National Community Oncology Dispensing Association, Inc.
PASSION FOR PATIENTS

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Positive Quality Intervention: Selinexor (Xpovio®) Patient Management

Description: This PQI will provide background on the novel medication selinexor for patients with multiple myeloma (MM) who have received at least one prior therapy, relapsed, refractory multiple myeloma (RR-MM), and relapsed, refractory diffuse large b-cell lymphoma (RR-DLBCL) and discuss effective practices to maximize the use of selinexor therapy.

Background: Selinexor is an oral, selective inhibitor of nuclear export (SINE) that blocks exportin 1 (XPO1). Selinexor is indicated:

1. In combination with bortezomib and dexamethasone for the treatment of adult patients with multiple myeloma who have received at least one prior therapy
2. In combination with dexamethasone, for the treatment of adult patients with relapsed refractory multiple myeloma (RRMM) who have received at least 4 prior therapies and whose disease is refractory to at least 2 proteasome inhibitors (PI), at least 2 immunomodulatory agents (IMiD), and an anti-CD38 monoclonal antibody (mAb)
3. For the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL), not otherwise specified, including DLBCL arising from follicular lymphoma, after at least 2 lines of systemic therapy

PQI Process:

Upon receiving a new prescription for selinexor

- Confirm appropriate dosing and schedule **based on diagnosis and prescribed regimen (MM, RR-MM or RR-DLBCL)**
- Confirm receipt of dexamethasone (requirement for RR-MM indication only)
- Confirm prophylactic anti-emetic for moderate to high emetogenicity
    - See ***Chemotherapy-Induced Nausea and Vomiting*** *PQI*
    - See **CINV Assessment Tool**
- Advise patients to maintain adequate fluid and caloric intake throughout treatment. Consider intravenous hydration for patients at risk of dehydration
- Provide prophylactic antiemetics. Administer a 5-HT3 receptor antagonist and other anti-nausea agents (such as NK-1 RA and/or olanzapine) prior to and during treatment with selinexor
- Ensure appropriate monitoring with a CBC, CMP, and body weight at baseline, then at least weekly for the first 3 months, then at least monthly thereafter. Consider monitoring more frequently during the first three months of treatment

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PQI Process Continued:

- Monitor patients closely for side effects including:
  - Cytopenia (thrombocytopenia, anemia, neutropenia)
  - GI intolerance (nausea, vomiting, diarrhea)
  - Fatigue
  - Weight loss
  - Hyponatremia
  - Potential side effects involved with utilizing bortezomib in combination (peripheral neuropathy, blurred vision)
- Educate patients on side effects and report adverse effects to prescriber

Dosing:

- RR-MM in combination with dexamethasone **Xd**: Selinexor 80 mg (4 x 20 mg tablets) by mouth twice weekly on Days 1 and 3 until disease progression or unacceptable toxicity. Dexamethasone 20 mg by mouth twice weekly on Days 1 and 3 until disease progression or unacceptable toxicity
- MM in combination with bortezomib and dexamethasone **XVd**: Selinexor is 100 mg (2 x 50mg) by mouth once weekly on day 1 of each week until disease progression or unacceptable toxicity. Bortezomib 1.3 mg/m2 administered subcutaneously once weekly on Day 1 of each week for 4 weeks followed by 1 week off. Dexamethasone 20mg by mouth twice weekly on Days 1 and 2 of each week
- RR-DLBCL: Selinexor 60 mg (3 x 20 mg tablets) by mouth twice weekly on days 1 and 3 until disease progression or unacceptable toxicity

Supportive Care/Adverse Effect Management

Xd Dose Reduction Steps for RR-MM Adverse Reactions

Selinexor starting dose	**1st Reduction**	**2nd Reduction**	**3rd Reduction**	**Discontinue**
80 mg <u>Days 1 and 3</u> of each week (160 mg total per week)	**100 mg ONCE Weekly**	**80 mg ONCE Weekly**	**60 mg ONCE Weekly**	

53% of patients had a reduction in dose, and 65% had a dose interrupted[3]

XVd Dose Reduction Steps for MM Adverse Reactions

Selinexor starting dose	**1st Reduction**	**2nd Reduction**	**3rd Reduction**	**Discontinue**
100 mg <u>ONCE Weekly on Day 1 of each week</u> (100 mg total per week)	**80 mg ONCE Weekly**	**60 mg ONCE Weekly**	**40 mg ONCE Weekly**	

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64% of patients had a reduction in dose, and 83% had a dose interrupted[3]

Dose Reduction Steps for RR-DLBCL Adverse Reactions[5]

Selinexor starting dose	1st Reduction	2nd Reduction	3rd Reduction	
60 mg Days 1 and 3 of each week (120 mg total per week)	**40 mg Days 1 and 3 of each week (80 mg total per week)**	**60 mg ONCE Weekly**	**40 mg ONCE Weekly**	**Discontinue**

49% of patients had a reduction in dose, and 61% had a dose interrupted[5]

- Gastrointestinal
  - Dose reduction and/or drug holiday
  - Addition of olanzapine or NK1R antagonist for nausea and vomiting
  - Addition of loperamide for diarrhea
- Hyponatremia
  - Interrupt when Sodium level ≤ 130 mmol/L
  - Oral and IV fluids and/or salt tablets
- Weight Loss
  - Interrupt when weight loss between 10% to ≤ 20%
  - Consider Nutritionist consult and supplements such as Boost®, Ensure®
    - Consider addition of low dose olanzapine and/or megesterol acetate

Patient Centered Activities:

- Provide Oncology Chemotherapy Education (OCE) sheet
- Consider providing Selinexor (Xpovio®) Treatment Support Kit (TSK)
- Ensure patient knows dosing schedule including dexamethasone (if applicable) and prophylactic anti-nausea medications
- Ensure patient knows to swallow the tablet whole with water. The tablet should not be broken, chewed, crushed, or divided
- Ensure patient knows that blood tests and body weight will be monitored closely
- Ensure patient knows the importance of maintaining adequate fluid and **caloric intake** throughout treatment

References:
1. Vogl DT, Dingli D, Cornell RF, et al. Selective inhibition of nuclear export with oral selinexor for treatment of relapsed or refractory multiple myeloma. Journal of Clinical Oncology. 2018; 36: 859-866.
2. Chen C, Siegel D, Gutierrez M, et al. Safety and efficacy of selinexor in relapsed or refractory multiple myeloma and waldenstrom macroglobulinemia. Blood. 2018; 131(8): 855-963.
3. Xpovio® (selinexor) [package insert]. Newton, MA: Karyopharm Therapeutics Inc; 2021.
4. Chari A, Vogl DT, Gavriatopoulou M, et al. Oral selinexor-dexamethasone for triple-class refractory multiple myeloma. New England Journal of Medicine. 2019; 381:727-738.

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5. Kalakonda N, Maerevoet M, Cavallo F, et al. Selinexor in patients with relapsed or refractory diffuse large B-cell lymphoma (SADAL): a single-arm, multinational, multicentre, open-label, phase 2 trial. Lancet Haematol 2020; 7: e511–22.