Administration of Darzalex Faspro® (daratumumab-hyaluronidase fihj) for treatment of patients with newly diagnosed light chain amyloidosis

Center for Medicare & Medicaid Services
ICD-10 Coordination and Maintenance Committee Meeting
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janssen | PHARMACEUTICAL COMPANIES OF Johnson & Johnson

Light chain amyloidosis

- AL amyloidosis is a **life-threatening** blood disorder caused by increased production of **misfolded immunoglobulin light chains** by an abnormal proliferation of malignant CD38+ plasma cells.

- These deficient immunoglobulin light chains **will aggregate into highly ordered amyloid fibrils that deposit in tissues, resulting over time in progressive organ dysfunction and damage** due to the toxic effect of the misfolded proteins and the distortion of the normal tissue architecture by the amyloid deposits[1].

- The most frequently **affected organs are the heart, kidney, liver, spleen, gastrointestinal tract and nervous system**.

- Patients often have a **poor prognosis**, and as many as 30 percent of patients with AL amyloidosis die within the first year after diagnosis. Approximately 4,500 people in the US develop AL amyloidosis each year[2]

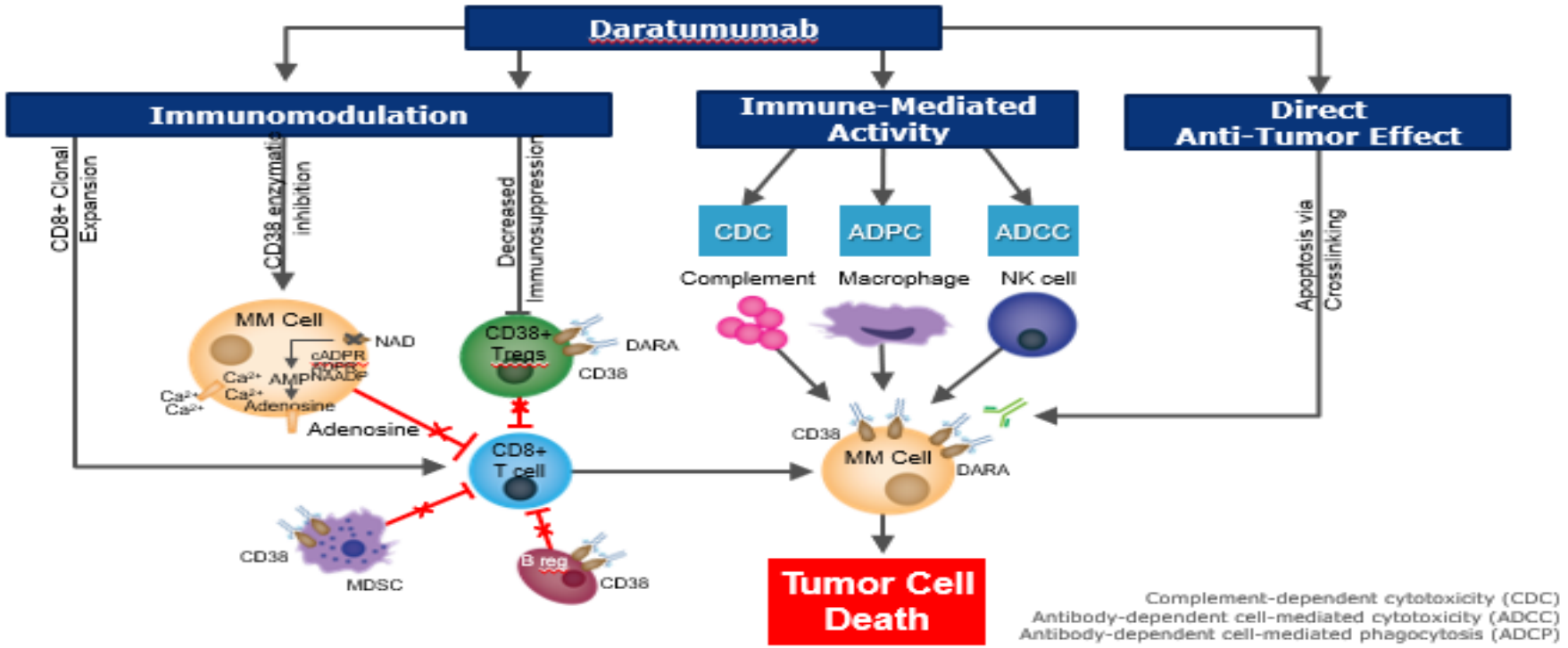
1. Merlini et al. Nat Rev Dis Primers. 2018; 4:38 19
2. Amyloidosis Foundation. AL amyloidosis facts. http://www.amyloidosis.org/facts/al/. Accessed September 2021

