CARFILZOMIB with LENALIDOMIDE and DEXAMETHASONE (KRD)

INDICATIONS

Multiple myeloma at first relapse, having previously responded to therapy containing bortezomib and without prior exposure to immunomodulatory treatment with lenalidomide* (NICE TA695)

*Unless received as part of induction therapy prior to a stem cell transplant.

Blueteq approval required.

TREATMENT INTENT

Disease modification

GENERAL PRE-ASSESSMENT

1. Ensure all the following staging investigations are done:
   - FBC & film
   - Clotting screen
   - U&Es
   - LFTs
   - Calcium
   - Albumin
   - Uric acid
   - Virology: HIV, Hepatitis B (including core antibody), and Hepatitis C
   - Calculated creatinine clearance (CrCl), urine protein/creatinine ratio
   - Electrophoresis and immunofixation for quantitation of serum paraprotein and immunoglobulins
   - Serum free light chain assay (Freelite)
   - Heavylite analysis (if paraprotein level difficult to quantify)
   - LDH
   - Bone marrow aspirate and trephine (with immunophenotyping for kappa/lambda if appropriate)
   - Myeloma FISH should be performed in all patients at diagnosis, and in selected patients at relapse/progression to help guide treatment decisions. Samples should be sent to Wessex Regional Genetics Laboratory (address below)
   - Group and save
   - Imaging as per NICE/network guidance and clinical presentation

Wessex Regional Genetic Laboratory
Salisbury NHS Foundation Trust
Salisbury District Hospital
Salisbury
Wiltshire, SP2 8BJ
ADDITIONAL INVESTIGATIONS

1. Plasma viscosity if hyperviscosity suspected.
2. If allogeneic transplant an option: Tissue typing of patient and siblings and CMV serology.
3. Consent - ensure patient has received adequate verbal and written information regarding their disease, treatment and potential side effects. Document in medical notes all information that has been given.
4. Fertility - all patients should be offered fertility advice, as appropriate.
5. Hydration - fluid intake of at least 3 litres /day should be attempted.
8. Treatment must be agreed at the relevant MDT.

REGIMEN SPECIFIC INVESTGATIONS

1. Evaluate for presence of cardiac issues in all patients, especially in those > 60yo, history of hypertension, prior cardiac arrhythmias or IHD. Clinical assessment, echocardiogram (where indicated) and ECG are recommended in all patients as a baseline.
2. Baseline lying and standing blood pressure should be recorded prior to administration of cycle 1. Ensure BP well controlled prior to starting therapy.
4. Baseline thyroid function – hypothyroidism reported with lenalidomide use.
5. Urine pregnancy testing for pre-menopausal women younger than 55 before each cycle.
6. Counselling - all patients should receive verbal and written information on oral chemotherapy.
7. Ensure pre-chemotherapy counselling in line with NPSA recommendation and chemotherapy measures.
8. The conditions of the Lenalidomide Pregnancy Prevention Programme must be fulfilled for all male and female patients.

DRUG REGIMEN

All carfilzomib doses should be capped at BSA 2.2m².
Patients should attempt to drink 3 litres of fluid 24 hours before, and on treatment days and avoid sugary or caffeine-based drinks where clinical situation permits.

Pre- and post- IV hydration

Pre- and post-hydration should continue beyond Cycle 2 day 1 if patient is still considered at risk for TLS.
In other patients, encourage at least 1L oral fluids before and after each carfilzomib dose to maintain adequate hydration.
## Cycle 1:

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Days</th>
<th>Administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre and post hydration</td>
<td><strong>500ml sodium chloride 0.9%</strong></td>
<td>1, 2, 8, 9, 15 and 16</td>
<td>IVI Before and after dosing</td>
</tr>
<tr>
<td>Dexamethasone</td>
<td><strong>20 mg OD</strong> Consider reduction in elderly or if poor steroid tolerance</td>
<td>1, 2, 8, 9, 15, 16, 22, 23</td>
<td>Oral 30mins before carfilzomib as pre-med when due</td>
</tr>
<tr>
<td>Carfilzomib</td>
<td><strong>20 mg/m² – max. 44mg</strong></td>
<td>1 and 2</td>
<td>IVI over 10mins in 50 - 100mL 5% glucose Monitor patient for 1hr following infusion</td>
</tr>
<tr>
<td></td>
<td><strong>27 mg/m² – max. 60mg</strong></td>
<td>8, 9, 15 and 16</td>
<td></td>
</tr>
<tr>
<td>Lenalidomide</td>
<td><strong>25 mg once daily, at night</strong></td>
<td>1 – 21</td>
<td>Oral With or without food</td>
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</table>

