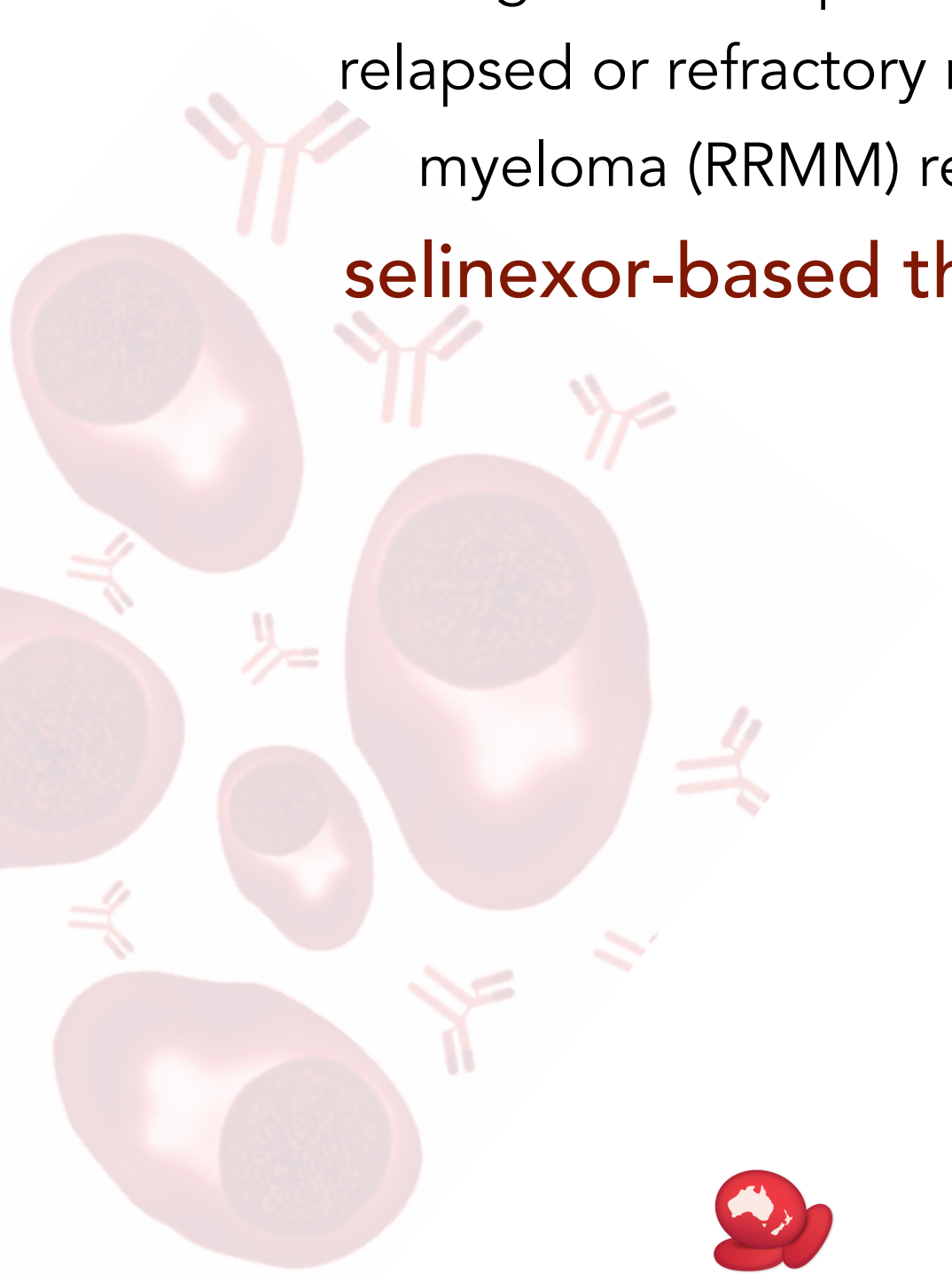
Best Practice Consensus Recommendations

For optimal use and local management for patients with relapsed or refractory multiple myeloma (RRMM) receiving

selinexor-based therapy



MyeSPN MYELOMA SPECIALIST PRACTICE NETWORK

HSANZ Haematology Society of Australia and New Zealand

Foreword

Haematology Society of Australia and New Zealand Nurses' Group (HSANZ-NG) is a sub-group within the HSANZ that represents the interests of its nurse members. Their mission is to enhance the care of patients undergoing treatment for haematological conditions and support their relatives and caregivers through the development and promotion of information and education aimed at improving the standards of care. The Myeloma Specialists Practice Network (M-SPN) was specifically formed to focus on enhancing care of those affected by multiple myeloma (MM). The M-SPN identified an opportunity to improve the management of myeloma patients receiving treatment with selinexor based therapy and a lack of standardised supportive care guidelines. These consensus recommendations regarding best supportive care for myeloma patients receiving selinexor have been developed by the M-SPN drawing on evidence available at the time of writing.

