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Avapritinib (Ayvakit®) for Indolent Systemic Mastocytosis

Description:
This PQI will discuss the use of oral avapritinib in patients with indolent systemic mastocytosis (ISM).

Background:
Avapritinib is a highly selective and potent tyrosine kinase inhibitor that blocks D816V-mutated KIT and D842V platelet-derived growth factor receptor alpha (PDGFRA), which are mutations that confer resistance to other kinase inhibitors. It is approved in patients with:[1,2,3]

- Indolent systemic mastocytosis
- Additional indications – see prescribing information[1]

Most common adverse events (< 20%) in patients with ISM: eye edema, dizziness, peripheral edema and flushing

PQI Process:

- Confirm diagnosis for ISM
- Dosing: avapritinib 25 mg by mouth once daily on an empty stomach (**note:** dosing differs for GIST and advanced systemic mastocytosis [AdvSM] indications).
- Avapritinib is associated with moderate to high emetic risk[4] in patients with AdvSM (24%) and GIST (64%), and prophylactic antiemetics are recommended for these indications.
  In the treatment of ISM, nausea occurred in 13% of patients treated with avapritinib compared to 17% in the placebo group.
    - Consider use of an antiemetic to be given as needed for nausea/vomiting
- Avapritinib is not recommended for patients with platelet counts <50,000/mm^3
- Assess for potential drug interactions
    - Avoid concomitant use of strong/moderate CYP3A inhibitors and/or inducers.
- No dose modifications are recommended for adverse reactions
    - Dose modifications for renal impairment
        - No dose adjustment is recommended for patients with mild to moderate renal impairment (creatinine clearance 30-89 mL/min)
        - Not studied in patients with creatinine clearance < 30 mL/min
    - Dose modifications for hepatic impairment
        - No dose adjustment is recommended for patients with mild to moderate hepatic impairment
        - Severe hepatic impairment (Child-Pugh Class C): 25 mg orally every other day
- No specific laboratory parameter monitoring is recommended for treatment of patients with ISM

Patient-Centered Activities:

- Provide Patient Education Sheet for avapritinib
- Administer avapritinib on an empty stomach ≥1 hour before or ≥2 hours after a meal.
- Do not make up for a missed dose within 8 hours of the next scheduled dose. Do not repeat dose if vomiting occurs after avapritinib but continue with the next scheduled dose.
- Discuss the most common side effects: nausea/vomiting/diarrhea or constipation, anorexia, abdominal pain, edema (peripheral, facial, periorbital), photosensitivity (rash, flushing, hair color changes), increased tearing, fatigue, headache, insomnia, dizziness.
- Report any signs of intracranial bleeding immediately including headache, nausea, vomiting, vision changes, or altered mental status.
- Educate the patient on the risk of photosensitivity reactions, importance of limiting ultraviolet exposure during treatment and 1 week after treatment; use sunscreen and protective clothing
- Use effective contraception during treatment and for 6 weeks after; applies to both sexes.
    - Coadministration of avapritinib with ethinyl estradiol-containing contraceptives may increase the exposure of ethinyl estradiol, which may lead to increased risk of ethinyl estradiol-associated adverse reactions; see avapritinib PI for more information (section 7.2)
- Counsel patients on potential drug interactions.
    - Grapefruit or grapefruit juice may interact with avapritinib; patients should avoid eating or drinking this during treatment with avapritinib
- Patient Assistance: NCODA Financial Assistance Tool

References:

1. AYVAKIT® (avapritinib) [prescribing information].
2. Gotlib J, Castells M, Oude Elberink H, et al. Avapritinib versus placebo in indolent systemic mastocytosis. *NEJM Evid.* 2023;2(6).
3. FDA approves Ayvakit (avapritinib) as the first and only treatment for indolent systemic mastocytosis. News release. Blueprint Medicines Corporation. May 22, 2023. Accessed May 25, 2023. https://ir.blueprintmedicines.com/news-releases/news-release-details/fda-approves-ayvakitr-avapritinib-first-and-only-treatment.
4. NCCN Clinical Practice Guidelines in Oncology: Systemic Mastocytosis. Version 1.2025. Accessed October 25, 2025. https://www.nccn.org/professionals/physician_gls/pdf/mastocytosis.pdf