes</td>
<td>65</td>
<td>19</td>
</tr>
<tr>
<td>Decreased lymphocytes</td>
<td>59</td>
<td>36</td>
</tr>
<tr>
<td>Decreased neutrophils</td>
<td>55</td>
<td>19</td>
</tr>
<tr>
<td>Decreased platelets</td>
<td>43</td>
<td>16</td>
</tr>
<tr>
<td>Decreased hemoglobin</td>
<td>42</td>
<td>14</td>
</tr>
</tbody>
</table>

a Denominator is based on the safety population treated with DARZALEX FASPRO (N=260) and Intravenous Daratumumab (N=258).

Light Chain Amyloidosis

In Combination with Bortezomib, Cyclophosphamide and Dexamethasone

The safety of DARZALEX FASPRO with bortezomib, cyclophosphamide and dexamethasone (DARZALEX FASPRO-VCd) was evaluated in ANDROMEDA (see Clinical Studies (14.3)). Patients received DARZALEX FASPRO 1,800 mg/30,000 units administered subcutaneously once weekly from weeks 1 to 8, once every 2 weeks from weeks 9 to 24 and once every 4 weeks starting with week 25 until disease progression or unacceptable toxicity or a maximum of 2 years. Among patients who received DARZALEX FASPRO-VCd, 74% were exposed for 6 months or longer and 32% were exposed for greater than one year.

Serious adverse reactions occurred in 43% of patients who received DARZALEX FASPRO in combination with VCd. Serious adverse reactions that occurred in at least 5% of patients in the DARZALEX FASPRO-VCd arm were pneumonia (9%), cardiac failure (8%), and sepsis (5%). Fatal adverse reactions occurred in 11% of patients. Fatal adverse reactions that occurred in more than one patient included cardiac arrest (4%), sudden death (3%), cardiac failure (3%), and sepsis (1%).

Permanent discontinuation of DARZALEX FASPRO due to an adverse reaction occurred in 5% of patients. Adverse reactions resulting in permanent discontinuation of DARZALEX FASPRO in more than one patient were pneumonia, sepsis, and cardiac failure.

Dosage interruptions (defined as dose delays or skipped doses) due to an adverse reaction occurred in 36% of patients who received DARZALEX FASPRO. Adverse reactions which required a dosage interruption in ≥3% of patients included upper respiratory tract infection (9%), pneumonia (6%), cardiac failure (4%), fatigue (3%), herpes zoster (3%), dyspnea (3%), and neutropenia (3%).

The most common adverse reactions (≥20%) were upper respiratory tract infection, diarrhea, peripheral edema, constipation, fatigue, peripheral sensory neuropathy, nausea, insomnia, dyspnea, and cough.

Table 16 below summarizes the adverse reactions in patients who received DARZALEX FASPRO in ANDROMEDA.

Table 16: Adverse Reactions (≥10%) in Patients with AL Amyloidosis Who Received DARZALEX FASPRO with Bortezomib, Cyclophosphamide and Dexamethasone (DARZALEX FASPRO-VCd) with a Difference Between Arms of >5% Compared to VCd in ANDROMEDA

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>DARZALEX FASPRO-VCd (N=193)</th>
<th>VCd (N=188)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All Grades (%)</td>
<td>Grades 3-4 (%)</td>
</tr>
<tr>
<td>Infections</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Upper respiratory tract infectiona</td>
<td>40</td>
<td>1f</td>
</tr>
<tr>
<td>Pneumoniab</td>
<td>15</td>
<td>10</td>
</tr>
<tr>
<td>Gastrointestinal disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diarrhea</td>
<td>36</td>
<td>6f</td>
</tr>
<tr>
<td>Constipation</td>
<td>34</td>
<td>2f</td>
</tr>
<tr>
<td>Nervous system disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peripheral sensory neuropathy</td>
<td>31</td>
<td>3f</td>
</tr>
<tr>
<td>Respiratory, thoracic and mediastinal disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dyspnea</td>
<td>26</td>
<td>4</td>
</tr>
<tr>
<td>Cough</td>
<td>20</td>
<td>1f</td>
</tr>
<tr>
<td>Musculoskeletal and connective tissue disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Back pain</td>
<td>12</td>
<td>2f</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>10</td>
<td>0</td>
</tr>
<tr>
<td>Muscle spasms</td>
<td>10</td>
<td>1f</td>
</tr>
<tr>
<td>Cardiac disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arrhythmia</td>
<td>11</td>
<td>4</td>
</tr>
<tr>
<td>General disorders and administration site conditions</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Injection site reactionsf</td>
<td>11</td>
<td>0</td>
</tr>
</tbody>
</table>

a Only grade 3 adverse reactions occurred.

b Upper respiratory tract infection includes laryngitis, nasopharyngitis, pharyngitis, respiratory syncytial virus infection, respiratory tract infection, respiratory tract infection viral, rhinitis, rhinovirus infection, sinusitis, tonsilitis, tracheitis, upper respiratory tract infection, upper respiratory tract infection bacterial, and viral upper respiratory tract infection.

c Pneumonia includes lower respiratory tract infection, pneumonia, pneumonia aspiration, and pneumonia pneumococcal.

c Dyspnea includes dyspnea, and dyspnea exertional.

c Cough includes cough, and productive cough.

d Arrhythmia includes atrial flutter, atrial fibrillation, supraventricular tachycardia, bradycardia, atrhythymia, bradyarrhythmia, cardiac flutter, extrasystoles, supraventricular extrasystoles, ventricular arrhythmia, ventricular extrasystoles, atrial tachycardia, ventricular tachycardia

f Injection site reactions includes terms determined by investigators to be related to daratumumab injection.

Clinically relevant adverse reactions not included in Table 16 and occurred in patients who received DARZALEX FASPRO with bortezomib, cyclophosphamide and dexamethasone included:

- Skin and subcutaneous tissue disorders: rash, pruritus
- Nervous system disorders: paresthesia
- General disorders and administration site conditions: infusion reaction, chills
- Cardiac disorders: cardiac failure, cardiac arrest
- Metabolism and nutrition disorders: hyperglycemia, hypocalcemia, dehydration
- Infections: bronchitis, herpes zoster, sepsis, urinary tract infection, influenza
- Vascular disorders: hypertension
- Musculoskeletal and connective tissue disorders: musculoskeletal chest pain
- Gastrointestinal disorders: pancreatitis
- Respiratory, thoracic and mediastinal disorders: pulmonary edema

c Cardiac failure includes cardiac dysfunction, cardiac failure, cardiac failure congestive, cardiovascular insufficiency, diastolic dysfunction, pulmonary edema, and left ventricular dysfunction occurred in 11% of patients.

