NCODA Positive Quality Interventions

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Avapritinib (Ayvakit) Management for Advanced Systemic Mastocytosis

Description: This PQI will discuss the initiation and management of patients receiving avapritinib for advanced systemic mastocytosis (AdvSM).

Background: Avapritinib is a potent tyrosine kinase inhibitor that targets platelet-derived growth factor receptor alpha (PDGFRA) and KIT exon mutants. Avapritinb selectively targets and inhibits the autophosphorylation of KIT D816V mutation, which is expressed in 90-95% of patients with:[1]

- Advanced systemic mast cell disease
- Additional indications – see prescribing information[1]

Most common adverse reactions in AdvSM (≥ 20%):[1]

- Edema, diarrhea, nausea, and fatigue/asthenia

PQI Process: Upon receiving a prescription for avapritinib[1]

- Confirm diagnosis for AdvSM (**Advanced Systemic Mastocytosis Patient Diagnostic Algorithm** PQI)
- Avapritinib is not recommended in patients with platelet counts of < 50,000/mm^3
- Verify AdvSM dose: 200 mg orally once daily (Note: dosing varies for other indications)
  - Dose should be taken on an empty stomach (≥1 hour prior to or ≥ 2 hours after a meal)
  - Dose modifications for toxicity in AdvSM patients

First Dose Reduction	100 mg once daily
Second Dose Reduction	50 mg once daily
Third Dose Reduction	25 mg once daily
Fourth Dose Reduction	Permanently discontinue

- Assess drug-drug interactions
  - Avoid avapritinib administration with moderate or strong CYP3A4 inhibitors or inducers
    - If concomitant is unavoidable, reduce starting avapritinib dose to 50 mg once daily
  - Avapritinib may increase ethinyl estradiol exposure, increasing the risk of estrogen-related adverse effects
    - If non-hormonal or non-estrogen contraceptives are not an option, use an ethinyl estradiol formulation with ≤20 mcg unless a higher dose is required
- Monitor platelet counts every 2 weeks for the first 8 weeks
  - After 8 weeks, frequency of monitoring is dependent on the platelet count at that time:
    - Platelets < 75,000/mm^3: monitor every 2 weeks
    - Platelets 75,000 – 100,000/mm^3: monitor every 4 weeks
    - Platelets >100,000/mm^3: monitor as clinically indicated
- Dose modification for renal impairment
  - No dose adjustment is recommended for patients with mild to moderate renal impairment
  - Not studied in patients with creatinine clearance < 30 mL/min

- Dose modification for hepatic impairment
  - No dose adjustment is recommended for patients with mild to moderate hepatic impairment
  - Severe hepatic impairment (Child-Pugh Class C): reduce dose to 100 mg once daily
- Dose modifications for specific adverse reactions:

Adverse Effect	Grade	Recommendation
Intracranial Hemorrhage	Any Grade	Permanently discontinue.
Cognitive Effects	Grade 1	Continue avapritinib at same dose or reduced dose, or hold treatment until improvement to baseline or resolution of symptoms. Resume at same or reduced dose.
	Grade 2/3	Hold avapritinib until improvement to baseline/Grade 1/resolution. Resume at same or reduced dose.
	Grade 4	Permanently discontinue.
Thrombocytopenia (platelet < 50,000/mm^3)		Hold avapritinib until resolution (platelet ≥ 50,000/mm^3). Resume avapritinib at reduced dose. Consider platelet support if platelet counts do not recover.
Other Adverse Reactions	Grade 3/4	Hold until improvement to ≤ Grade 2. Resume at same or reduced dose as clinically appropriate.

  - Moderate to high emetic risk (per NCCN®)[4]: ensure patient has prn antiemetic available

Patient-Centered Activities:

- Provide Patient Education Sheet (PES)
- Patient counseling
  - Take avapritinib on an empty stomach (≥ 1 hr before or ≥ 2-hr after a meal)
  - If you miss a dose and it is less than 8 hours until the next scheduled dose, skip the missed dose. Do not take an extra dose if you vomit after taking avapritinib
  - Advise patient to avoid grapefruit and grapefruit juice
  - Possible side effects and when to seek care:
    - Nausea/vomiting/diarrhea: take antiemetic as prescribed. Call your care team if symptoms are persistent or severe
    - Other common side effects: fatigue, edema
    - Monitor and report any central nervous side effects such as dizziness, trouble sleeping, confusion, or changes in mood
    - Seek immediate care for any symptoms suggestive of intracranial bleed (headache, nausea, vomiting, vision changes, or altered mental status)
    - Photosensitivity: limit sun exposure during treatment and for 1 week after discontinuation; use sunscreen and wear protective clothing
- Patient Assistance: NCODA Financial Assistance Tool

References:

1. AYVAKIT® (avapritinib) [prescribing information].
2. Gotlib J, Radia D, George T. Pure Pathologic Response Is Associated with Improved Overall Survival in Patients with Advanced Systemic Mastocytosis Receiving Avapritinib in the Phase I EXPLORER Study *Blood* (2020) 136 (Supplement 1): 37–38.
3. DeAngelo DJ, Reiter A, Radia D, et al. CT023 – PATHFINDER: Interim analysis of avapritinib (ava) in patients (pts) with advanced systemic mastocytosis (AdvSM). Abstract #CT023. Presented at the 2021 American Association for Cancer Research Annual Meeting, April 11, 2021.
4. National Comprehensive Cancer Network. *NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Antiemesis.* Version 2.2025. Published March 2025. Accessed August 20, 2025. https://www.nccn.org.