Darzalex Faspro® is a drug with multiple indications and usage.

- Darzalex Faspro® is a **combination** of daratumumab, a CD38-directed cytolytic antibody, and hyaluronidase, an endoglycosidase
- Darzalex Faspro® is **indicated for the treatment of light chain (AL) amyloidosis** in combination with bortezomib, cyclophosphamide and dexamethasone (CyBorD) in newly diagnosed patients and is administered through a subcutaneous injection.
- Darazalex Faspro ® in combination with **Cy**clophosphamide - **Bor**tezomib – **D**examethasone (CyBorD) **is approved under accelerated approval** based on response rate[1]. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s). 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.
- Darzalex Faspro® is **the first and only FDA-approved treatment** for patients with AL amyloidosis.
- Darzalex Faspro® is **also approved for multiple indications** for treatment of patients with multiple myeloma (MM), from newly diagnosed MM (NDMM) to relapsed/refractory MM (RRMM).
- This coding application focuses on the light chain (AL) amyloidosis indication

1. Kastritis E, et al. N Engl J Med. 2021; 385:46 58.

Darzalex Faspro®: Mechanism of Action



Darzalex Faspro is human IgG monoclonal antibody that targets CD38. CD38 is a plasma cell surface protein. Plasma cells are specialized white blood cells which normally produce antibodies to fight infection. However in specific circumstances, this plasma cell can turn malignant, leading to amyloidosis.

1. de Weers et al. J Immunol 2011;186:1840 1848)
2. Overdijk et al. MAbs.2015;7:311 321).
3. Krejcik J, Casneuf T, Nijhof IS, et al. Blood 2016; 128: 384 94.

Darzalex Faspro® Drug preparation and administration

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

Step 2. Drug preparation
Inspect vial – Liquid product comes in a single-use sterile glass vial with gray flip-cap.
Fill syringe – Withdraw the full content of the vial into a 20 mL dosing syringe with approved filters.
Prime the Syringe

Step 3. Site Preparation
Select site – The injection site should be approximately 3 inches to the right or left of the navel.
Prepare site – Cleanse the area around the site with a fresh alcohol wipe.

Step 4. Inject the drug
Insert the needle at a 45-degree angle and deliver the drug. The injection should be completed in between 3 and 5 minutes. If the subject is experiencing pain, the rate of delivery may be slowed down.

Step 5. Post-medication
Consider administering corticosteroids and other medications after the administration of DARZALEX FASPRO® depending on dosing regiment and medical history to minimize the risk of delayed (defined as occurring the day after administration) systemic administration-related reactions (ARRs).[2]

1. Darzalex Faspro® Prescribing Info
2. Daratumumab SC 1800mg Investigational Product Preparation Instructions for IPPI 5476741 v3.0. 2018

Darzalex Faspro® administration schedule in AL amyloidosis

In combination with bortezomib (VELCADE®), cyclophosphamide (CYTOXAN®), and dexamethasone (4-week cycle).

Weeks	Schedule for Darzalex Faspro® administration*
1-8	Weekly (total of 8 doses)
9-24	Every 2 weeks (total of 8 doses)
25 onward until disease progression or a maximum of 2 years	Every 4 weeks

* Provided schedule is only applicable for Darzalex Faspro. Per the ANDROMEDA study, Bortezomib, Cyclophosphamide and dexamethasone was given on a weekly basis for 6 cycles.