Table 17 summarizes the laboratory abnormalities in patients who received DARZALEX FASPRO in ANDROMEDA.
DARZALEX FASPRO® (daratumumab and hyaluronidase-fihj) injection

Interference with Indirect Antiglobulin Tests (Indirect Coombs Test)

† Daratumumab binds to CD38 on RBCs and interferes with compatibility testing, including antibody screening and cross matching. Daratumumab interference mitigation methods include treating reagent RBCs with dithiothreitol (DTT) to disrupt daratumumab binding (see References (15)) or genotyping. Since the Kell blood group system is also sensitive to DTT treatment, supply K-negative units after ruling out or identifying alloantibodies using DTT-treated RBCs. If an emergency transfusion is required, administer non-cross-matched AB0/RhD-compatible RBCs per local blood bank practices.

Interference with Serum Protein Electrophoresis and Immunofixation Tests

Rare cases of daratumumab antibodies have been detected in the serum of patients who received DARZALEX FASPRO as monotherapy or as part of a combination therapy. The antibody response to daratumumab is generally seen within the first 12 weeks of therapy. The antibody response appears to be dose-dependent. The anti-daratumumab antibodies do not affect daratumumab pharmacokinetics.

The immunoglobulin G1 (IgG1) monoclonal antibodies are transferred across the placenta. Based on its mechanism of action, DARZALEX FASPRO may cause depletion of fetal CD38 positive immune cells and decreased bone density. Defer administering live vaccines to neonates and infants exposed to daratumumab in utero until a hematologic evaluation is completed.

8.2 Lactation

Risk Summary

There is no data on the presence of daratumumab and hyaluronidase in human milk, the effects on the breastfed child, or the effects on milk production. Maternal immunoglobulin G is known to be present in human milk. Published data suggest that antibodies in breast milk do not enter the neonatal and infant circulations in substantial amounts. Because of the potential for serious adverse reactions in the breastfed child when DARZALEX FASPRO is administered with lenalidomide, thalidomide or pomalidomide, advise women not to breastfeed during treatment with DARZALEX FASPRO. Refer to lenalidomide, thalidomide or pomalidomide prescribing information for additional information.

Data

Animal Data

DARZALEX FASPRO for subcutaneous injection contains daratumumab and hyaluronidase. Mice that were genetically modified to eliminate all CD38 expression (CD38 knockout mice) had reduced bone density at birth that recovered by 5 months of age. Data from studies using CD38 knockout animal models also suggest the involvement of CD38 in the regulation of humoral immune responses (mice), fetomaternal immune tolerance (mice), and early embryonic development (frogs).

No systemic exposure of hyaluronidase was detected in monkeys given 22,000 U/kg subcutaneously (12 times higher than the human dose) and there were no effects on embryo-fetal development in pregnant mice given 330,000 U/kg hyaluronidase subcutaneously during organogenesis, which is 45 times higher than the human dose.

There were no effects on pre- and post-natal development through sexual maturity in offspring of mice treated daily from implantation through lactation with 990,000 U/kg hyaluronidase subcutaneously, which is 134 times higher than the human doses.

8.1 Pregnancy

Risk Summary

There are no available data on the use of DARZALEX FASPRO in pregnant women to evaluate drug-associated risk of major birth defects, miscarriage or adverse maternal or fetal outcomes. Animal reproduction studies have not been conducted.

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

The combination of DARZALEX FASPRO and lenalidomide, thalidomide or pomalidomide is contraindicated in pregnant women, because lenalidomide, thalidomide and pomalidomide may cause birth defects and death of the unborn child. Lenalidomide, thalidomide and pomalidomide are only available through a REMS program. Refer to the lenalidomide, thalidomide or pomalidomide prescribing information on use during pregnancy.

Clinical Considerations

Fetal/Neonatal Adverse Reactions

IgG1 monoclonal antibodies are transferred across the placenta. Based on its mechanism of action, DARZALEX FASPRO may cause depletion of fetal CD38 positive immune cells and decreased bone density. Defer administering live vaccines to neonates and infants exposed to daratumumab in utero until a hematologic evaluation is completed.

Data

Animal Data

DARZALEX FASPRO for subcutaneous injection contains daratumumab and hyaluronidase. Mice that were genetically modified to eliminate all CD38 expression (CD38 knockout mice) had reduced bone density at birth that recovered by 5 months of age. Data from studies using CD38 knockout animal models also suggest the involvement of CD38 in the regulation of humoral immune responses (mice), fetomaternal immune tolerance (mice), and early embryonic development (frogs).

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There were no effects on pre- and post-natal development through sexual maturity in offspring of mice treated daily from implantation through lactation with 990,000 U/kg hyaluronidase subcutaneously, which is 134 times higher than the human doses.

8.3 Females and Males of Reproductive Potential

DARZALEX FASPRO can cause fetal harm when administered to a pregnant woman. The assessment of associated risks with daratumumab products is based on the mechanism of action and data from target antigen CD38 knockout animal models (see Data). There are no available data on the use of DARZALEX FASPRO in pregnant women to evaluate drug-associated risk of major birth defects, miscarriage or adverse maternal or fetal outcomes. Animal reproduction studies have not been conducted.

Teratogenic Effects

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

The combination of DARZALEX FASPRO and lenalidomide, thalidomide or pomalidomide is contraindicated in pregnant women, because lenalidomide, thalidomide and pomalidomide may cause birth defects and death of the unborn child. Lenalidomide, thalidomide and pomalidomide are only available through a REMS program. Refer to the lenalidomide, thalidomide or pomalidomide prescribing information on use during pregnancy.

Clinical Considerations

Fetal/Neonatal Adverse Reactions

IgG1 monoclonal antibodies are transferred across the placenta. Based on its mechanism of action, DARZALEX FASPRO may cause depletion of fetal CD38 positive immune cells and decreased bone density. Defer administering live vaccines to neonates and infants exposed to daratumumab in utero until a hematologic evaluation is completed.

Data

Animal Data

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There were no effects on pre- and post-natal development through sexual maturity in offspring of mice treated daily from implantation through lactation with 990,000 U/kg hyaluronidase subcutaneously, which is 134 times higher than the human doses.

8.2 Lactation

Risk Summary

There is no data on the presence of daratumumab and hyaluronidase in human milk, the effects on the breastfed child, or the effects on milk production. Maternal immunoglobulin G is known to be present in human milk. Published data suggest that antibodies in breast milk do not enter the neonatal and infant circulations in substantial amounts. Because of the potential for serious adverse reactions in the breastfed child when DARZALEX FASPRO is administered with lenalidomide, thalidomide or pomalidomide, advise women not to breastfeed during treatment with DARZALEX FASPRO. Refer to lenalidomide, thalidomide or pomalidomide prescribing information for additional information.

Data

Animal Data

DARZALEX FASPRO for subcutaneous injection contains daratumumab and hyaluronidase. Mice that were genetically modified to eliminate all CD38 expression (CD38 knockout mice) had reduced bone density at birth that recovered by 5 months of age. Data from studies using CD38 knockout animal models also suggest the involvement of CD38 in the regulation of humoral immune responses (mice), fetomaternal immune tolerance (mice), and early embryonic development (frogs).

No systemic exposure of hyaluronidase was detected in monkeys given 22,000 U/kg subcutaneously (12 times higher than the human dose) and there were no effects on embryo-fetal development in pregnant mice given 330,000 U/kg hyaluronidase subcutaneously during organogenesis, which is 45 times higher than the human dose.