Selinexor (Xpovio®) Consensus Recommendations

Written by members of the M-SPN, the recommendations represent a summary of evidence and clinical experience and aim to inform Health Care Professionals in providing best supportive care to patients receiving selinexor-based therapy. They provide an overview of selinexor dosing and schedules, common treatment related adverse effects (TRAE's), supportive care and practical management recommendations.

The following people have provided expert review of the final recommendations.

- **Professor Hang Quach**, Deputy Chair of Myeloma Scientific Advisory Group (MSAG) and lead MSAG guideline pillar, provided medical expert opinion and review of consensus recommendations.
- **Professor Kate White,** Cancer/Haematology Research Academic reviewer.
- **Donna Catamero**, Myeloma Nurse Practitioner, Associate Director, Myeloma Translational Research, Mount Sinai Health System, USA provided international expert review.

Draft consensus recommendations were presented to the wider M-SPN membership at a meeting during Blood 2022 Sydney (Sept 2022) and further consensus gained. Desktop publishing provided by Natalie D'Abrew and funded by an educational grant from Antengene.

Every effort is made to ensure content is correct at time of publishing August 2023
Minor update November 2023: Akynzeo (netupitant 300mg + palonosetron 0.5mg) reimbursed

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Members of the M-SPN who have been involved in writing the selinexor-based therapy recommendations.

M-SPN Member Authors	Affiliation
A/Prof Tracy King PhD, RN, MN Lead author	Myeloma CNC, Royal Prince Alfred, The University of Sydney - Sydney
Jacqueline Jagger RN, BA (Hons), MN (NP)	Haematology NP, Central Coast LHD, Central Coast Haematology, The University of Sydney, Gosford
Hayley Beer RN, Grad Cert (Onc)	Myeloma CNC, Peter McCallum, Myeloma Australia – Melbourne
Daniela Klarica RN, MN (NP)	Myeloma NP, Alfred Hospital - Melbourne
Alicia Snowden RN, Grad Cert (Onc)	Haematology CNC, Precision Haematology - Melbourne
Jessica Demajo RN, MN	Myeloma CNC, St Vincent's Hospital - Melbourne
Carmel Woodrow BSc (Nurs)	Myeloma CNC, Princess Alexandra Hospital - Brisbane

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Introduction

Selinexor represents a new class of drug for relapsed refractory multiple myeloma (RRMM) and has a unique mechanism of action and a different toxicity profile compared to other more commonly used MM treatments. Utilised in the RRMM treatment phase, patients have commonly received many lines of previous therapy and may be living with existing treatment related adverse effects (TRAEs), disease morbidities and comorbidities of an older patient group. The most common TRAE's associated with selinexor are gastrointestinal (GI) (nausea, vomiting and diarrhoea), anorexia and weight loss, thrombocytopenia, neutropenia, hyponatremia, and fatigue. Gastrointestinal side effects are more commonly experienced in the first few cycles of therapy and can improve over time.

A patient's ability to continue with selinexor therapy is dependent on effective management of side effects. Supportive care includes multi-agent prophylactic antiemetics, adequate hydration, maintaining calorific input and blood count/electrolyte monitoring. Patient and carer education focused on symptom management, need for concurrent supportive medications such as regular antiemetics, is vital in ensuring tolerance and adherence, in this often medically fragile population. Prompt and proactive symptom management in the first few cycles of therapy can reduce the risk of treatment discontinuation due to toxicity. A 'go slow and low' approach to selinexor dosing can further help patients better adjust to therapy.

SELINEXOR MECHANISM OF ACTION

Selinexor is a first-in-class, oral, selective inhibitor of nuclear export (SINE) compound which inhibits the nuclear export protein XPO1[1]. Inhibition of XPO1 results in accumulation of tumour suppressor proteins (TSPs) in the nucleus and reduction of oncoproteins (c-myc and cyclin D1), cell cycle arrest and apoptosis of myeloma cells[1].

SELINEXOR INDICATION

The Australian indication for selinexor is:

- In combination with bortezomib and dexamethasone (SVd) for the treatment of adult patients with multiple myeloma who have received at least one prior therapy based on the phase III BOSTON study[2].
- In combination with dexamethasone (Sd) based on the STORM study[3] for the treatment of adult patients with RRMM who have received at least three prior therapies and whose disease is refractory to at least one proteasome inhibitor (PI), at least one immunomodulatory medicinal product (IMiD), and an anti CD38 monoclonal antibody (moAb).

SELINEXOR PBS Listing (01.06.23)

Selinexor in combination with bortezomib and dexamethasone (SVd) for the treatment of adult patients with MM who have received at least one prior therapy.

And

Selinexor in combination with dexamethasone (Sd) for the treatment of adult patients with RRMM who have received at least three prior therapies and whose disease is refractory to at least one proteasome inhibitor (PI), at least one immunomodulatory agents (IMiD), and an anti-CD38 monoclonal antibody (moAb).

SELINEXOR SCHEDULES AND APPROPRIATE STARTING DOSES[1].

The efficacy of selinexor was evaluated in two principal studies, STORM[3], and BOSTON[2]. The drug dose and scheduling are listed below alongside outcomes relating to response.