Site of Care & Documentation

Darzalex Faspro® will typically be administered in the outpatient setting.

However, if a patient is admitted for inpatient care, the patient may need to receive Darzalex Faspro® during the inpatient stay (depending on the patient's treatment schedule).

Darzalex Faspro® administration should be documented consistent with the documentation associated with other subcutaneous infusions.

Documentation of administration within the medical record would most commonly be found in the Medication Administration Record (MAR), physician orders, and progress notes.

Darzalex Faspro® safety profile in patients with AL amyloidosis was consistent with known safety data

- In the D-VCd arm, 1 additional grade 3/4 TEAE (fatigue) occurred over 25.8 months of follow-up versus 20.3 months of follow-up (119 [61.7%] versus 118 [61.1%] patients)

Any grade		
	D-VCd	VCd
Patients, %	**N=193**	**N=188**
≥1 TEAE	98	98
Peripheral edema	37	36
Diarrhea	36	30
Constipation	36	29
Fatigue	29	28
Peripheral sensory neuropathy	34	20
Nausea	29	28
Insomnia	25	25
Upper respiratory tract infection	26	11
Anemia	25	23
Dyspnea	25	17

Grade ¾		
	D-VCd	VCd
Patients, %	**N=193**	**N=188**
≥1 TEAE of grade 3/4	62	57
Lymphopenia	13	10
Pneumonia	8	4
Fatigue	5	3
Syncope	6	6
Diarrhea	6	4
Cardiac failure	6	3
Neutropenia	5	3
Peripheral edema	3	6
Hypokalemia	2	5

D VCd, daratumumab, bortezomib, cyclophosphamide, dexamethasone; TEAE, treatment emergent adverse event; VCd, bortezomib, cyclophosphamide, dexamethasone

Darzalex Faspro® adverse reactions

- The most common adverse reaction (≥20%) in patients with multiple myeloma who received DARZALEX FASPRO monotherapy is upper respiratory tract infection.
- 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.
- 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.
- 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
- 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.
- **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.**
- The most common (≥40%) hematology laboratory abnormalities with DARZALEX FASPRO are decreased leukocytes, decreased lymphocytes, decreased neutrophils, decreased platelets, and decreased hemoglobin.
- 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.

Darzalex Faspro® - Summary

- Darazalex Faspro ® in combination with **Cy**clophosphamide - **Bor**tezomib – **D**examethasone (CyBorD) is approved under **accelerated approval** based on response rate[1]. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s). 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.
  - ❑ **Darzalex Faspro® is the first and only FDA-approved treatment for patients with AL amyloidosis**. Darzalex Faspro® is also approved for multiple indications for treatment of patients with multiple myeloma (MM), from newly diagnosed (NDMM) to relapsed/refractory MM (RRMM)
  - ❑ From a clinical standpoint, **subcutaneous daratumumab provides important advantages** for the population of patients with AL amyloidosis. Nearly 3x reduction in systemic administration-related reactions (ARRs) with Darzalex Faspro® vs Darzalex® were observed in the COLUMBA trial[2].

- Darzalex Faspro® safety profile in AL amyloidosis was consistent with known safety data.
- Johnson & Johnson Health Care Systems Inc., on behalf of Janssen Biotech, Inc., has submitted a New Technology Add-On Payment (NTAP) application to CMS for Darzalex Faspro® for amyloidosis for FY 2023 consideration
- Currently, there is no ICD-10-PCS code for the use of Darzalex Faspro® for newly diagnosed light chain amyloidosis.
- To support program efficiency and patient access we request issuance of a new ICD-10-PCS code for the administration of Darzalex Faspro®.

1. Kastritis E, et al. N Engl J Med. 2021; 385:46 58.
2. Mateos MV, et al. Lancet Haematol. 2020;7:E370 E380