There were no effects on pre- and post-natal development through sexual maturity in offspring of mice treated daily from implantation through lactation with 990,000 U/kg hyaluronidase subcutaneously, which is 134 times higher than the human doses.

8.3 Females and Males of Reproductive Potential

DARZALEX FASPRO can cause fetal harm when administered to a pregnant woman. The assessment of associated risks with daratumumab products is based on the mechanism of action and data from target antigen CD38 knockout animal models (see Data). There are no available data on the use of DARZALEX FASPRO in pregnant women to evaluate drug-associated risk of major birth defects, miscarriage or adverse maternal or fetal outcomes. Animal reproduction studies have not been conducted.

Teratogenic Effects

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

The combination of DARZALEX FASPRO and lenalidomide, thalidomide or pomalidomide is contraindicated in pregnant women, because lenalidomide, thalidomide and pomalidomide may cause birth defects and death of the unborn child. Lenalidomide, thalidomide and pomalidomide are only available through a REMS program. Refer to the lenalidomide, thalidomide or pomalidomide prescribing information on use during pregnancy.
DARZALEX FASPRO® (daratumumab and hyaluronidase-fihj) injection

Safety and effectiveness of DARZALEX FASPRO in pediatric patients have not been established.

8.5 Geriatric Use

Of the 291 patients who received DARZALEX FASPRO as monotherapy for relapsed and refractory multiple myeloma, 37% were 65 to <75 years of age, and 19% were 75 years of age or older. No overall differences in effectiveness of DARZALEX FASPRO have been observed between patients ≥85 years of age and younger patients. Adverse reactions that occurred at a higher frequency (≥5% difference) in patients ≥85 years of age included upper respiratory tract infection, urinary tract infection, dizziness, cough, dyspnea, diarrhea, nausea, fatigue, and peripheral edema. Serious adverse reactions that occurred at a higher frequency (≥2% difference) in patients ≥85 years of age included pneumonia.

Of the 214 patients who received DARZALEX FASPRO as combination therapy with pomalidomide and dexamethasone or DARZALEX FASPRO as combination therapy with lenalidomide and low-dose dexamethasone for relapsed and refractory multiple myeloma, 43% were ≥65 years of age, and 18% were ≥75 years of age or older. No overall differences in effectiveness were observed between patients ≥65 years (n=131) and <65 years (n=85). Adverse reactions occurring at a higher frequency (≥5% difference) in patients ≥65 years of age included fatigue, pyrexia, peripheral edema, urinary tract infection, diarrhea, constipation, vomiting, dyspnea, cough, and hypoglycemia. Serious adverse reactions occurring at a higher frequency (≥2% difference) in patients ≥65 years of age included neutropenia, thrombocytopenia, diarrhea, anemia, COVID-19, ischemic colitis, deep vein thrombosis, general physical health deterioration, pulmonary embolism, and urinary tract infection.

Of the 193 patients who received DARZALEX FASPRO as part of a combination therapy for light chain (AL) amyloidosis, 35% were ≥65 to <75 years of age, and 10% were ≥75 years of age or older. Clinical studies of DARZALEX FASPRO as part of a combination therapy for patients with light chain (AL) amyloidosis did not include sufficient numbers of patients aged 65 and older to determine whether effectiveness differs from that of younger patients. Adverse reactions that occurred at a higher frequency in patients ≥65 years of age were peripheral edema, asthenia, pneumonia and hypotension.

No clinically meaningful differences in the pharmacokinetics of daratumumab were observed in geriatric patients compared to younger adult patients [see Clinical Pharmacology (12.3)].

11 DESCRIPTION

Daratumumab is an immunoglobulin G1 kappa (IgG1k) human monoclonal antibody that binds to the CD38 antigen. Daratumumab is produced in Chinese Hamster Ovary (CHO) cells using recombinant DNA technology. The molecular weight of daratumumab is approximately 148 kDa.

Hyaluronidase (recombinant human) is an endoglycosidase used to increase the dispersion and absorption of co-administered drugs when administered subcutaneously. It is a glycosylated single-chain protein produced by Chinese Hamster Ovary cells containing a DNA plasmid encoding for a soluble fragment of human hyaluronidase (PH20). Hyaluronidase (recombinant human) has a molecular weight of approximately 61 kDa.

DARZALEX FASPRO® (daratumumab and hyaluronidase-fihj) injection is a sterile, preservative-free, colorless to yellow, and clear to opalescent solution supplied in a single-dose vial for subcutaneous administration.

Each DARZALEX FASPRO FASPRO 15 mL single-dose vial contains 1,800 mg of daratumumab and 30,000 units of hyaluronidase, L-histidine (4.9 mg), L-histidine hydrochloride monohydrate (18.4 mg), L-methionine (13.5 mg), polysorbate 20 (6 mg), sorbitol (735.1 mg), and Water for Injection, USP.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

CD38 is a transmembrane glycoprotein (48 kDa) expressed on the surface of hematopoietic cells, including clonal plasma cells in multiple myeloma and light chain (AL) amyloidosis, as well as other cell types. Surface CD38 has multiple functions, including receptor mediated adhesion, signaling, and modulation of cyclic AMP and hydrolysis activity. Daratumumab is an IgG1κ human monoclonal antibody (mAb) that binds to CD38 and inhibits the growth of CD38 expressing tumor cells by inducing apoptosis directly through Fc receptor cross linking as well as by immune-mediated tumor cell lysis through complement dependent cytotoxicity (CDC), antibody dependent cell mediated cytotoxicity (ADCC) and antibody dependent cellular phagocytosis (ADCP). A subset of myeloid derived suppressor cells (CD38+MDSCs), regulatory T cells (CD38+CD45RA) and B cells (CD38+CD19) are decreased by daratumumab.

Hyaluronan is a polysaccharide found in the extracellular matrix of the subcutaneous tissue. It is depolymerized by the naturally occurring enzyme hyaluronidase. Unlike the stable structural components of the interstitial connective tissue, hyaluronan has a half-life of approximately 0.5 days. Hyaluronidase increases permeability of the subcutaneous tissue by depolymerizing hyaluronan. In the doses administered, hyaluronidase in DARZALEX FASPRO acts locally. The effects of hyaluronidase are reversible and permeability of the subcutaneous tissue is restored within 24 to 48 hours.

12.2 Pharmacodynamics

NK cells express CD38 and are susceptible to daratumumab mediated cell lysis. Decreases in absolute counts and percentages of total NK cells (CD16+CD56+) and activated (CD16+CD56dim) NK cells in peripheral whole blood and bone marrow were observed with DARZALEX FASPRO treatment.

Cardiac Electrophysiology

DARZALEX FASPRO as a large protein has a low likelihood of direct ion channel interactions. There is no evidence from non-clinical or clinical data to suggest that DARZALEX FASPRO has the potential to delay ventricular repolarization.