Treatment	**RRMM in combination with bortezomib and dexamethasone (SVd)** **1-3 prior lines therapy - BOSTON study[2]** 35-day cycle		
	Selinexor	**Bortezomib**	**Dexamethasone***
Dose	100 mg PO	1.3 mg/m² SC	20 mg PO
Schedule	Once weekly (1,8,15,22,29)	Once weekly (1,8,15,22) for 4 weeks, then 1 week off	Twice weekly (1,2,8,9,15,16,22,23, 29,30)
Response	Median progression-free survival – 13.93 months Median overall survival not reached (NR) after a median follow up of 16.5 months. NOTE The median delivered dose of selinexor in the BOSTON (SVd) study was 80mg weekly[1]. Dose adjustment may be indicated as early as 2nd week to aid tolerability		
Treatment	**RRMM in combination with dexamethasone (Sd)** **Penta-refractory patients - STORM study[3]** 28-day cycle		
	Selinexor	**Dexamethasone***	
Dose	80 mg PO	20 mg PO	
Schedule	Twice weekly (Day 1 and 3 of each week)	Twice weekly (Day 1 and 3 of each week)	
Response	Median duration of response – 4.4 months Median progression-free survival – 3.7 months Median overall survival – 8.6 months **NOTE:** The median delivered dose of selinexor in the STORM (Sd) study was 113.6mg/week (approx. 60mg twice weekly)[1] Dose adjustment may be indicated as early as 2nd week to aid tolerability.		

*In those >75yrs or who are frail, a lower starting dose of dexamethasone, 20mg weekly should be considered[4].

DUAL ANTI-EMETIC PROPHYLAXIS

The most common non-haematologic adverse event with selinexor is nausea[1]. Before commencing treatment with selinexor, all patients should commence treatment with two prophylactic antiemetics.

Dual antiemetic approach including a 5-HT3 antagonist, is recommended for the first 2 cycles of treatment then taper as required.

1. Ondansetron 8 mg PO 30 to 60 minutes prior to each dose and continued every 8-12 hours for 2-3 days following dose.

OR

Akynzeo (netupitant 300 mg + palonosetron 0.5 mg) once weekly dosing

If Akynzeo utilised as primary antiemetic, additional 5-HT3 antagonist may be used after 72hrs of Akynzeo dosing if required.

AND

2. Olanzapine 2.5 mg – 5 mg PO nocte and continued each night for 2-3 days following dose

Add third as required

- Metoclopramide
- Prochlorperazine

RECOMMENDED DOSE ADJUSTMENT AND MONITORING

Monitor patients carefully during cycle 1 & 2 of therapy to assess for tolerability.

- **Monitor patients weekly during the first cycle of therapy**
  - Weekly phone review to assess and manage TRAE's
  - Adverse events are largely dose and schedule dependent[7]
  - Consider weekly full blood count (FBC), blood chemistries including sodium (EUCs) and complete metabolic profile (CMP)
  - Low platelets and/or low sodium can be predictors of TRAE's
  - Weekly weight – patient self-report
- **Face to face review beginning of each new cycle**
  - Maintain low threshold for dose reduction as early as week two

SELINEXOR DOSE REDUCTIONS

	RRMM in combination with bortezomib and dexamethasone BOSTON (SVd)	RRMM in combination with dexamethasone STORM (Sd)
Recommend starting dosage[1]	100 mg once weekly	80 mg Days 1 and 3 of each week (160 mg total per week)
	Prompt dose reduction in presence of AEs	Prompt reduction to weekly dosing is often required
First Reduction	80 mg once weekly	100 mg once weekly
Second Reduction	60 mg once weekly	80 mg once weekly
Third Reduction	40 mg once weekly	60 mg once weekly
Fourth Reduction	Permanently discontinue	

TREATMENT RELATED ADVERSE EFFECTS (TRAE's)

The TRAE's associated with selinexor-based therapy in the STORM (Sd) and BOSTON (SVd) studies, are shown below. The most common AE's being GI (nausea, vomiting, diarrhoea), haematologic (thrombocytopenia, anaemia, neutropenia), fatigue and hyponatremia.

TEAE, n (%)	SVd (n=195) BOSTON		Sd (n=123) STORM	
	All Grades	Grade 3/4	All Grades	Grade 3/4
Haematologic				
Thrombocytopenia	117 (60%)	77 (39%)	90 (73%)	72 (59%)
Anaemia	71 (36%)	31 (16%)	83 (67%)	54 (44%)
Neutropenia	29 (15%)	17 (9%)	49 (40%)	26 (21%)
Hyponatremia	58%	14%	39%	22%
Non-Haematologic				
Fatigue	82 (42%)	26 (13%)	90 (73%)	31 (25%)
Nausea	98 (50%)	15 (8%)	88 (72%)	12 (10%)
Diarrhoea	63 (32%)	12 (6%)	56 (46%)	9 (7%)
Peripheral neuropathy	63 (32%)	9 (5%)		
Decreased Appetite	69 (35%)	7 (4%)	69 (56%)	6 (5%)
Weight Loss	51 (26%)	4 (2%)	62 (50%)	1 (1%)
Asthenia	48 (25%)	16 (8%)		
Constipation	33 (17%)	0	50 (25%)	3 (1.5%)
Cough	35 (18%)	1 (1%)	33 (16%)	0
Insomnia	31 (16%)	2 (1%)	21 (17%)	2 (2%)
Back Pain	30 (15%)	1 (1%)		
Pneumonia	35 (18%)	24 (12%)	26 (13%)	18 (9%)
Pyrexia	30 (15%)	3 (2 %)	32 (16%)	1 (0.5%)
Cataract	42 (22%)	17 (9%)		
Blurred Vision	(13%)	(>1%)	21 (10%)	1 (0.5%)
Vomiting	40 (21%)	8 (4%)	47 (38%)	4 (3%)
Peripheral Oedema	23 (12%)	1 (1%)		
Dyspnoea	18 (9%)	1 (1%)	48 (24%)	7 (3.5%)
Bronchitis	24 (12%)	3 (2%)		
Upper Respiratory Tract Infection	35 (18%)	5 (3%)	42 (21%)	6 (3%)

