PROTOCOL

The Clatterbridge Cancer Centre NHS Foundation Trust

Systemic Anti Cancer Therapy Protocol

# BORTEZOMIB & DEXAMETHASONE (Vel/Dex) MULTIPLE MYELOMA

PROTOCOL REF: MPHABDVDMM
(Version No. 1.0)

## Approved for use in:

The following patients with multiple myeloma:

- Patients who have received one prior line of therapy and have undergone, or are unsuitable for, a bone marrow transplant **(NICE TA129)**.Treatment should only be continued after 4 cycles if there is a complete or partial response (ie reduction in serum M protein of ≥50% or if not measurable then an appropriate alternative biochemical measure of response).
- Induction treatment of patients with untreated multiple myeloma, who are eligible for high dose chemotherapy with haematopoeitic stem cell transplant **(NICE TA311)**
- Bortezomib is routinely commissioned for
    - 1st line treatment of patients presenting with severe renal failure or haemodialysis (contraindicating standard therapy)
    - Patients with multisystem amyloidosis (on review from National Amyloid Centre)
    - 1st line treatment in patients unsuitable for haematopoietic stem cell transplant

**Blueteq is not required for the above indications**

## Dosage:

### 21 Day – Twice Weekly

| Drug | Dosage | Route | Frequency |
|---|---|---|---|
| **Bortezomib** | **1.3mg/m$^2$** | S/C | Day 1, 4, 8 and 11 |
| **Dexamethasone** | **20mg*** | Oral | Days 1, 2, 4, 5, 8, 9, 11, 12 |

**Dexamethasone dose may be altered at clinician discretion.

**Cycle length every 21 days. Max 8 cycles.**

### 35 Day – Weekly

| Drug | Dosage | Route | Frequency |
|---|---|---|---|
| **Bortezomib** | **1.3mg/m$^2$** | S/C | Day 1, 8, 15, 22 |
| **Dexamethasone** | **20mg*** | Oral | Days 1, 2, 8, 9, 15, 16, 22 and 23 |

**Dexamethasone dose may be altered at clinician discretion.

**Cycle length every 35 days. Max 8 cycles.**

## Administration and counselling points:

- Dexamethasone tablets should be taken in the morning after food.
- At least 72 hours should elapse between bortezomib administrations.
- Bortezomib should be administered subcutaneously through the thighs (right or left) or abdomen (right or left). The solution should be injected subcutaneously, at a 45-90° angle. Injection sites should be rotated for successive injections.

## Emetogenic risk:

Mildly emetogenic.

## Supportive Medication:

- Allopurinol 300mg oral once daily (cycle 1 only)
- Aciclovir oral 400mg oral twice a day

- Co-trimoxazole 480mg oral once daily
- Metoclopramide 10mg oral three times a day when required for up to 7 days
- Nystatin oral suspension 1mL four times daily or fluconazole 50mg oral once daily (higher risk patients only)
- Omeprazole 20mg oral once daily

## Dosing in renal and hepatic impairment:

| Bortezomib | |
|---|---|
| **Renal** | |
| No dose adjustments required but bortezomib should be administered after dialysis. | |
| **Hepatic** | |
| **Liver function** | **Dose adjustment** |
| Moderate to severe impairment (bilirubin >1.5xULN) | Reduce to 0.7mg/m$^2$. Consider dose escalation to 1.0 mg/m$^2$ or further dose reduction to 0.5 mg/m$^2$ in subsequent cycles based on patient tolerability. |

## Extravasation Risk:

Bortezomib – non-vesicant

## Interactions:

- Monitor closely for side effects when giving bortezomib in combination with potent CYP3A4 inhibitors (e.g. ketoconazole, ritonavir) due to potential for increased exposure to bortezomib.
- Concomitant use of bortezomib with strong CYP3A4 inducers (e.g., rifampicin, carbamazepine, phenytoin, phenobarbital and St. John's Wort) is not recommended, as efficacy may be reduced

## Treatment schedule:

### 21 day Cycle:

| Day | Drug | Dose | Route | Diluent and rate |
|---|---|---|---|---|
| 1 | **Dexamethasone** | **20mg** | **PO** | Mane day 1, 2, 4, 5, 8, 9, 11, 12 (TTO) |
| | **Bortezomib** | **1.3mg/m$^2$** | **S/C** | |
| 4 | **Bortezomib** | **1.3mg/m$^2$** | **S/C** | |
| 8 | **Bortezomib** | **1.3mg/m$^2$** | **S/C** | |
| 11 | **Bortezomib** | **1.3mg/m$^2$** | **S/C** | |

### 35 day Cycle:

| Day | Drug | Dose | Route | Diluent and rate |
|---|---|---|---|---|
| 1 | **Dexamethasone** | **20mg** | **PO** | Mane day 1, 2, 8, 9, 15, 16, 22 and 23 (TTO) |
| | **Bortezomib** | **1.3mg/m$^2$** | **S/C** | |
| 8 | **Bortezomib** | **1.3mg/m$^2$** | **S/C** | |
| 15 | **Bortezomib** | **1.3mg/m$^2$** | **S/C** | |
| 22 | **Bortezomib** | **1.3mg/m$^2$** | **S/C** | |

