Darzalex Faspro® (daratumumab/hyaluronidase-fihj) – New indication, expanded indication

- On January 15, 2021, Janssen announced the FDA approval of Darzalex Faspro (daratumumab/hyaluronidase-fihj), in combination with bortezomib, cyclophosphamide, and dexamethasone for the treatment of adult patients with newly diagnosed light chain (AL) amyloidosis.
    - 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).
    - Darzalex Faspro is not indicated and is not recommended for the treatment of patients with AL amyloidosis who have NYHA Class IIIB or Class IV cardiac disease or Mayo Stage IIIB outside of controlled clinical trials.
- Darzalex Faspro is also approved as monotherapy and as part of various combination treatment regimens for the treatment of adult patients with multiple myeloma.
    - In addition to its previous uses in multiple myeloma, the FDA also approved Darzalex Faspro in combination with bortezomib, thalidomide, and dexamethasone in newly diagnosed multiple myeloma patients who are eligible for autologous stem cell transplant.
- AL amyloidosis is a rare, life-threatening blood cell disorder that occurs when blood plasma cells in the bone marrow produce amyloid deposits, which build up in vital organs and eventually cause organ deterioration. It affects an estimated 4,500 people in the U.S. annually and as many as 30% of patients with AL amyloidosis die within the first year after diagnosis.
    - Darzalex Faspro is the first FDA approved treatment for newly diagnosed AL amyloidosis.
- The approval of Darzalex Faspro for the new indication was based on ANDROMEDA, an open-label, randomized, and active-controlled study in 388 newly diagnosed AL amyloidosis patients with at least one affected organ and measurable hematologic disease. Patients were randomized to receive Darzalex Faspro plus bortezomib, cyclophosphamide, and dexamethasone (VCd) or VCd alone. The primary endpoint was overall complete hematologic response rate.
    - The complete hematologic response rate was 42% with Darzalex Faspro plus VCd vs. 13% with VCd alone ($p < 0.0001$).
    - Overall survival data were not mature. A total of 56 deaths were observed (13.8% with Darzalex Faspro plus VCd vs. 15% with VCd alone).
- The most common adverse reactions (≥ 20%) with Darzalex Faspro use in patients with AL amyloidosis were upper respiratory tract infection, diarrhea, peripheral edema, constipation, fatigue, peripheral sensory neuropathy, nausea, insomnia, dyspnea, and cough.
- 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 to 5 minutes. For AL amyloidosis, Darzalex Faspro should be administered weekly (total of 8 doses) during weeks 1 to 8, every two weeks (total of 8 doses) for weeks 9 to 24, and then every four weeks for weeks 25 onwards until disease progression or a maximum of 2 years.

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- For AL amyloidosis, Darzalex Faspro is used in combination with bortezomib, cyclophosphamide and dexamethasone. Refer to the drug labels for the other drugs for dosage recommendations.
- Darzalex Faspro should be administered by a healthcare provider.
- Refer to the Darzalex Faspro drug label for dosing and administration recommendations for multiple myeloma.
- Patients should be pre-medicated with a corticosteroid, acetaminophen and a histamine-1 receptor antagonist 1 to 3 hours before each dose of Darzalex Faspro.

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