MANAGEMENT OF MORE COMMON TRAE's

GASTROINTESTINAL TOXICITIES

Nausea and Vomiting (N&V)

Nausea is a common side effect of Selinexor-based therapy reported in 73% of patients on the STORM study (Sd) and 50% of those in the BOSTON study (SVd). Even mild (grade 1) nausea can adversely impact quality of life (QOL) and supportive care to prevent and manage N&V is a priority of care. Median time to onset of nausea in the BOSTON study was **6-days**[2]. Effective prophylaxis with a dual antiemetic approach is recommended in all patients from 1st dose of selinexor and for the first 2 cycles of therapy. Antiemetics may be tapered after 2 cycles if tolerance improves. Patient education that nausea is best managed preventively rather reactively can ensure best adherence to antiemetic drug regimes.

See CINSW eviQ information on prevention of anti-cancer therapy induced nausea and vomiting (AINV)- selinexor listing pending at time of writing.
7-Prevention of anti-cancer therapy induced nausea and vomiting (AINV) | eviQ

Prophylaxis – Dual antiemetic recommended for all patients during cycle 1 & 2 [8,9,10]

Dual antiemetic regimen containing a 5-HT3 antagonist
Ondansetron 8mg PO 30-60 mins prior to each dose and continued every 8-12hrs for 2-3 days following dose **OR** **Akynzeo** (netupitant 300mg + palonosetron 0.5mg) once weekly dosing If Akynzeo utilised as primary antiemetic, additional 5-HT3 antagonist may be used after 72hrs of Akynzeo dosing if required.
AND
Olanzapine 2.5 mg – 5 mg PO nocte and continued each night

OR/Add third as required

- Metoclopramide
- Prochlorperazine

Constipation is a commonly associated with antiemetic therapies – careful monitoring is required to ensure regular soft-formed bowel movement in context of higher risk of diarrhoea with selinexor. Educate patients and family with strategies to minimise risk of constipation including optimal hydration, high fibre diet and potential use of laxatives.

Management of Nausea and Vomiting: Supportive care and dosing recommendations[8,9,10]

https://ctep.cancer.gov/protocolDevelopment/electronic_applications/ctc.htm (CTCAE) Version 5.0

Nausea and Vomiting	Action
Grade 1 or 2 nausea Oral intake decreased without significant weight loss, dehydration, or malnutrition **OR** **Grade 1 or 2 vomiting** 5 or fewer episodes per day	▪ **Maintain** selinexor dose ▪ **Implement additional** anti-nausea medications to supplement the required 5-HT3 antagonists using institutional guidelines, eviQ and NCCN ▪ If not already taking - Add olanzapine daily for 1-2 cycles – if appropriate ▪ Consider outpatient IV hydration; clinical review
Grade 3 nausea Inadequate oral caloric or fluid intake **OR** **Grade ≥ 3 vomiting** ≥6 or more episodes per day	▪ **Interrupt** dosing with selinexor until improved to ≤ Grade 2 or baseline ▪ **Initiate** additional antiemetics ▪ **Add** additional supportive care e.g increased frequency of clinical review, IV hydration, tube feeding, TPN or hospitalisation ▪ **Restart** selinexor at 1 dose level lower

***Consensus opinion:**

Consider holding selinexor for 1 week for any Grade vomiting per doctors' discretion. If vomiting occurs again – consider hold until resolved and reintroduce at lower dose.

Antiemetic may be required regularly each day through cycles 1 & 2.

Diarrhoea

Diarrhoea occurred in 46% of patients in the STORM (Sd) study and 32% of patients in the BOSTON (SVd) study. If not effectively managed, diarrhoea can lead to dehydration and weight loss. Effective management includes monitoring for episodes of diarrhoea and managing with timely dose adjustments and anti-diarrhoeal agents.