12.3 Pharmacokinetics

Following the recommended dose of DARZALEX FASPRO 1,800 mg/30,000 units subcutaneously once weekly for 8 weeks, daratumumab peak concentration (Cmax) increased 4.8-fold and area under the curve (AUC0-7 days) increased 5.4-fold from the 1st dose to the 8th dose as monotherapy. Maximum trough concentrations for DARZALEX FASPRO are typically observed at the midpoint of the weekly dosing regimens for both monotherapy and combination therapies. The mean ± standard deviation (SD) maximum trough serum concentration (Cmax) and area under the curve from time zero to 7 days (AUC0-7 days) after the 8th dose were 563 ± 306 µg/mL when DARZALEX FASPRO was administered as monotherapy and 537 ± 277 µg/mL, 526 ± 226 µg/mL, and 766 ± 276 µg/mL when DARZALEX FASPRO was administered as combination with Pd, Rd, and Rd, respectively.

Table 18 lists the observed mean (±SD) maximum trough concentrations (Cmax) after the 8th dose, simulated median (5th-95th percentiles) maximum Cmax after the 8th dose, simulated median (5th-95th percentiles) Cmax after the 8th dose, and simulated median (5th-95th percentiles) area under the curve after the 8th dose following DARZALEX FASPRO 1,800 mg/30,000 units administered subcutaneously in patients with multiple myeloma or light chain (AL) amyloidosis.

Table 18: Daratumumab Exposure for Patients with Multiple Myeloma or Light Chain (AL) Amyloidosis

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Intravenous</th>
<th>DARZALEX FASPRO 1,800 mg/30,000 units</th>
<th>DARZALEX FASPRO 1,800 mg/30,000 units</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observed mean±SD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cmax after 8th dose (µg/mL)</td>
<td>522±226</td>
<td>593±306</td>
<td>597±232</td>
</tr>
<tr>
<td>Simulated median (5th-95th percentiles)</td>
<td>472 (144-809)</td>
<td>583 (177-1063)</td>
<td>662 (315-1037)</td>
</tr>
<tr>
<td>Simulated median (5th-95th percentiles) Cmax after 8th dose (µg/mL)</td>
<td>688 (369-1061)</td>
<td>592 (234-1114)</td>
<td>729 (390-1105)</td>
</tr>
<tr>
<td>Simulated median (5th-95th percentiles) AUC0-7 days after 8th dose (µg/mL/day)</td>
<td>4019 (1740-6370)</td>
<td>4017 (1515-7564)</td>
<td>4855 (2562-7522)</td>
</tr>
</tbody>
</table>

4 Geometric mean ratio between 1,800 mg SC and 16 mg/kg was 108% (90% CI: 98-122) in patients with multiple myeloma.

Source: AMY3001 Primary Analysis Clinical Study Report

a Patients with multiple myeloma who received daratumumab monotherapy

b Patients with AL amyloidosis who received daratumumab in combination with Multiple Myeloma or Light Chain (AL) Amyloidosis

c Source: MMY3012 Primary Analysis Clinical Study Report

d Source: AMY3001 Primary Analysis Clinical Study Report

e Source: Population Pharmacokinetics and Exposure-response Analysis Report for Subcutaneously Administered Daratumumab in Multiple Myeloma Subjects

f Source: Population Pharmacokinetics and Exposure-response Analysis Report for Daratumumab Subcutaneous Administration for the Treatment of Subjects with AL Amyloidosis
Absorption
At the recommended dose of DARZALEX FASPRO 1,800 mg/30,000 units, the absolute bioavailability is 89%, with peak concentrations occurring around 3 days (Tmax) in patients with multiple myeloma. Peak concentrations occurred around 4 days in patients with light chain (AL) amyloidosis.

Distribution
The estimated mean (coefficient of variation, CV) volume of distribution for the central compartment is 5.2 L (37%) and peripheral compartment was 3.8 L in patients with multiple myeloma. The estimated mean volume of distribution was 10.8 L (28%) in patients with light chain (AL) amyloidosis.

Elimination
Daratumumab is cleared by parallel linear and nonlinear saturable target mediated clearances. The estimated mean (CV%) linear clearance of daratumumab is 119 mL/day (93%) in patients with multiple myeloma and is 210 mL/day (42%) in patients with light chain (AL) amyloidosis. The estimated mean (CV%) elimination half-life associated with linear clearance is 20 days (22%) in patients with multiple myeloma and 28 days (74%) in patients with light chain (AL) amyloidosis.

Specific Populations
The following population characteristics have no clinically meaningful effect on the pharmacokinetics of daratumumab in patients administered DARZALEX FASPRO as monotherapy or as combination therapy: sex, age (33 to 92 years), renal impairment (Creatinine clearance (ClCr) 15 to 89 mL/min as determined by the Cockcroft-Gault formula), and mild hepatic impairment (total bilirubin 1 to 1.5 times ULN and AST:ULN). The effect of moderate and severe hepatic impairment on daratumumab pharmacokinetics is unknown.

Racial or Ethnic Groups
Of 190 patients with light chain (AL) amyloidosis who received DARZALEX FASPRO and had a maximum Cmax after the 8th dose, African-Americans (4%) had 24% higher daratumumab mean maximum Cmax after the 8th dose compared to that of Whites (83%) and Asians (10%) had 16% higher mean maximum Cmax after the 8th dose compared to that of Whites. The difference in exposure between that of Asians and Whites could be explained in part by differences in body size. The effect of African-American race on exposure and related safety and efficacy of daratumumab is unknown.

Body Weight
In patients with multiple myeloma who received DARZALEX FASPRO 1,800 mg/30,000 units as monotherapy, the mean maximum Cmax after the 8th dose was 12% lower in the higher body weight (BW) group (>85 kg), while the mean maximum Cmax after the 8th dose was 81% higher in the lower BW group (<50 kg) compared to the corresponding BW groups in the intravenous daratumumab arm.

In patients with light chain (AL) amyloidosis who received DARZALEX FASPRO 1,800 mg/30,000 units in combination and had a maximum Cmax after the 8th dose, the mean maximum Cmax after the 8th dose was 22% lower in the higher BW group (>85 kg) while the mean maximum Cmax after the 8th dose was 27% higher in the lower BW group (<50 kg) compared to the patients with body weight of 51-85 kg.

13 NONCLINICAL TOXICOLOGY
13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
No carcinogenicity or genotoxicity studies have been conducted with daratumumab. No animal studies have been performed to evaluate the potential effects of daratumumab on reproduction or development, or to determine potential effects on fertility in males or females.

No carcinogenicity, genotoxicity, or fertility studies were conducted for recombinant human hyaluronidase. There were no effects on reproductive tissues and function and no systemic exposure of hyaluronidase in monkeys given 22,000 U/kg/week subcutaneously (12 times higher than the human dose) for 29 weeks. As hyaluronidase is a recombinant form of the endogenous human hyaluronidase, no carcinogenicity, mutagenesis, or effects on fertility are expected.

