



Positive Quality Intervention: Duvelisib for Chronic Lymphocytic Leukemia and Follicular Lymphoma

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 (Copiktra) is an oral dual PI3K- δ and PI3K- γ inhibitor that targets malignant B cells and the tumor microenvironment. Duvelisib is a kinase inhibitor indicated for the treatment of adult patients with relapsed or refractory chronic lymphocytic leukemia (CLL), small lymphocytic lymphoma (SLL), or follicular lymphoma (FL) 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. In the Phase III DUO study involving patients with CLL/SLL, duvelisib showed superior progression-free survival and overall response rate compared with ofatumumab.

PQI Process:

Upon receiving a new prescription for Duvelisib (Copiktra):

- Verify dose of Duvelisib 25 mg orally twice daily with or without food. A cycle is 28 days. Reduce Duvelisib dose to 15 mg twice daily when co-administered with strong CYP3A4 inhibitors (e.g. ketoconazole).
- Verify that the patient has been given prophylaxis for *Pneumocystis jirovecii* (PJP) during treatment with Duvelisib. *Pneumocystis jirovecii* pneumonia (PJP) occurred in 1% of patients taking Duvelisib. Following completion of Duvelisib treatment, the PJP prophylaxis should be continued until the absolute CD4+ T cell count is greater than 200 cells/ μ L. Withhold Duvelisib in patients with suspected PJP of any grade, and discontinue if PJP is confirmed.
- Consider prophylactic antivirals during treatment to prevent cytomegalovirus (CMV) infection including CMV reactivation.
- Treat 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

Patient Centered Activities:

- Provide Oral Chemotherapy Education Sheet (oralchemoedsheets.com)
- Provide patient with the medication guide located on the Verastem Copiktra website
- Counsel patients to utilize the COPIKTRA Patient Safety Wallet Card available on website.
- Review baseline labs
- Review concurrent medications and instruct patient to inform provider of *any new medications*
 - Avoid strong CYP3A4 inducers; reduce dose to 15mg twice daily for strong inhibitors; substrates of CYP3A4 may require dose reduction as duvelisib itself is an inhibitor

Important notice: National Community Oncology Dispensing Association, Inc. (NCODA), has developed this Positive Quality Intervention platform. This platform represents a brief summary of medication uses and therapy options derived from information provided by the drug manufacturer and other resources. This platform is intended as an educational aid and does not provide individual medical advice and does not substitute for the advice of a qualified healthcare professional. This platform does not cover all existing information related to the possible uses, directions, doses, precautions, warning, interactions, adverse effects, or risks associated with the medication discussed in the platform and is not intended as a substitute for the advice of a qualified healthcare professional. The materials contained in this platform are for informational purposes only and do not constitute or imply endorsement, recommendation, or favoring of this medication by NCODA, which assumes no liability for and does not ensure the accuracy of the information presented. NCODA does not make any representations with respect to the medications whatsoever, and any and all decisions, with respect to such medications, are at the sole risk of the individual consuming the medication. All decisions related to taking this medication should be made with the guidance and under the direction of a qualified healthcare professional.



- Recommend anti-diarrheals and moisturizing cream (i.e Urea 20%)
- **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 to the patient
- Educate when to call their provider
- Educate the importance of keeping lab appointments
- Duvelisib dose Modifications: Initial_Dose
25 mg twice daily 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*

References:

1. Copiktra (duvelisib) Package Insert Revised: 07/2019
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.

Supplemental Information:

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.

Verastem Cares programs:

Patient Assistance Program (PAP) Co-pay / Co-Insurance Assistance:

- Co-pays adjusted may be as little as \$5/prescription
- No patient income requirement
- Annual benefit limit of \$25,000
- Must have commercial insurance
- (No Medicare, Medicaid, or any other government programs)

Bridge Rx Program

- For coverage delays or loss of insurance lasting longer than 5 days
- On-label indications only
- Free 14-day supply (Until coverage is obtained or 4 shipments have been received)

*All Verastem Cares programs are subject to eligibility requirements. Restrictions apply

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