- Loperamide (4 mg followed by 2 mg every 4 hours or after every unformed stool. Max 16 mg per 24 hours)
- Replace electrolytes if clinically indicated

See CINSW eviQ information on treatment induced diarrhoea and its management.
779-Treatment induced diarrhoea | eviQ
3237-Algorithm - treatment induced diarrhoea management | eviQ

Management of diarrhoea: Supportive care and dosing recommendations[8,9]

Diarrhoea	Action
Grade 2 (1st occurrence) Increase of 4 - 6 stools per day over baseline	▪ **Interrupt** selinexor dose ▪ **Initiate** anti-diarrhoeal treatment per institutional guidelines ▪ **Monitor** until diarrhoea resolves to Grade 1 or lower ▪ **Restart** at current dose
Grade 2 (2nd occurrence)	▪ **Interrupt** selinexor dose ▪ **Initiate** anti-diarrhoeal treatment per institutional guidelines ▪ **Monitor** until diarrhoea resolves to Grade 1 or lower ▪ **Reduce** selinexor dose by 1 dose level
Grade ≥3 Increase of ≥7 stools per day over baseline; hospitalisation indicated	▪ **Interrupt** selinexor dose ▪ **Monitor** until diarrhoea resolved to Grade 1 ▪ **Restart** selinexor at 1 dose level lower

Anorexia and weight loss

Anorexia was present in 53% (Sd) and 35% (SVd) patients with weight loss in 47% (Sd) and 26% (SVd). The presence of GI side effects (e.g., nausea, vomiting, diarrhoea) associated with selinexor contributes to loss of appetite, dehydration, and weight loss. Use of 2 antiemetics to prevent N&V and maintaining hydration and calorific input, can help reduce risk of anorexia and weight loss. A malnutrition screening tool (MST) (https://www.health.qld.gov.au/__data/assets/pdf_file/0029/148826/hphe_mst_pstr.pdf) is a useful instrument to assess and monitor for patients at risk of loss of appetite +/- weight.

Consider review by dietician, as available, before commencing therapy to optimise nutrition. Suggested recommendations to optimise appetite and reduce risk of weight loss:

- Small, frequent meals – grazing diet 2 hourly initially
- High calorie snacks
- High protein/energy drinks (as recommended by dietician)
- Fruit tingles, sour gums/babies (fizzy and sour lollies) – can help with loss of appetite and loss of taste buds, stimulate salivary production and acid secretion in stomach and can help with appetite.
- Monitor weight weekly during cycles 1 & 2
- If diarrhoea present, increase frequency of monitoring[8,9]

High energy food & drinks information sheets:

https://www.leukaemia.org.au/wp-content/uploads/2022/08/Eating-Well_Leukaemia-Foundation_FINAL.pdf

https://www.cancerresearchuk.org/about-cancer/coping/physically/diet-pr

Myeloma Australia MyeConversations podcast – All things nutrition part 1 and 2
https://myeloma.org.au/podcast

Management of anorexia and weight loss: Supportive care and dosing recommendations [1,8,9]

Anorexia and Weight Loss	Action
Grade 2 Weight loss of 10% to < 20% **OR** **Grade ≥3** Anorexia associated with significant weight loss or malnutrition	▪ **Interrupt** selinexor dose ▪ **Rule out** other causes ▪ **Consider** a repeat nutritional consultation and nutritional supplements ▪ **Institute** supportive care medications per institutional guidelines, eviQ and NCCN ▪ **Monitor** until weight returns to more than 90% of baseline weight. ▪ **Restart** selinexor at 1 dose level lower

Fatigue

Fatigue is commonly reported in those with myeloma throughout their course of disease and can have significant impact on physical, role and social functioning negatively impacting quality of life. Strategies to minimize fatigue include managing contributing factors (e.g., anaemia) and increasing exercise tolerance[11]. Patient education should be focused on improving sleep hygiene, pacing, prioritising activity and setting realistic expectations.

Regular exercise as tolerated alongside mind, body and spirit practices can be effective in minimizing fatigue. Referral to an exercise physiologist with experience in working with people with cancer, can help facilitate appropriate and individualized exercise programs.

See CINSW eviQ Patient and Carer Information Fatigue

3424-Feeling tired (fatigue) during cancer treatment | eviQ

Sleep hygiene - Better Health Channel

Management of fatigue: Supportive care and dosing recommendations[1]

Fatigue	**Action**
Grade 1 Fatigue relieved by rest[2]	▪ **Maintain** selinexor dose ▪ **Institute** supportive care per institutional guidelines, eviQ and NCCN
Grade 2 Lasting > 7 day **OR** **Grade 3** Fatigue not relieved by rest, limiting self care ADL[2]	▪ **Institute** supportive care per institutional guidelines, eviQ and NCCN ▪ **Interrupt** selinexor dose until resolved to Grade 1 or baseline ▪ **Monitor** for anaemia ▪ **Restart** selinexor at 1 dose level lower

ADL: Activities of Daily Living[8,11]

HAEMATOLOGICAL TOXICITY

Cytopenia's are more common in those with poor bone marrow reserve at baseline. Weekly FBC during first 2 cycles of treatment is recommended and then taper frequency as indicated. Thrombocytopenia was the leading cause of dose modification in the BOSTON study[2]. Patients should be instructed to report any bruising and bleeding. Provide platelet support as per institutional guidelines to facilitate dosing. Note that RRMM patients are commonly on a form of anti-platelet therapy due to previous thrombotic episodes or prophylaxis. Dosing and scheduling may need to be adapted in presence of thrombocytopenia. For example, anti-thrombotic's are commonly omitted with platelet count < 50. Timely dose reductions of selinexor are included below.