14 CLINICAL STUDIES
14.1 Newly Diagnosed Multiple Myeloma
In Combination with Bortezomib, Melphalan and Prednisone
The efficacy of DARZALEX FASPRO with bortezomib, melphalan and prednisone was evaluated in a single-arm cohort of PLEIADES (NCT03412665), a multi-cohort, open-label trial. Patients received DARZALEX FASPRO 1,800 mg/30,000 units administered subcutaneously once weekly from weeks 1 to 8, once every 3 weeks from weeks 9 to 54 and once every 4 weeks starting with week 55 until disease progression or unacceptable toxicity; bortezomib 1.3 mg/m2 subcutaneously twice weekly on Weeks 1, 3 and 5 for the first 8-week cycle (Cycle 1; 8 doses), followed by once weekly on Weeks 1, 2, 4, and 5 for eight more 6-week cycles (Cycles 2-9; 4 doses per cycle); and melphalan 9 mg/m2 and prednisone 60 mg/m2 orally on Days 1 to 4 of the nine 6-week cycles (Cycles 1-9). The major efficacy outcome measure was overall response rate (ORR).

A total of 67 patients received DARZALEX FASPRO with VMP. The median age was 75 years (range: 66 to 86 years); 46% were male; 69% were White, 8% Asian, and 2% Black or African American; and 33% had ISS Stage I, 45% had ISS Stage II, and 22% had ISS Stage III disease. Efficacy results are summarized in Table 19. The median duration of follow-up for patients was 6.9 months.

14.2 Relapsed/Refractory Multiple Myeloma
In Combination with Lenalidomide and Dexamethasone
The efficacy of DARZALEX FASPRO with lenalidomide and dexamethasone (DARZALEX FASPRO-Rd) was evaluated in a single-arm cohort of PLEIADES (NCT03412665), a multi-cohort, open-label trial. Patients received DARZALEX FASPRO 1,800 mg/30,000 units administered subcutaneously once weekly from weeks 1 to 8, once every 2 weeks from weeks 9 to 24 and once every 4 weeks starting with week 25 until disease progression or unacceptable toxicity with lenalidomide 25 mg once daily orally on Days 1-21 of each 28-day cycle; and dexamethasone 40 mg per week (or a reduced dose of 20 mg per week for patients >75 years or BMI <18.5). The major efficacy outcome measure was ORR.

A total of 65 patients received DARZALEX FASPRO with Rd. The median age was 69 years (range: 33 to 82 years); 69% were male; 69% were White, and 3% Black or African American; and 42% had ISS Stage I, 30% had ISS Stage II, and 28% had ISS Stage III disease. Patients had received a median of 1 prior line of therapy. A total of 52% of patients had a prior ASCT; 35% of patients received a prior PI; 59% received a prior immunomodulatory agent, including 22% who received prior lenalidomide; and 54% of patients received both a prior PI and immunomodulatory agent.

Efficacy results are summarized in Table 20. The median duration of follow-up for patients was 7.1 months.
APOLLO demonstrated an improvement in PFS in the DARZALEX FASPRO-Pd treatment group as compared to the Pd treatment group; the median PFS was 12.4 months in the DARZALEX FASPRO-Pd treatment group and 6.9 months in the Pd treatment group (HR [95% CI]: 0.63 [0.47, 0.86]; p-value = 0.0018), representing a 37% reduction in the risk of disease progression or death for patients treated with DARZALEX FASPRO-Pd versus Pd.

In responders, the median time to response was 1 month (range: 0.9 to 24 months) with relapsed or refractory multiple myeloma excluding patients with left ventricular ejection fraction (LVEF) less than 40%, myocardial infarction within 6 months, uncontrolled cardiac arrhythmia, or uncontrolled hypertension.

Figure 1: Kaplan-Meier Curve of PFS in APOLLO

![Kaplan-Meier Curve of PFS in APOLLO](image)

Additional efficacy results from APOLLO are presented in Table 21.

Table 21: Efficacy results from APOLLO

<table>
<thead>
<tr>
<th>DARZALEX FASPRO-Pd (n=151)</th>
<th>Pd (n=153)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall response (sCR+CR+VGPR+PR) n (%)</td>
<td>104 (68.9%)</td>
</tr>
<tr>
<td>P-value</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Stringent complete response (sCR)</td>
<td>14 (9.3%)</td>
</tr>
<tr>
<td>Complete response (CR)</td>
<td>23 (15.2%)</td>
</tr>
<tr>
<td>Very good partial response (VGPR)</td>
<td>40 (26.5%)</td>
</tr>
<tr>
<td>Partial response (PR)</td>
<td>27 (17.3%)</td>
</tr>
<tr>
<td>MRD negativity rate</td>
<td>13 (8.6%)</td>
</tr>
<tr>
<td>95% CI (%)</td>
<td>(4.7%, 14.3%)</td>
</tr>
</tbody>
</table>

Pd=pomalidomide-dexamethasone; MRD=minimal residual disease; CI=confidence interval

* Based on intent-to-treat population

1. **Prevalence of MRD negativity in patients with CR or better**
   - Number of patients with CR or better: N=37
   - Number of patients: N=6
   - MRD negativity rate: 13 (35.1%)
   - 95% CI: (20.2%, 52.5%)

2. For Pd arm, median OS was not reached for either treatment group.

In Combination with Carfilzomib and Dexamethasone

The efficacy of DARZALEX FASPRO with carfilzomib and dexamethasone (DARZALEX FASPRO-Kd) was evaluated in a single-arm cohort of PLEIADES (NCT03412565), a multi-cohort, open-label trial. This cohort enrolled patients with relapsed or refractory multiple myeloma excluding patients with left ventricular ejection fraction (LVEF) less than 40%, myocardial infarction within 6 months, uncontrolled cardiac arrhythmia, or uncontrolled hypertension.

Additional efficacy results from PLEIADES are presented in Table 22.

Table 22: Efficacy Results from PLEIADES in Patients Who Received DARZALEX FASPRO-Kd

<table>
<thead>
<tr>
<th>DARZALEX FASPRO-Kd (N=66)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall response (sCR+CR+VGPR+PR) n (%)</td>
</tr>
<tr>
<td>95% CI (%)</td>
</tr>
<tr>
<td>Stringent complete response (sCR)</td>
</tr>
<tr>
<td>Complete response (CR)</td>
</tr>
<tr>
<td>Very good partial response (VGPR)</td>
</tr>
<tr>
<td>Partial response (PR)</td>
</tr>
</tbody>
</table>

CI=confidence interval

* Based on treated patients

Monotherapy

The efficacy of DARZALEX FASPRO as monotherapy was evaluated in COLUMBA (NCT03277105), an open-label, randomized, non-inferiority study. Eligible patients were required to have relapsed or refractory multiple myeloma who had received at least 3 prior lines of therapy including a proteasome inhibitor and an immunomodulatory agent or who were double-refractory to a proteasome inhibitor and an immunomodulatory agent. Patients were randomized to receive DARZALEX FASPRO 1,800 mg/30,000 units administered subcutaneously or daratumumab 16 mg/kg administered intravenously; each administered once weekly from weeks 1 to 8, once every 2 weeks from Weeks 9 to 24 and once every 4 weeks starting with Week 25 until unacceptable toxicity or disease progression. The major efficacy outcome measure was ORR. A total of 56 patients received DARZALEX FASPRO with Kd. The median age was 61 years (range: 42 to 84); 52% were male; 73% were White and 3% Black or African American; and 66% had ISS Stage I, 18% had ISS Stage II, and 14% had ISS Stage III disease. A total of 79% of patients had a prior ASCCT; 91% of patients received a prior PI. All patients received 1 prior line of therapy with exposure to lenalidomide and 62% of patients were refractory to lenalidomide.

