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Gilteritinib (Xospata) for Relapsed/Refractory Acute Myeloid Leukemia

Description: This PQI will discuss proper patient selection and management of adverse events related to the administration of oral gilteritinib in patients with relapsed/refractory (R/R) acute myeloid leukemia (AML) that have an FMS-like tyrosine kinase 3 (FLT3) mutation as detected by an FDA-approved test.

Background:
Gilteritinib is a tyrosine kinase inhibitor that inhibits FLT3 and is indicated for use in adult patients with:[1,2]

- R/R AML with a FLT3 mutation

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

- Increased transaminases, myalgia/arthralgia, fatigue/malaise, fever, mucositis, edema, rash, noninfectious diarrhea, dyspnea, nausea, cough, constipation, eye disorders, headache, dizziness, hypotension, vomiting, and renal impairment

PQI Process:

- Verify genetic testing is complete with positive FLT3 mutations and appropriate prior lines of therapy
- Consider checking for pregnancy prior to initiation in female patients of childbearing age.
- Ensure that the correct dose is prescribed: 120 mg (three 40 mg oral tablets) by mouth once daily
- Verify that baseline blood counts, chemistries, as well as creatine phosphokinase (CPK) have been assessed prior to initiation of gilteritinib
  - Schedule these labs for every week for the first month, every other week for the second month, and once monthly thereafter for the duration of therapy
- Ensure ECG results obtained prior to treatment initiation, on days 8 and 15 of cycle 1, and consider prior to cycles 2 and 3 to monitor for prolonged QTc interval
- Monitor for any signs/symptoms of pancreatitis, posterior reversible encephalopathy syndrome (PRES), differentiation syndrome (DS) during treatment
  - DS symptoms include: fever, dyspnea, hypoxia, pulmonary infiltrates, pleural effusions, edema
- Dosage modifications as described in the table below in Supplemental Information
- Important: Upon refill, check and clarify dosing, quantity, and instructions to the patient (number of tablets per dose, etc.)

Patient-Centered Activities:

- Provide Patient Education Sheet (PES) sheet
- Educate patient on dosing and schedule: 120 mg (3 x 40 mg oral tablets) once daily continuously at the same time each day
- Ensure patient knows that the drug may be taken without regard to meals and that the tablets should not be broken or crushed

- If dose is missed, take as soon as possible if at least 12 hours before next scheduled dose. Do **not** take two doses within 12 hours.
- Counsel female patients of childbearing age to use effective contraception during treatment and for at least 6 months after the last dose of gilteritinib; male patients should utilize contraception during treatment and for at least 4 months after the last dose of gilteritinib
- Educate patient to call office at first sign of fever (>100.4°F)
- Counsel patient on the appropriate use of antidiarrheals if diarrhea occurs
- Patient Assistance: NCODA Financial Assistance Tool

References:

1. XOSPATA® (gilteritinib) [package insert].
2. *NCCN*. (n.d.). Retrieved August 25, 2022, from https://www.nccn.org/professionals/physician_gls/pdf/aml.pdf
3. Perl AE, Cortes JE, Strickland SA, et al. An open-label, randomized phase III study of gilteritinib versus salvage chemotherapy in relapsed or refractory FLT3 mutation- positive acute myeloid leukemia. *Journal of Clinical Oncology*. DOI: 10.1200/JCO.2017.35.15_suppl.TPS7067

Supplemental Information:

Dose Modifications

Adverse Event	Recommended Action
Differentiation Syndrome	Systemic steroids until resolved for a minimum of 3 days (hold if signs remain > 48 hr); resume when symptoms improve to Grade 2
PRES	Discontinue gilteritinib
QTc interval > 500 msec	Interrupt gilteritinib and resume at reduced dose of 80 mg daily when QTc interval returns within 30 msec of baseline or ≤480 msec
QTc interval increased by > 30 msec on ECG on day 8 of cycle 1	If confirmed on day 9, consider dose reduction to 80 mg daily
Pancreatitis	Hold until resolved and resume at a reduced dose of 80 mg daily
Other Grade 3 or higher toxicity	Hold until toxicity resolves or improves to Grade 1 and reduce dose to 80 mg daily

Common adverse events	Rare and serious adverse events
Transaminase increase (51%)	QTc prolongation (9%)
Fatigue/malaise (44%)	Hypersensitivity (8%)
Fever (41%)	Pancreatitis (5%)
Mucositis (41%)	Cardiac failure (4%)
Edema (40%)	Pericardial effusion (4%)
Rash (36%)	Differentiation syndrome (3%) [Boxed Warning]
Diarrhea (35%)	PRES (1%)
Dyspnea (35%)	
Nausea (30%)	