Thrombocytopenia: Supportive care and dosing recommendations[1]

Thrombocytopenia	**Action**
Platelet Count 25 to < 75 X 10^9/L	▪ **Reduce** selinexor by 1 dose
Platelet Count 25 to < 75 X 10^9/L with concurrent bleeding	▪ **Interrupt** dose ▪ **Restart** selinexor at 1 dose lower after bleeding has resolved
Platelet Count < 25 X 10^9/L	▪ **Interrupt** dose and consider supportive care ▪ **Monitor** – until platelet count returns to at least 50 x 10^9/L ▪ **Restart** selinexor at 1 dose level lower

Neutropenia

Weekly FBC during the first cycle is recommended and then titrated as indicated. Patients should be instructed to report any signs and symptoms of infection (e.g., temperature >38oC) immediately. Febrile neutropenia alert cards as per institutional policy, should be provided and the importance of acting upon symptoms, reinforced. Note, RRMM patients who have received multiple previous lines of therapy, are more commonly cytopenic at baseline of new treatment initiation. Consider the use of antimicrobials and growth factors as per institutional guidelines, to facilitate continuation of therapy[9].

G-CSF agents

- Filgrastim: 5 mcg/kg SC or IV
- Pegfilgrastim: 6 mg SC

Neutropenia: Dose reduction recommendations[1]

Neutropenia:	**Action**
Absolute neutrophil count (ANC) of 0.5 to 1.0 x 10^9/L without fever	▪ **Reduce** selinexor by 1 dose level
Absolute neutrophil count < 0.5 x 10^9/L OR febrile neutropenia	▪ **Interrupt** dose and provide supportive care ▪ **Monitor** until neutrophil counts return to 1.0 x 10^9/L or higher ▪ **Restart** selinexor at 1 dose level lower

ANC: absolute neutrophil count; G-CSF: granulocyte colony-stimulating factor; IV: intraveneous; SC: subcutaneous

Hyponatremia

Hyponatremia commonly occurs within the 1st cycle with median time to onset of 21 days (SVd any grade) and 8 days (Sd any grade). The cause of this is not completely understood. Weekly monitoring of blood chemistries including sodium, during the first 1 or 2 cycles is recommended and monthly thereafter or as indicated. Sodium replacement can be managed with IV saline or salt tablets as indicated. Hyponatremia occurred more commonly in the presence of GI effects, nausea, vomiting and diarrhoea. Timely management of GI effects may reduce risk of hyponatremia. Be alert for signs of confusion and drowsiness and educate carer to be aware of subtle signs of confusion.

Hyponatremia: Supportive care and dosing recommendations for treatment[1,8,9]

Hyponatremia:	Action
Sodium level ≤ 130 nmol/L	▪ Interrupt selinexor dose, evaluate and provide supportive care ▪ Monitor until sodium levels return to > 130 nmol/L ▪ Restart selinexor at 1 dose level lower

Examples of supportive care[8,9]**:**

- Monitor hydration status and serum sodium levels
- Saline/salt tablets
- Salty snacks e.g. nuts, crackers, chips, sweet/salty energy bites, popcorn

PRACTICAL MANAGEMENT RECOMMENDATIONS

Health Care Professionals (HCPs)

Selinexor-based therapy represents a unique targeted drug for the treatment of RRMM and has a differing toxicity profile to other more commonly used MM treatments (e.g., PIs IMiDs, alkylators, corticosteroids, moAbs). Preparation of supportive care protocols including those focused on assessment and management, are a critical first step in optimizing management for patients. Patients receiving oral cancer therapy regimens may have reduced opportunity for repeat education, clarification of understanding and reduced treatment monitoring compared to patients attending day therapy to receive infusional cancer therapies. Nurse led review (face to face or telephone) of myeloma patients on oral therapies provides a useful framework for assessment review of TRAE's and medication adherence.

Gastrointestinal toxicity can be particularly challenging during the first 1-2 cycles of therapy and baseline assessment and review by dietician, where available, is recommended.

Patients who are heavily pre-treated, have poor bone marrow reserve, are elderly, frail, do not have a carer, have a low BMI (BMI <18.5) or history of treatment associated N&V - may experience increased levels of symptoms or concerns, or find it harder to tolerate therapy. This group of patients would benefit from more intensive supportive care strategies. These may include more regular (e.g., weekly) face-to-face assessment and review, pre-planned IV hydration and more frequent blood monitoring.

HCPs may consider the use of automated alerts (e.g., on EMR or oncology scheduling systems) to focus clinical reviews for individual patients.

In this heavily pre-treated population who may have significant co-morbidities of older age, disease morbidities (e.g., bone disease, renal impairment, immune compromise), pre-existing TRAE's (e.g. peripheral neuropathy, fatigue or cytopenia's) and are high risk for TRAE's, early referral to a palliative care service should be considered. Early palliative care referral aims to manage both disease and treatment related effects, complex symptomatology and improve quality of life. This also provides an opportunity for early engagement in end-of life discussions, including advanced care planning, a vital component in the multiply relapsed myeloma patient population.