Efficacy results are summarized in Table 22. At a median follow-up of 9.2 months, the median duration of response had not been reached and an estimated 85.2% (95% CI: 72.5, 92.3) maintained response for at least 6 months and 82.5% (95% CI: 68.9, 90.6) maintained response for at least 9 months.

Table 22: Efficacy Results from PLEIADES in Patients Who Received DARZALEX FASPRO-Kd

<table>
<thead>
<tr>
<th>DARZALEX FASPRO-Kd (N=66)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall response (sCR+CR+VGPR+PR) n (%)</td>
</tr>
<tr>
<td>95% CI (%)</td>
</tr>
<tr>
<td>Stringent complete response (sCR)</td>
</tr>
<tr>
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</tr>
<tr>
<td>Very good partial response (VGPR)</td>
</tr>
<tr>
<td>Partial response (PR)</td>
</tr>
</tbody>
</table>

CI=confidence interval

* Based on treated patients

In response, the median time to response was 1 month (range: 0.9 to 9.1 months) in the DARZALEX FASPRO-Pd group and 1.9 months (range: 0.9 to 17.3 months) in the Pd group. The median duration of response had not been reached in the DARZALEX FASPRO-Pd group (range: 1 to 24.5 months) and was 15.9 months (range: 1 to 24.8 months) in the Pd group.

With a median follow-up of 16.9 months, 99 deaths were observed; 48 in the DARZALEX FASPRO-Pd group and 51 in the Pd group. Median OS was not reached for either treatment group.

In Combination with Carfilzomib and Dexamethasone

The efficacy of DARZALEX FASPRO with carfilzomib and dexamethasone (DARZALEX FASPRO-Kd) was evaluated in a single-arm cohort of PLEIADES (NCT03412565), a multi-cohort, open-label trial. This cohort enrolled patients with relapsed or refractory multiple myeloma excluding patients with left ventricular ejection fraction (LVEF) less than 40%, myocardial infarction within 6 months, uncontrolled cardiac arrhythmia, or uncontrolled hypertension.

Additional efficacy results from PLEIADES are presented in Table 22.

Table 22: Efficacy Results from PLEIADES in Patients Who Received DARZALEX FASPRO-Kd

<table>
<thead>
<tr>
<th>DARZALEX FASPRO-Kd (N=66)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall response (sCR+CR+VGPR+PR) n (%)</td>
</tr>
<tr>
<td>95% CI (%)</td>
</tr>
<tr>
<td>Stringent complete response (sCR)</td>
</tr>
<tr>
<td>Complete response (CR)</td>
</tr>
<tr>
<td>Very good partial response (VGPR)</td>
</tr>
<tr>
<td>Partial response (PR)</td>
</tr>
</tbody>
</table>

CI=confidence interval

* Based on treated patients

The results show that DARZALEX FASPRO 1,800 mg/30,000 units administered subcutaneously or daratumumab 16 mg/kg administered intravenously; each administered once weekly from weeks 1 to 8, once every 2 weeks from Weeks 9 to 24 and once every 4 weeks starting with Week 25 until unacceptable toxicity or disease progression. The major efficacy outcome measures were ORR by the IMWG response criteria and maximum C trough at pre-dose Cycle 3 Day 1 (see Clinical Pharmacology (12.3)). Randomization was stratified by body weight, myeloma type, and number of prior lines of therapy.

A total of 522 patients were randomized: 263 to the DARZALEX FASPRO arm and 259 to the intravenous daratumumab arm. The median age was 67 years (range: 33 to 92 years); 55% were male; and 78% were White, 14% Asian, and 25% to the intravenous daratumumab arm. The median age was 73 kg (range: 29 to 138). Patients had received a median of 4 prior lines of therapy. A total of 51% of patients had a prior ASCCT; 100% of patients received both a PI and an immunomodulatory agent. Forty-nine percent of patients were refractory to both a PI and an immunomodulatory agent. Eighty-two percent of patients were refractory to their last line of prior systemic therapy.

The results show that DARZALEX FASPRO 1,800 mg/30,000 units administered subcutaneously is non-inferior to daratumumab 16 mg/kg administered intravenously in terms of ORR and maximum trough concentration (see Clinical Pharmacology (12.3)). Median progression-free survival was 5.6 months in the DARZALEX FASPRO arm and 6.1 months in the intravenous daratumumab arm. ORR results are provided in Table 23.

Table 23: Efficacy Results from COLUMBA

<table>
<thead>
<tr>
<th>DARZALEX FASPRO (N=263)</th>
<th>Intravenous Daratumumab (N=259)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall response (sCR+CR+VGPR+PR) n (%)</td>
<td>108 (41%)</td>
</tr>
<tr>
<td>95% CI (%)</td>
<td>(35%, 47%)</td>
</tr>
<tr>
<td>Ratio of response rates (95% CI)</td>
<td>1.11 (1.08, 1.37)</td>
</tr>
<tr>
<td>CR or better, n (%)</td>
<td>51 (19%)</td>
</tr>
<tr>
<td>Very good partial response (VGPR)</td>
<td>45 (17%)</td>
</tr>
<tr>
<td>Partial response (PR)</td>
<td>58 (22%)</td>
</tr>
</tbody>
</table>

* Based on intent-to-treat population.
14.3 Light Chain Amyloidosis

In Combination with Bortezomib, Cyclophosphamide and Dexamethasone

The efficacy of DARZALEX FASPRO with Vcd was evaluated in ANDROMEDA (NCT03201965), an open-label, randomized, active-controlled trial. Eligible patients were required to have newly diagnosed light chain (AL) amyloidosis with at least one affected organ, measurable hematologic disease, Cardiac Stage I-IIIA (based on European Modification of Mayo 2004 Cardiac Stage), and NYHA Class I-IIIA. Patients with NYHA Class IIIB and IV were excluded. Patients were randomized to receive bortezomib 1.3 mg/m² administered subcutaneously, cyclophosphamide 300 mg/m² (max dose 500 mg) administered orally or intravenously, and dexamethasone 40 mg (or a reduced dose of 20 mg for patients >70 years or body mass index <18.5) or who have hypervolemia, poorly controlled diabetes mellitus or prior intolerance to steroid therapy) administered orally or intravenously on Days 1, 8, 15, and 22 of each 28-day cycle with or without DARZALEX FASPRO 1,800 mg/30,000 units subcutaneously once weekly from weeks 1 to 8, every 2 weeks from weeks 9 to 24 and once every 4 weeks starting with week 25 until disease progression or a maximum of two years. When DARZALEX FASPRO and dexamethasone were administered on the same day, dexamethasone 20 mg was administered before DARZALEX FASPRO with the remaining dose of dexamethasone administered after DARZALEX FASPRO if applicable. The major efficacy outcome measure was confirmed hematologic complete response (HemCR) rate based on Consensus Criteria as determined by the Independent Review Committee (negative serum and urine immunofixation, involved free light chain level decrease to less than the upper limit of normal, and normal free light chain ratio). Randomization stratification was stratified by Cardiac Stage (European Modification of Mayo 2004 Cardiac Stage) countries that typically offer autologous stem cell transplant (ASCT) for patients with light chain (AL) amyloidosis, and renal function.

