Azedra® (iobenguane I 131) – New orphan drug approval

- On July 30, 2018, the FDA announced the approval of Progenics Pharmaceuticals' Azedra (iobenguane I 131) for the treatment of adult and pediatric patients 12 years and older with iobenguane scan positive, unresectable, locally advanced or metastatic pheochromocytoma or paraganglioma (PPGL) who require systemic anticancer therapy.

- Pheochromocytomas are rare tumors of the adrenal glands. These glands are located right above the kidneys and make hormones including stress hormones called epinephrine and norepinephrine (NE). Pheochromocytomas increase the production of these hormones, leading to hypertension, headaches, irritability, sweating, tachycardia, nausea, vomiting, weight loss, weakness, chest pain or anxiety. When this type of tumor occurs outside the adrenal gland, it is called a paraganglioma.

    - Metastatic PPGL may result in unresectable disease with a poor prognosis, including a five-year survival rate as low as 12%.

- Azedra is the first drug approved to treat patients with PPGL who require systemic treatment. It is an I 131 labeled iobenguane. Iobenguane is similar in structure to the neurotransmitter NE and is subject to the same uptake and accumulation pathways as NE. Following intravenous (IV) administration, Azedra is taken up and accumulates within PPGL cells. Radiation resulting from radioactive decay of I 131 causes cell death and tumor necrosis.

- The efficacy of Azedra was demonstrated in a single-arm, open-label study of 68 patients with iobenguane scan-positive, unresectable, locally advanced or metastatic PPGL. The major efficacy outcome was the proportion of patients who experienced a 50% or greater reduction of all antihypertensive medication(s) lasting for at least six months (28 days per month).

    - The major efficacy outcome was achieved by 25% (95% CI: 16, 37) of patients.
    - In addition, the overall response rate was 22% (95%: 14, 33), with 53% of the patients experiencing a response for ≥ 6 months.

- Warnings and precautions of Azedra include risk from radiation exposure; myelosuppression; secondary myelodysplastic syndrome, leukemia and other malignancies; hypothyroidism; elevations in blood pressure; renal toxicity; pneumonitis; embryo-fetal toxicity and risk of infertility.

- The most common adverse reactions (grade 3 – 4, ≥ 10%) with Azedra use were lymphopenia, neutropenia, thrombocytopenia, fatigue, anemia, increased international normalized ratio, nausea, dizziness, hypertension, and vomiting.

- The recommended dose of Azedra is given IV as a dosimetric dose followed by two therapeutic doses given 90 days apart.

    - The dosimetric dose of Azedra is 185 to 222 MBq (5 to 6 mCi) in patients > 50 kg and 3.7 MBq/kg (0.1 mCi/kg) in patients ≤ 50 kg.
    - The Azedra therapeutic dose is based on body weight and reduced, if necessary, based on the dosimetry data.
    - Administer thyroid blockade and other pre- and concomitant medications as recommended.
    - Radiopharmaceuticals, including Azedra, should be used by or under the control of physicians who are qualified by specific training and experience in the safe use and handling of radiopharmaceuticals, and whose experience and training have been approved by the appropriate governmental agency authorized to license the use of radiopharmaceuticals.
    - Consult the Azedra drug label for additional dosing recommendations.

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- Azedra is stored at -70°C (-94°F). The shelf-life is 6 days post calibration time and must be discarded within 144 hours.

- Progenics' launch plans for Azedra are pending. Azedra will be available as 555 MBq/mL (15 mCi/ml) in a single-dose vial. The product vial is in a lead shielded container placed in a re-sealable plastic bag. The product will be shipped on dry ice in a USA DOT Type A Radioactive package.

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