A strong motivation for patients' ability to tolerate side effects, is being able to see how they are responding to treatment. Finding ways of communicating this with patients clearly will help to get patients onboard to working with HCPs to minimize side effects and remain on treatment. For example, graphing M-protein readings in EMR to demonstrate disease response or blood count recovery.

EMR – electronic medical records

Patients & Carers

Various strategies can be implemented to help those with myeloma to better tolerate therapy. Education should empower the patient/carer and provide clear instructions on how to manage TRAE's. If no carer is available, patient should have expectation of more frequent (e.g., weekly) in person day unit reviews. Link patients and carer into the wider support available from patient organisations such as Myeloma Australia, Cancer Council and Leukaemia Foundation.

MEDICATION SCHEDULES

Myeloma treatment regimens are complex, patients and carers require medication schedules to aid their understanding of the treatment regimen. Myeloma Treatment Scheduler is an online tool developed by M-SPN members. Based on eviQ (CINSW) treatment protocols and with flexibility to adapt to real world use. Selinexor-based protocols, including supportive measures (e.g., anti-emetics) can be produced in minutes.

Register via: https://rego.interact.technology/myetx/

Examples of SVd and Sd schedules are provided in the Appendix.

Summary Statement: M-SPN Consensus recommendations regarding selinexor dosing and supportive care.

- Best supportive care for those receiving selinexor-based therapies includes provision of dual antiemetic prophylaxis and prompt dose adjustment to aid tolerability.
- Maintain low threshold for dose reduction as early as week two.
- The most common selinexor associated AEs are GI (nausea, vomiting, diarrhoea), haematologic (thrombocytopenia, anaemia, neutropenia), fatigue and hyponatremia.
- Nurses are well placed to advocate for timely dose adjustments in the presence of TRAE's.
- Twice weekly dosing of Selinexor and dexamethasone (Sd) doublet therapy can be hard to tolerate long-term. Prompt reduction to weekly dosing of selinexor is often required.
- Dose reductions of selinexor in combination with bortezomib and dexamethasone (SVd Boston study) were associated with longer progression free survival (PFS), duration on response (DOR), time to next treatment (TTNT), and significantly reduced AEs with improved tolerability, highlighting dose reductions as an important tool to optimise clinical outcomes for patients[11].
- Suggested timing of selinexor and associated drugs (EVENING)
    - Dexamethasone with/after breakfast
    - Akynzeo (netupitant 300 mg + palonosetron 0.5 mg) once weekly dosing
        OR
    - Ondansetron 30-60 mins before bedtime
    - Selinexor & olanzapine nocte
- Alternate timing for selinexor and associated drugs (MORNING)
    - Dexamethasone with/after breakfast
    - Akynzeo (netupitant 300 mg + palonosetron 0.5 mg) once weekly dosing, min 60 mins before selinexor
        OR
    - Ondansetron
    - Selinexor 30-60 mins later
    - Olanzapine nocte
- Continue antiemetics for 2-3 days post selinexor dosing.
- Consider tapering antiemetics after 2 cycles as indicated.
- Gastrointestinal (GI) side effects are seen more commonly during cycle 1 & 2 and may improve over time.

- Focused and frequent communication, education and supportive care during cycle 1 & 2 is critical and reduces risk of discontinuation due to TRAE's
    - Patient & carer education, weekly bloods, N&V prophylaxis. Encourage patients to maintain symptom diary for first 1-2 cycles to help with proactive assessment and management of symptoms and concerns
- Where available – provide regular nurse led follow-up during cycle 1 & 2 focused on identification of, assessment and management of TRAE's
- Provide in person reviews in presence of red flags (e.g., patient lives alone, has high disease burden or emergent treatment related effects)
- Myeloma Australia nurse-led support line (1800 693 566) can supplement site specific management.

Intensive supportive care of people commencing selinexor-based therapy has been shown to aid tolerance and reduce risk of treatment discontinuation[11]. Regular review that focus on early identification and management of toxicity and timely dose or scheduling adjustments enhances adherence and drug tolerance.

ADDITIONAL READING

Selinexor Treatment Protocol/s eviQ

Product Information vs 3.0 Jan 2023. Product Information (tga.gov.au)

Consumer Medical Information vs 3.0 2023. pdf (tga.gov.au)

Selinexor Treatment Fact Sheet - Myeloma Australia Selinexor_may22.pdf (myeloma.org.au)

International Myeloma Foundation Information
Xpovio (selinexor) | International Myeloma Foundation

Myeloma UK Information
Myeloma-UK-Selinexor-Horizons-Infosheet.pdf

For further information on XPOVIO (Selinexor), please contact:
Antengene Australia on
1800 978 284
Medinfo.au@antengene.com