A total of 388 patients were randomized: 195 to DARZALEX FASPRO-Vcd and 193 to Vcd. The median patient age was 64 years (range: 34 to 87 years); 58% were male; 78% White, 17% Asian, and 5% Black or African American; 22% had light chain (AL) amyloidosis Cardiac Stage I, 40% had Stage II, and 37% had Stage IIIA. The median number of organs involved was 2 (range: 1-6) and 66% of patients had 2 or more organs involved. Vital organ involvement was: cardiac 71%, renal 59% and hepatic 8%. The majority (79%) of patients had lambda free light chain disease.

Efficacy results are summarized in Table 24.

Table 24: Efficacy results from ANDROMEDA

<table>
<thead>
<tr>
<th>DARZALEX FASPRO-Vcd (n=195)</th>
<th>Vcd (n=193)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hematologic complete response (HemCR), n (%)</td>
<td>82 (42%)</td>
</tr>
<tr>
<td>p-value</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Very good partial response (VGPR), n (%)</td>
<td>71 (36%)</td>
</tr>
<tr>
<td>Partial response (PR), n (%)</td>
<td>26 (13%)</td>
</tr>
<tr>
<td>Hematologic VGPR or better (HemCR + VGPR), n (%)</td>
<td>153 (78%)</td>
</tr>
<tr>
<td>Major organ deterioration progression-free survival, Hazard ratio with 95% CI</td>
<td>0.58 (0.37, 0.92)</td>
</tr>
</tbody>
</table>

Vcd=bortezomib-cyclophosphamide-dexamethasone

a Based on intent-to-treat population

b p-value from Cochran Mantel-Haenszel Chi-Squared test.

15 REFERENCES


16 HOW SUPPLIED/STORAGE AND HANDLING

DARZALEX FASPRO® (daratumumab and hyaluronidase-fihj) injection is a sterile, preservative-free, colorless to yellow, and clear to opalescent solution for subcutaneous use supplied as individually packaged single-dose vials providing 1,800 mg of daratumumab and 30,000 units of hyaluronidase per 15 mL (NDC 57964-503-01).

Store DARZALEX FASPRO vials in a refrigerator at 2ºC to 8ºC (36ºF to 46ºF) in the original carton to protect from light.

Do not freeze or shake.

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Patient Information).

Hypersensitivity and Other Administration Reactions

Advise patients to seek immediate medical attention for any of the following signs and symptoms of systemic administration-related reactions: itchy, runny or blocked nose; chills, nausea, throat irritation, cough, headache, shortness of breath or difficulty breathing [see Warnings and Precautions (5.1)].

Cardiac Toxicity in Patients with Light Chain (AL) Amyloidosis

Advise patients immediately to contact their healthcare provider if they have signs or symptoms of cardiac adverse reactions [see Warnings and Precautions (5.2)].

Neutropenia

Advise patients to contact their healthcare provider if they have a fever [see Warnings and Precautions (5.3)].

Thrombocytopenia

Advise patients to contact their healthcare provider if they have bruising or bleeding [see Warnings and Precautions (5.4)].

Embryo-Fetal Toxicity

Advise pregnant women of the potential hazard to a fetus. Advise females of reproductive potential to inform their healthcare provider of a known or suspected pregnancy [see Warnings and Precautions (5.5), Use in Specific Populations (8.1, 8.3)].

Advise females of reproductive potential to avoid becoming pregnant during treatment with DARZALEX FASPRO and for 3 months after the last dose [see Use in Specific Populations (8.1, 8.3)].

Advise patients that lenalidomide, thalidomide and pomalidomide have the potential to cause fetal harm and have specific requirements regarding contraception, pregnancy testing, blood and sperm donation, and transmission in sperm. Lenalidomide, thalidomide and pomalidomide are only available through a REMS program [see Use in Specific Populations (8.1, 8.3)].

Interference with Laboratory Tests

Advise patients to inform their healthcare provider, including personnel at blood transfusion centers, that they are taking DARZALEX FASPRO, in the event of a planned transfusion [see Warnings and Precautions (5.5)].

Advise patients that DARZALEX FASPRO can affect the results of some tests used to determine complete response in some patients and additional tests may be needed to evaluate response [see Warnings and Precautions (5.7)].

Hepatitis B Virus (HBV) Reactivation

Advise patients to inform healthcare providers if they have ever had or might have a hepatitis B infection and that DARZALEX FASPRO could cause hepatitis B virus to become active again [see Adverse Reactions (6.1)].

Product of Switzerland

Manufactured by: Janssen Biotech, Inc.

Horsham, PA 19044

U.S. License Number 1864

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DARZALEX FASPRO® (daratumumab and hyaluronidase-fihj) injection

PATIENT INFORMATION
DARZALEX (Dar'-zah-lex) FASPRO® (Fas-pro)
daratatumumab and hyaluronidase-fihj) injection, for subcutaneous use

DARZALEX FASPRO may be used with other medicines called lenalidomide, thalidomide or pomalidomide. You should also read the Medication Guide that comes with lenalidomide, thalidomide or pomalidomide if you use DARZALEX FASPRO with these medicines.

What is DARZALEX FASPRO?
DARZALEX FASPRO is a prescription medicine used to treat adult patients with multiple myeloma:
• in combination with the medicines bortezomib, melphalan and prednisone, in people with newly diagnosed multiple myeloma who cannot receive a type of stem cell transplant that uses their own stem cells (autologous stem cell transplant).
• in combination with the medicines lenalidomide and dexamethasone in people with newly diagnosed multiple myeloma who cannot receive a type of stem cell transplant that uses their own stem cells (autologous stem cell transplant) and in people whose multiple myeloma has come back or did not respond to treatment, who have received at least one prior medicine to treat multiple myeloma.
• in combination with the medicines bortezomib, thalidomide, and dexamethasone in newly diagnosed people who are eligible to receive a type of stem cell transplant that uses their own stem cells (autologous stem cell transplant).
• in combination with the medicines bortezomib and dexamethasone in people who have received at least one prior medicine to treat multiple myeloma.
• in combination with the medicines pomalidomide and dexamethasone in people who have received at least one prior medicine including lenalidomide and a proteasome inhibitor to treat multiple myeloma.
• in combination with the medicines carfilzomib and dexamethasone in people who have received one to three prior medicines to treat multiple myeloma.
• alone in people who have received at least three prior medicines, including a proteasome inhibitor and an immunomodulatory agent, or did not respond to a proteasome inhibitor and an immunomodulatory agent.

