Written By: Josh Nubla, PharmD
Institution: NCODA

Avapritinib (Ayvakit®) Management for Gastrointestinal Stromal Tumor

Description:

- This PQI will discuss the initiation and management of avapritinib in patients with gastrointestinal stromal tumor (GIST).

Background[1,2]:

- Avapritinib is a tyrosine kinase inhibitor that targets KIT D816V, platelet-derived growth factor receptor alpha (PDGFRA) and PDGFRA D842 mutants as well as multiple KIT exon 11, 11/17 and 17 mutants
- Avapritinib FDA approved indications include:
  - Treatment of adults with unresectable or metastatic GIST harboring a PDGFRA exon 18 mutation, including PDGFRA D842V mutations
  - See avapritinib prescribing information for other indications
- Adverse reactions occurring ≥ 20% of GIST patients treated with avapritinib: edema, nausea, fatigue/asthenia, cognitive impairment, vomiting, decreased appetite, diarrhea, increased lacrimation, abdominal pain, constipation, rash, dizziness, and hair color changes

PQI Process:

- Confirm appropriate diagnosis and verify genetic testing for PDGFRA exon 18 and PDGFRA D842V mutations
- Verify dose – Usual dose 300 mg orally once daily on empty stomach (1hr before/2hr after eating)

Table 1. Dose Modifications

First dose reduction	200 mg once daily
Second dose reduction	100 mg once daily
Third dose reduction	Permanently discontinue in patients unable to tolerate 100 mg daily

- Moderate emetogenic potential, consider 5HT3 antagonist prior to avapritinib doses
- Check for drug interactions
  - Avoid avapritinib co-administration with strong or moderate CYP3A inhibitors; If concomitant use is unavoidable, reduce dose of avapritinib to 100 mg once daily
  - Avoid avapritinib administration with strong or moderate CYP3A inducers

Table 2. Dose Modifications for Specific Adverse Reactions

Adverse Effect	Grade	Recommendation
Intracranial Hemorrhage	Any Grade	Permanently discontinue
Central Nervous System Effects	Grade 1	Continue avapritinib, reduce dose or hold treatment until improvement to baseline or resolution of symptoms and resume at same/reduced dose
	Grade 2/3	Hold avapritinib until improvement to baseline/Grade 1/resolution Resume at same or reduced dose
	Grade 4	Permanently discontinue
Other adverse reactions	Grade 3/4	Hold until improvement to > Grade 2 Resume at same or reduced dose as clinically appropriate

Patient-Centered Activities:

- Provide Patient Education Sheet for avapritinib
- Counsel patient that medication should be taken on empty stomach
- 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
- Counsel patient on potential drug, OTC, dietary, and supplement interactions with avapritinib
    - 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)
    - Grapefruit or grapefruit juice may interact with avapritinib; patients should avoid eating or drinking this during treatment with avapritinib
- Monitor patient for central nervous side effects such as dizziness, trouble sleeping, changes in mood or behavior as well as any neurological signs and symptoms related with intracranial hemorrhage
    - Report new cognitive changes such as memory loss, forgetfulness and confusion
- Patient Assistance: NCODA Financial Assistance Tool

References:

1. Heinrich MC, Jones RL, von Mehren M, et al. Avapritinib in advanced PDGFRA D842V-mutant gastrointestinal stromal tumour (NAVIGATOR): a multicentre, open-label, phase 1 trial. Lancet Oncol. 2020;21(7):935-946. doi:10.1016/S1470-2045(20)30269-2
2. AYVAKIT® (avapritinib) [prescribing information].