IVI= Intravenous infusion

## Cycle 2 - 12 onwards:

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<th>Dose</th>
<th>Days</th>
<th>Administration</th>
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<tr>
<td>Pre and post hydration*</td>
<td><strong>500ml sodium chloride 0.9%</strong> (Cycle 2 only) D1</td>
<td>1, 2, 8, 9, 15, 16</td>
<td>IVI Before and after dosing</td>
</tr>
<tr>
<td></td>
<td>Minimum 1L oral hydration</td>
<td></td>
<td>Oral Before and after dosing</td>
</tr>
<tr>
<td>Dexamethasone</td>
<td><strong>20 mg OD</strong> Consider reduction in elderly or if poor steroid tolerance</td>
<td>1, 2, 8, 9, 15, 16, 22, 23</td>
<td>Oral 30mins before carfilzomib as pre-med when due</td>
</tr>
<tr>
<td>Carfilzomib</td>
<td><strong>27 mg/m² – max. 60mg</strong></td>
<td>1, 2, 8, 9, 15, 16</td>
<td>IVI over 10mins in 50 - 100mL 5% glucose C2 day 1 - Monitor patient for 1hr following infusion</td>
</tr>
<tr>
<td>Lenalidomide</td>
<td><strong>25 mg once daily, at night</strong></td>
<td>1 – 21</td>
<td>Oral With or without food</td>
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## Cycle 13 to 18 onwards:

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<td>Minimum 1L oral hydration</td>
<td>1,2,15, 16,</td>
<td>Oral Before and after dosing</td>
</tr>
<tr>
<td>Dexamethasone</td>
<td><strong>20 mg OD</strong> Consider reduction in elderly or if poor steroid tolerance</td>
<td>1, 2, 8, 9, 15, 16, 22, 23</td>
<td>Oral 30mins before carfilzomib as pre-med when due</td>
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<tr>
<td>Carfilzomib</td>
<td><strong>27 mg/m² – max. 60mg</strong></td>
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<td>IVI over 10mins in 50 - 100mL 5% glucose</td>
</tr>
<tr>
<td>Lenalidomide</td>
<td><strong>25 mg once daily, at night</strong></td>
<td>1 – 21</td>
<td>Oral With or without food</td>
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</table>
**Cycle 19 onwards, until progression or intolerance:**

<table>
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<th>Dose</th>
<th>Days</th>
<th>Administration</th>
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</thead>
<tbody>
<tr>
<td>Lenalidomide</td>
<td>25 mg once daily, at night</td>
<td>1 – 21</td>
<td>Oral</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>With or without food</td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>40 mg OD</td>
<td>1, 8, 15, 22</td>
<td>Oral, With food, in the morning</td>
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<tr>
<td></td>
<td>Consider reduction in elderly or if poor steroid tolerance</td>
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Continue lenalidomide and dexamethasone until progression as per ASPIRE trial.

In clinical trials for cycles 19 onwards dexamethasone was dosed at 40mg weekly (D1,8,15,22), but it is recommended that clinicians also take into account tolerability as well as the dexamethasone dose that the patient previously received and tolerated, especially if myeloma is optimally controlled. Clinicians may elect to re-escalate dosing to 40mg weekly as required.

**CYCLE FREQUENCY**

Repeat every 28 days. Maximum 18 cycles of carfilzomib.

Lenalidomide and dexamethasone continue until signs of disease progression or unacceptable toxicity.

**DOSE MODIFICATIONS - CARFILZOMIB**

**Prior to initiating a new cycle of therapy:**

- Platelets ≥ 75 x 10^9/L and ANC ≥ 1.0 x 10^9/L – in the event of lower counts, discuss with consultant.
- Non-haem toxicities should resolve to G1 or baseline.

**Carfilzomib dose reduction levels**

<table>
<thead>
<tr>
<th>Starting Dose</th>
<th>1st level</th>
<th>2nd level</th>
<th>Discontinue</th>
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<tbody>
<tr>
<td>27 mg/m²</td>
<td>20 mg/m²</td>
<td>15 mg/m²</td>
<td></td>
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</tbody>
</table>

A once weekly dosing schedule can also be considered for toxicity management. If toxicity does not resolve after reducing to 15 mg/m², discontinue carfilzomib.

