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Positive Quality Intervention: Duvelisib (Copiktra®) for Chronic Lymphocytic Leukemia

Description: The purpose of this PQI is to provide background on PI3K inhibition and review clinical considerations for duvelisib therapy in order to optimize outcomes for cancer patients as well as identifying the patients with malignant lymphoma who may be candidates for duvelisib.

Background: Duvelisib is an oral dual PI3K-δ and PI3K-γ inhibitor that targets malignant B cells and the tumor microenvironment.[3] Duvelisib is a kinase inhibitor indicated for the treatment of adult patients with relapsed or refractory chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) after at least two prior systemic therapies. A patient may receive prior anti-CD-20 +/- chemotherapy, or oral therapy with a Bruton's kinase inhibitor or a BCL-2 inhibitor. [1] In the Phase III DUO study involving patients with CLL/SLL, duvelisib showed superior progression-free survival and overall response rate compared with ofatumumab.[3]

*** The U.S. Food and Drug Administration (FDA) is warning that results from the DUO trial (CLL/SLL) show a possible increased risk of death with Copiktra® (duvelisib). The trial also found Copiktra was associated with a higher risk of serious side effects, including infections, diarrhea, inflammation of the intestines and lungs, skin reactions, and high liver enzyme levels in the blood (6/30/22).**
**** The indication for relapsed/refractory Follicular lymphoma has been withdrawn (4/13/22).**

PQI Process: Upon receiving a new prescription for duvelisib

- Verify dose of duvelisib 25 mg orally twice daily with or without food (28 day cycle)
  - Reduce duvelisib dose to 15 mg twice daily when co-administered with strong CYP3A4 inhibitors (eg. ketoconazole)[1]
- Duvelisib dose modifications
  - Dose reduction 15 mg twice daily
  - Subsequent dose modification: discontinue if patient is unable to tolerate 15 mg twice daily

  **see full prescribing information for detailed guidance on specific dose modification by AE*
- Verify that the patient has been given prophylaxis for pneumocystis jirovecii pneumonia (PJP) during treatment with duvelisib and should be continued until the absolute CD4+ T cell count is greater than 200 cells/µL
  - Hold duvelisib in patients with suspected PJP of any grade and discontinue if PJP is confirmed[1]
- Consider prophylactic antivirals during treatment to prevent cytomegalovirus (CMV) infection including CMV reactivation[1]
- Treat any infections prior to initiation of duvelisib
- Verify Monitoring Parameters
  - CBC with differential - at least every 2 weeks for the first 2 months of duvelisib therapy, and at least weekly in patients with grade 3-4 neutropenia
- **REMS Components**: Communication Plan to inform healthcare professionals about the risks of fatal and/or serious toxicities including infections, diarrhea or colitis, cutaneous reactions, and pneumonitis associated with duvelisib use

Patient-Centered Activities:

- Provide Oral Chemotherapy Education (OCE) Sheet
- Provide patient with the medication guide located on the manufacturer website
- Counsel patients to utilize the Copiktra® Patient Safety Wallet Card available on website
- Review baseline labs and educate the importance of keeping lab appointments

- Review concurrent medications and instruct patient to inform provider of *any new medications*
- Recommend anti-diarrheal and moisturizing cream
- **Educate patient around black box warning and the adverse effects like diarrhea, pneumonitis and cutaneous reactions which often occur several months later in therapy**
    - Median time to onset of diarrhea and colitis is 4 months
    - Median time to dose reduction was also 4 months
    - Median time to onset of any grade transaminase elevation was 2 months
- Verify PJP prophylaxis is ordered and explain the importance of taking these medications
- Educate the patient when to call their provider
- Patient Assistance: NCODA Financial Assistance Tool

References:

1. Copiktra® (duvelisib) Package Insert.
2. Greenwell I Brian, Ip Andrew, et al. PI3K inhibitors: understanding toxicity mechanisms and management. Oncology. 2017 Nov 15; 31(11):1-10.
3. Flinn IW, Hillmen P, Montillo M, Nagy Z, Illés Á, Etienne G, Delgado J, Kuss BJ, Tam CS, Gasztonyi Z, Offner F, Lunin S, Bosch F, Davids MS, Lamanna N, Jaeger U, Ghia P, Cymbalista F, Portell CA, Skarbnik AP, Cashen AF, Weaver DT, Kelly VM, Turnbull B, Stilgenbauer S. The phase 3 DUO trial: duvelisib vs ofatumumab in relapsed and refractory CLL/SLL. Blood. 2018 Dec 6;132(23):2446-2455.