DARZALEX FASPRO is a prescription medicine also used in combination with the medicines bortezomib, cyclophosphamide and dexamethasone in patients with newly diagnosed light chain (AL) amyloidosis. It is not known if DARZALEX FASPRO is safe and effective in children.

Do not receive DARZALEX FASPRO if you have a history of a severe allergic reaction to daratumumab, hyaluronidase or any of the ingredients in DARZALEX FASPRO. See the end of this leaflet for a complete list of ingredients in DARZALEX FASPRO.

Before you receive DARZALEX FASPRO, tell your healthcare provider about all of your medical conditions, including if you:
• have a history of breathing problems
• have had shingles (herpes zoster)
• have ever had or might now have a hepatitis B infection as DARZALEX FASPRO could cause hepatitis B virus to become active again. Your healthcare provider will check you for signs of this infection before, during and for some time after treatment with DARZALEX FASPRO. Tell your healthcare provider right away if you get worsening tiredness or yellowing of your skin or white part of your eyes.
• are pregnant or plan to become pregnant. DARZALEX FASPRO may harm your unborn baby. Tell your healthcare provider right away if you become pregnant or think that you may be pregnant during treatment with DARZALEX FASPRO.
  ○ Females who are able to become pregnant should use an effective method of birth control (contraception) during treatment and for 3 months after your last dose of DARZALEX FASPRO. Talk to your healthcare provider about birth control methods that you can use during this time.
  ○ Before starting DARZALEX FASPRO in combination with lenalidomide, thalidomide or pomalidomide, females and males must agree to the instructions in the lenalidomide, thalidomide or pomalidomide REMS program.
    ▪ The lenalidomide, thalidomide and pomalidomide REMS have more information about effective methods of birth control, pregnancy testing, and blood donation for females who can become pregnant.
    ▪ For males who have female partners who can become pregnant, there is information in the lenalidomide, thalidomide and pomalidomide REMS about sperm donation and how lenalidomide, thalidomide and pomalidomide can pass into human semen.
• are breastfeeding or plan to breastfeed. It is not known if DARZALEX FASPRO passes into your breast milk. You should not breastfeed during treatment with DARZALEX FASPRO. Talk to your healthcare provider about the best way to feed your baby during treatment with DARZALEX FASPRO.
Before you receive DARZALEX FASPRO for light chain (AL) amyloidosis, tell your healthcare provider if you have a history of heart problems. DARZALEX FASPRO should not be used in light chain (AL) amyloidosis patients with highly advanced heart disease outside of clinical trials.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

How will I receive DARZALEX FASPRO?
- DARZALEX FASPRO may be given alone or together with other medicines used to treat multiple myeloma.
- DARZALEX FASPRO will be given to you by your healthcare provider as an injection under the skin, in the stomach area (abdomen).
- DARZALEX FASPRO is injected over 3 to 5 minutes.
- Your healthcare provider will decide the time between doses as well as how many treatments you will receive.
- Your healthcare provider will give you medicines before each dose of DARZALEX FASPRO and after each dose of DARZALEX FASPRO to help reduce the risk of serious allergic reactions and other reactions due to release of certain substances by your body (systemic).

If you miss any appointments, call your healthcare provider as soon as possible to reschedule your appointment.

What are the possible side effects of DARZALEX FASPRO?
DARZALEX FASPRO may cause serious reactions, including:

- **Serious allergic reactions and other severe injection-related reactions.** Serious allergic reactions and reactions due to release of certain substances by your body (systemic) that can lead to death, can happen with DARZALEX FASPRO. Tell your healthcare provider or get medical help right away if you get any of these symptoms during or after an injection of DARZALEX FASPRO.
  - shortness of breath or trouble breathing
  - dizziness or lightheadedness (hypotension)
  - cough
  - wheezing
  - heart beating faster than usual
  - low oxygen in the blood (hypoxia)
  - throat tightness
  - runny or stuffy nose
  - headache
  - itching
  - high blood pressure
  - nausea
  - vomiting
  - chills
  - fever
  - chest pain

- **Injection site reactions.** Skin reactions at or near the injection site (local), including injection site reactions, can happen with DARZALEX FASPRO. Symptoms at the site of injection may include itching, swelling, bruising, pain, rash, bleeding, or redness of the skin. These reactions sometimes happen more than 24 hours after an injection of DARZALEX FASPRO.

- **Heart problems in people with light chain (AL) amyloidosis.** Heart problems, in some cases fatal, have occurred. Your healthcare provider will monitor you closely during treatment with DARZALEX FASPRO. Call your healthcare provider right away if you get any of the following symptoms: chest pain, feeling faint, swollen legs, shortness of breath, or abnormal heart rhythm.

- **Decreases in blood cell counts.** DARZALEX FASPRO can decrease white blood cell counts which help fight infections and blood cells called platelets which help to clot blood. Your healthcare provider will check your blood cell counts during treatment with DARZALEX FASPRO. Tell your healthcare provider if you develop fever or have signs of bruising or bleeding.

- **Changes in blood tests.** DARZALEX FASPRO can affect the results of blood tests to match your blood type. These changes can last for up to 6 months after your final dose of DARZALEX FASPRO. Your healthcare provider will do blood tests to match your blood type before you start treatment with DARZALEX FASPRO. Tell all of your healthcare providers that you are being treated with DARZALEX FASPRO before receiving blood transfusions.

The most common side effects of DARZALEX FASPRO when used alone include: cold-like symptoms (upper respiratory infection) and decreased red blood cell counts.

The most common side effects of DARZALEX FASPRO used in combination therapy include:

- tiredness
- nausea
- diarrhea
- shortness of breath
- trouble sleeping
- headache
- fever
- cough
- muscle spasms
- back pain
- vomiting
- high blood pressure
- cold-like symptoms (upper-respiratory infection)
- nerve damage causing tingling, numbness or pain
- constipation
- lung infection (pneumonia)
- swollen hands, ankles, or feet
- decreased red blood cell counts

These are not all the possible side effects of DARZALEX FASPRO. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.
**General information about the safe and effective use of DARZALEX FASPRO.**
Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. You can ask your pharmacist or healthcare provider for information about DARZALEX FASPRO that is written for health professionals.

**What are the ingredients in DARZALEX FASPRO?**
**Active ingredient:** daratumumab and hyaluronidase-fihj

**Inactive ingredients:** L-histidine, L-histidine hydrochloride monohydrate, L-methionine, polysorbate 20, sorbitol, and water for injection.

Manufactured by: Janssen Biotech, Inc., Horsham, PA 19044 U.S. License Number 1864
For more information, call 1-800-526-7736 or go to www.DARZALEXFASPRO.com.

This Patient Information has been approved by the U.S. Food and Drug Administration. Revised: 11/2021

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