## Main toxicities:

| **Bortezomib** |
|---|
| Infections, herpes zoster reactivation, herpes simplex, pneumonia, thrombocytopenia, neutropenia, anaemia, leukopenia, lymphopenia, reduced appetite, hypokalaemia, hyponatraemia, dehydration, hypocalcaemia, mood disturbance, sleep disturbance, anxiety, neuropathies, peripheral sensory neuropathy, fatigue, eye swelling, conjunctivitis, vertigo, hypo/hyper-tension, nausea, vomiting, constipation, diarrhoea, abnormal hepatic enzymes, rash, pruritus, muscle pain/weakness, weight loss, hepatitis B reactivation.<br>Rare – seizures (review if additional risk factors for seizures) |

## Investigations and treatment plan:

| | Pre | Cycle 1+ D1 | Cycle 1 D2 | Cycle 1+ D4 | Cycle 1+ D8 | Cycle 1+ D11 | Ongoing |
|---|---|---|---|---|---|---|---|
| Informed consent | X | | | | | | |
| Clinical Assessment | X | X | | | | | Every cycle |
| SACT Assessment (including performance status toxicity assessment) | | X | | X | X | X | Every cycle |
| FBC, U&E, LFTs and calcium profile | X | X | | | | | Every cycle |
| Hepatitis B core antibody and surface antigens & Hep C & HIV 1+2 | X | | | | | | |
| Dental Assessment | X | | | | | | If clinically indicated |
| HbA1c and glucose | X | | | | | | Repeat if clinically indicated |
| Serum Igs/electrophoresis/serum free light chains (if indicated) | X | X | | | | | Every cycle |
| Neurological assessment (for neuropathy) – performed at medical review | X | X | | | | | Every cycle |
| Blood pressure | X | X | | X | X | X | |
| Weight | X | X | | | | | Every cycle |
| Height | X | | | | | | |
| Pregnancy test | X | | | | | | If clinically indicated. Repeat each cycle if women of childbearing potential |
| Imaging as per NICE/network guidance and clinical indication | X | | | | | | To restage as indicated |

## Dose Modifications and Toxicity Management:

## Haematological toxicity:

Proceed on day 1 if-

| | |
|---|---|
| ANC ≥ 0.5 x $10^9$/L | Platelets ≥ 25 x $10^9$/L |

Once the symptoms of the toxicity have resolved, bortezomib treatment may be re-initiated at a 25% reduced dose (1.3 mg/$m^2$ reduced to 1.0 mg/$m^2$; 1.0 mg/$m^2$ reduced to 0.7 mg/$m^2$). If the toxicity is not resolved or if it recurs at the lowest dose, discontinuation of bortezomib must be considered unless the benefit of treatment clearly outweighs the risk.

These haematological guidelines assume that patients are well with good performance status, that other acute toxicities have resolved and the patient has not had a previous episode of neutropenic sepsis.

## Non- Haematological toxicity:

Bortezomib treatment must be withheld at the onset of any Grade 3 non-haematological or any Grade 4 haematological toxicities, excluding neuropathy as discussed below. Once the symptoms of the toxicity have resolved, bortezomib treatment may be re-initiated at a 25 % reduced dose (1.3 mg/$m^2$ reduced to 1.0 mg/$m^2$; 1.0 mg/$m^2$ reduced to 0.7 mg/$m^2$). If the toxicity is not resolved or if it recurs at the lowest dose, discontinuation of bortezomib must be considered unless the benefit of treatment clearly outweighs the risk.

## Peripheral Neuropathy

| **Bortezomib** | |
|---|---|
| If there are symptoms of peripheral neuropathy the dose reduction schedule below must be invoked. Bortezomib should be stopped if symptoms or signs progress despite this | |
| Grade 1 with pain or grade 2 | Reduce to 1.0mg/$m^2$ or reduce to 1.3mg/$m^2$ weekly (day 1 and 8) |

| | |
|---|---|
| Grade 2 with pain of grade 3 | Withhold treatment until symptoms of toxicity have resolved. When toxicity resolves re-initiate treatment at 0.7mg/m$^2$ weekly (day 1 and 8) |
| Grade 4 and/or severe autonomic neuropathy | Discontinue |

## References:

1. https://www.medicines.org.uk/emc Bortezomib (updated Aug 2022, accessed Aug 2023)
2. Supplement to: Krens S D, Lassche, Jansman G F G A, et al. Dose recommendations for anticancer drugs in patients with renal or hepatic impairment. *Lancet Oncol* 2019; **20:** e201–08.
3. NICE: TA129: Bortezomib monotherapy for relapsed multiple myeloma. Published Oct 2007.
4. NICE: TA311: Bortezomib for induction therapy in multiple myeloma before high dose chemotherapy and autologous stem cell transplant. Published April 2014.

## Circulation/Dissemination

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|---|---|
| Date added into Q-Pulse | 1st February 2024 |
| Date document posted on the Intranet | N/A |

## Version History

| Date | Version | Author name and designation | Summary of main changes |
|---|---|---|---|
| Oct 2023 | 1.0 | **Jennifer Gibson Principal Pharmacist HO** | **New protocol** |
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