- XPOVIO Multiple Myeloma HCP Brochure
- Getting patients started on Selinexor

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Appendix

Selinexor Treatment Checklist Pre-Tx and Cycle 1				
Name:			**Start Date:** **Cycle No:**	
Selinexor regimen (circle)	**SVd**		**Sd**	
Selinexor start dose/schedule	Dose:		Frequency:	
Dexamethasone dose/schedule	Dose:		Frequency:	
Bortezomib dose/schedule (SVd)	Dose:		Frequency:	
Dual antiemetic regimen (circle)				
1. Ondansetron 8mg **OR** Akynzeo (netupitant 300mg + palonosetron 0.5mg)	Dose:		Frequency Weekly:	
2. Olanzapine 2.5-5mg	Dose:		At night:	
3rd agent as required Metoclopramide Prochlorperazine	Dose:		Frequency:	
Step down regimen (D4-7)				
Record weekly weight -baseline:	Wk1:	Wk2:	Wk3	Wk4:
Dietician: weight loss >10%, anorexia	Add MST			
Fluid status – is intake <2.5L/24hrs? Fluid status - Losses (diarrhoea, N&V)	Intake: Loss:	Intake: Loss:	Intake: Loss:	Intake: Loss:
Pathology monitoring (circle)	**Ticked Reviewed**			
FBC weekly/other	Wk1:	Wk2:	Wk3:	Wk4:
Biochem(Na+): weekly/other	Wk1:	Wk2:	Wk3:	Wk4:
Symptom monitoring	**Record issues & advice**			
Nausea & vomiting	Wk1:	Wk2:	Wk3:	Wk4:
Appetite/Nutrition	Wk1:	Wk2:	Wk3:	Wk4:
Fatigue	Wk1:	Wk2:	Wk3:	Wk4:
Diarrhoea or constipation	Wk1:	Wk2:	Wk3:	Wk4:
Cytopenias – record action e.g, blood product/GCSF or dose reduction	Wk1:	Wk2:	Wk3:	Wk4:
Infective symptoms	Wk1:	Wk2:	Wk3:	Wk4:

Patient Symptom Tracker

Name:_____ **Start date:** ___/____/_____

Week of Cycle (circle): Wk1 Wk2 Wk3 Wk4 Wk5 Wk6 Wk7 **(circle): SVd or Sd**

	Eating Normal Meals	Weight Kg	Nausea	Vomiting	Diarrhoea	Fatigue	How I have managed these side effects….
Monday	Yes / No		Yes / No	Yes / No	Yes / No	Yes / No	
Tuesday	Yes / No		Yes / No	Yes / No	Yes / No	Yes / No	
Wednesday	Yes / No		Yes / No	Yes / No	Yes / No	Yes / No	
Thursday	Yes / No		Yes / No	Yes / No	Yes / No	Yes / No	
Friday	Yes / No		Yes / No	Yes / No	Yes / No	Yes / No	
Saturday	Yes / No		Yes / No	Yes / No	Yes / No	Yes / No	
Sunday	Yes / No		Yes / No	Yes / No	Yes / No	Yes / No	

EXAMPLE: Selinexor + Bortezomib + Dexamethasone (SVD) 35-day cycle

Name: DOB: MRN:

CYCLE 1

Date																																
Day 1-35	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35
1. Akynzeo																																			
Anti-nausea medicaiton continaing 2 different drugs - slow release. Take 1 tablet, once per week.																																			
2. Olanzapine																																			
Anti-nausea medicaiton - taken each night to help prevent nausea associated with selinexor. Taken for 2-3 days following weekly selinexor dose																																			
Selinexor																																			
As tablets - taken once per week - every week, ongoing. Take _____ tablets (_____mg)																																			
Bortezomib (Velcade)																																			
As an injection under the skin of the abdomen. Given by nurses in day therapy once per week for 4 weeks followed by 1 week break																																			
Dexamethasone																																			
Steroid. Take _____ tablets (_____mg) day 1 and 2 of each week. Take in the morning with or after food.																																			
Anti-viral																																			
To help prevent shingles																																			
Ondansetron																																			
Anti-biotic																																			
PPI																																			
Weight	kg							kg							kg							kg							kg						
Monitor for loss of weight. Take your weight once per week and let your healthcare team know at each review																																			
Blood Test	YES							YES							YES							YES													
Frequency varies. Check with your team																																			
Dr/Nurse Review	YES							📞							📞							📞							📞						
In person or via phone																																			

EXAMPLE: Selinexor + Dexamethasone (Sd) 28-day cycle

Name: DOB: MRN:

CYCLE

Date																											
Day 1-28	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28
1. Akynzeo																												
Anti-nausea medicaiton - taken once per week (long acting) to help prevent nausea associated with selinexor. Suggested days shown																												
2. Olanzapine																												
Anti-nausea medicaiton - taken each night to help prevent nausea associated with selinexor. Suggested days shown																												
Selinexor																												
As a tablet - taken twice per week - every week, ongoing																												
Dexamethasone																												
Steroid. Take _____ tablets (_____mg) on same day as selinexor tablet. Take in the morning with or after food.																												
Ondansetron																												
PPI																												
Anti-biotic																												
Weight	kg							kg							kg							kg						
Monitor for loss of weight. Take your weight once per week and let your healthcare team know at each review																												
Blood Test	YES							YES							YES							YES						
Frequency varies. Check with your team																												
Dr/Nurse Review	YES							📞							📞							📞						
In person or via phone																												