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Positive Quality Intervention: Ibrutinib (Imbruvica®) Expansion with Obinutuzumab (Gazyva®)

Description: The purpose of this PQI is to expand on therapy management of ibrutinib (Imbruvica®) when used in combination with obinutuzumab (Gazyva®).

Background: This FDA has extended the indications for ibrutinib; already approved as a single agent OR in combination with bendamustine and rituximab. Ibrutinib is indicated for Mantle Cell Lymphoma (MCL) and Marginal Zone Lymphoma (MZL) at doses of 560 mg daily. Ibrutinib is also indicated for Waldenström's Macroglobulinemia (WM), chronic Graft versus Host disease (cGVHD) and Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (CLL/SLL) at doses of 420 mg daily. Ibrutinib in combination with obinutuzumab has been approved for adult patients with previously untreated CLL/SLL. This indication is a non-chemotherapy option for treatment naïve patients diagnosed with CLL/SLL, which may further help reduce the need for chemotherapy. As an oral and IV combination therapy, coordination of the medically integrated pharmacy team is critical. The Illuminate trial[4] found ibrutinib and obinutuzumab to show to be efficacious as first-line, non-chemotherapy regimen in CLL/SLL patients regardless of age or disease status. The median follow-up was 31.3 months and the most common grade 3 or 4 adverse effect was neutropenia and thrombocytopenia. After a median follow-up of 31.3 months (IQR 29.4–33.2), median progression-free survival was significantly longer in the ibrutinib plus obinutuzumab group (median not reached [95% CI 33.6–non-estimable]) than in the chlorambucil plus obinutuzumab group (19.0 months [15.1–22.1]; hazard ratio 0.23; 95% CI 0.15–0.37; $p<0.0001$). Estimated 30-month progression-free survival was 79% (95% CI 70–85) in the ibrutinib plus obinutuzumab group and 31% (23–40) in the chlorambucil plus obinutuzumab group.

PQI Process: Upon receiving a new prescription for ibrutinib for specific use in combination with obinutuzumab:

- Verify an established CLL/SLL diagnosis (independent of patient's del(17p) status, comorbidities and age) in the treatment naive patient and relevant dosing
- Assess risk for Tumor Lysis Syndrome (laboratory abnormalities of potassium, uric acid, phosphate, serum creatinine) which commonly occurs during the first cycle
- Dosing:
    - Ibrutinib 420 mg by mouth once daily with:
        - Obinutuzumab 100 mg IV on Day 1
        - then Obinutuzumab 900 mg IV on Day 2
        - then Obinutuzumab 1000 mg IV on Day 8 and Day 15 every 28 days for <u>1 Cycle</u>
    - Followed by Ibrutinib 420 mg by mouth once daily with:
        - Obinutuzumab 1000 mg IV on Day 1 every 28 Days for <u>5 Cycles</u>
- Consider administering ibrutinib prior to obinutuzumab when given on the same day
- Consider modification for ibrutinib if warranted due to hypertension, dermatologic toxicities, risk of bleeding, hepatic impairment, fluid retention, cardiac arrhythmias or abnormalities
- Verify scheduling of mremedications for obinutuzumab:
    - Acetaminophen 650 mg - 1000 mg at least 30 minutes prior
    - Antihistamine (ex: diphenhydramine 50 mg) at least 30 minutes prior
    - IV glucocorticoid (ex: dexamethasone 20 mg) at least 60 minutes prior
- Review CBC, CMP, hepatitis, LDH, and quantitative immunoglobulins monthly and as indicated
- Verify recommended antiviral (herpes and varicella virus) and pneumocystis prophylaxis are initiated

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- Review Ibrutinib (Imbruvica®) Management PQI
- Confirm baseline EKG has been obtained

Patient Centered Activities:

- Provide ibrutinib Oral Chemotherapy Education (OCE) sheet and written education for obinutuzumab
- Counsel patient on disease state, treatment regimen, what to expect and verify patient understanding
- Ibrutinib should be taken at the same time each day, swallowed whole, with a glass of water and prior to obinutuzumab infusion
- Avoid grapefruit and Seville orange products
- Advise patient to take a missed dose as soon as possible on the same day and to resume normal dosing schedule for the next day
- Patient Assistance: NCODA Financial Assistance Tool

Supplemental Information:

Ibrutinib is also considered as an option for the following populations:

- Patients with and without del(17p)/TP53 mutation who are:
    - 64 years old and younger without significant comorbidities
    - 65 years old and older with significant comorbidities

References:

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