Darzalex Faspro™ (daratumumab and hyaluronidase-fihj) – New formulation approval

- On May 1, 2020, the FDA announced the approval of Janssen's Darzalex Faspro (daratumumab and hyaluronidase-fihj), for the treatment of adult patients with multiple myeloma:

    - In combination with bortezomib (Velcade®), melphalan and prednisone in newly diagnosed patients who are ineligible for autologous stem cell transplant
    - In combination with lenalidomide (Revlimid®) and dexamethasone in newly diagnosed patients who are ineligible for autologous stem cell transplant and in patients with relapsed or refractory multiple myeloma who have received at least one prior therapy
    - In combination with bortezomib and dexamethasone in patients who have received at least one prior therapy
    - As monotherapy, in patients who have received at least three prior lines of therapy including a proteasome inhibitor (PI) and an immunomodulatory agent or who are double-refractory to a PI and an immunomodulatory agent.

- Daratumumab is also available as intravenously (IV) administered Darzalex® (daratumumab). Darzalex Faspro is administered subcutaneously (SC) over approximately 3 to 5 minutes. IV administered Darzalex is approved for the same indications as Darzalex Faspro but is also approved for two additional uses:

    - In combination with bortezomib, thalidomide (Thalomid®), and dexamethasone in newly diagnosed patients who are eligible for autologous stem cell transplant
    - In combination with pomalidomide (Pomalyst®) and dexamethasone in patients who have received at least two prior therapies including lenalidomide and a proteasome inhibitor.

- The efficacy of Darzalex Faspro in combination with bortezomib, melphalan and prednisone was established in a single-arm cohort (N = 67) of PLEIADES, a multi-cohort, open-label study. Eligible patients were required to have newly diagnosed multiple myeloma who are ineligible for transplant. The major efficacy outcome measure was overall response rate (ORR). ORR was 88% (95% CI: 78, 95).

- The efficacy of Darzalex Faspro in combination with lenalidomide and dexamethasone was evaluated in another single-arm cohort (N = 65) of the PLEIADES study. Eligible patients had received at least one prior line of therapy. ORR was 91% (95% CI: 81, 97).

- In addition, the efficacy of Darzalex Faspro as monotherapy was evaluated in COLUMBA, an open-label, randomized, non-inferiority study (N = 522). Eligible patients were required to have relapsed or refractory multiple myeloma who had received at least 3 prior lines of therapy including a PI and an immunomodulatory agent or who were double-refractory to a PI and an immunomodulatory agent. Patients received Darzalex Faspro or Darzalex.

    - Darzalex Faspro was non-inferior to Darzalex in terms of ORR (41% vs. 37%, respectively) and maximum trough concentration.
    - Median progression-free survival was 5.6 months in the Darzalex Faspro arm vs. 6.1 months in the Darzalex arm.

- Warnings and precautions for Darzalex Faspro include hypersensitivity and other administration reactions; neutropenia; thrombocytopenia; embryo-fetal toxicity; interference with serological testing; and interference with determination of complete response.

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- The most common adverse reaction (≥ 20%) with Darzalex Faspro monotherapy was upper respiratory tracts infection.

- The most common adverse reactions (≥ 20%) with Darzalex Faspro in combination with bortezomib, melphalan and prednisone was upper respiratory tract infection, constipation, nausea, fatigue, pyrexia, peripheral sensory neuropathy, diarrhea, cough, insomnia, vomiting, and back pain.

- The most common adverse reactions (≥ 20%) with Darzalex Faspro in combination with lenalidomide and dexamethasone were fatigue, diarrhea, upper respiratory tract infection, muscle spasms, constipation, pyrexia, pneumonia and dyspnea.

- The most common hematology laboratory abnormalities (≥ 40%) with Darzalex Faspro use were decreased leukocytes, decreased lymphocytes, decreased neutrophils, decreased platelets, and decreased hemoglobin.

- The recommended dose of Darzalex Faspro is 1,800 mg/30,000 units (1,800 mg daratumumab and 30,000 units hyaluronidase) administered SC over approximately 3 to 5 minutes. Refer to the Darzalex Faspro label for the complete recommended dosing schedule when Darzalex Faspro is administered as monotherapy or as part of a combination therapy.

    — Darzalex Faspro should be administered by a healthcare provider.
    — Medications should be administered before and after administration of Darzalex Faspro to minimize administration-related reactions.
    — Refer to the individual drug labels for dosing recommendations for drugs used in combination with Darzalex.

- Janssen plans to launch Darzalex Faspro as soon as the week of May 11, 2020. Darzalex Faspro will be available as a 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.