<table>
<thead>
<tr>
<th>Carfilzomib</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haematological toxicity</td>
</tr>
<tr>
<td>ANC &lt; 0.5 x10^9 /L</td>
</tr>
<tr>
<td>ANC= Absolute neutrophil count</td>
</tr>
<tr>
<td>Febrile neutropenia (ANC &lt; 0.5 x10^9 /L and temperature &gt; 37.5°C on 2 consecutive readings for 2 hours, or temperature &gt; 38°C)</td>
</tr>
</tbody>
</table>

This is a controlled document and therefore must not be changed.
### Myeloma group

#### Dose Modifications

**Platelets ≤ 10 x 10⁹/L or evidence of bleeding with thrombocytopenia**

| 1st occurrence - Withhold carfilzomib dose. If platelet recovers to ≥ 10 x10⁹/L and/or bleeding is controlled, continue at the same dose level. Subsequent occurrences - Withhold carfilzomib dose, consider 1 dose level reduction when restarting Carfilzomib. |

<table>
<thead>
<tr>
<th>Non-haematological toxicity</th>
<th>Recommended action</th>
</tr>
</thead>
<tbody>
<tr>
<td>CTCAE Grade 3 or 4 toxicities</td>
<td>Withhold carfilzomib dose until symptom resolution or return to baseline status. Consider dose reduction by 1 level</td>
</tr>
</tbody>
</table>

#### Renal Adjustments (starting treatment)

No dose adjustment is recommended for any grade of renal dysfunction at initiation. In patients with CrCl <30ml/min cautiously monitor renal function; adverse events are more likely. Follow dose reductions as below.

#### Renal Adjustments (during treatment)

| Withhold carfilzomib. Resume when renal function has recovered to within 25% of baseline and consider resuming at 1 dose level reduction. |
| Serum creatinine greater than, or equal to 2 x baseline (i.e., AKI Stage 2 or above), and/or |
| CrCl less than 15ml/min (or creatinine clearance decreases to ≤ 50% of baseline), and/or need for dialysis |

#### Hepatic Adjustments

**Mild/moderate impairment**

No starting dose adjustment is recommended. A higher incidence of hepatic function abnormalities, ≥ grade 3 adverse events and serious adverse events have been reported compared with patients with normal hepatic function. Monitor closely.

**Severe impairment**

No information available.

#### DOSE MODIFICATIONS - LENALIDOMIDE

**Prior to initiating a new cycle of therapy:**

New lenalidomide treatment cycles should not normally be started if ANC < 1x 10⁹/L, and/or platelet count < 75 x 10⁹/L. Or, exceptionally, dependent on existing bone marrow infiltration by plasma cells, platelet counts < 30 x 10⁹/L.

If the low counts are thought to be due to myeloma per se, the use of G-CSF and platelet support should be considered.

Dose adjustments, as summarized below, are recommended to manage grade 3 or 4 neutropenia or thrombocytopenia, or another grade 3 or 4 toxicity judged to be related to lenalidomide.

Consider re-escalating lenalidomide dose provide toxicities have completely resolved.
# Myeloma Group

## Lenalidomide

<table>
<thead>
<tr>
<th>Starting dose</th>
<th>1st reduction level</th>
<th>2nd reduction level</th>
<th>3rd reduction level</th>
</tr>
</thead>
<tbody>
<tr>
<td>25mg</td>
<td>15mg</td>
<td>10mg</td>
<td>5mg</td>
</tr>
</tbody>
</table>

## Thrombocytopenia

<table>
<thead>
<tr>
<th>Occurrence Type</th>
<th>Platelet Count</th>
<th>Treatment Protocol</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st occurrence</td>
<td>&lt; 30 x 10⁹/L</td>
<td>Interrupt lenalidomide treatment</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Return to ≥ 30 x 10⁹/L following 1st occurrence</td>
</tr>
<tr>
<td>2nd or more occurrences</td>
<td>&lt; 30 x 10⁹/L</td>
<td>Interrupt lenalidomide treatment</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Return to ≥ 30 x 10⁹/L following 2nd or more occurrences</td>
</tr>
</tbody>
</table>

## Neutropenia

<table>
<thead>
<tr>
<th>Occurrence Type</th>
<th>Neutrophil Count</th>
<th>Treatment Protocol</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st occurrence</td>
<td>&lt; 0.5 x 10⁹/L</td>
<td>Interrupt lenalidomide treatment, administer G-CSF for 3 days and recheck FBC.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Return to ≥ 0.5 x 10⁹/L when neutropenia is the only toxicity</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Resume lenalidomide at the starting dose level</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Return to ≥ 0.5 x 10⁹/L when dose-dependent haematological toxicities other than neutropenia are observed</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Resume lenalidomide at one level dose reduction</td>
</tr>
<tr>
<td>2nd or more occurrences</td>
<td>&lt; 0.5 x 10⁹/L</td>
<td>Interrupt lenalidomide treatment, administer G-CSF for 3 days and recheck FBC.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Return to ≥ 0.5 x 10⁹/L following 2nd or more occurrences</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Resume lenalidomide at next lower dose level. Do not dose below 5 mg once daily.</td>
</tr>
</tbody>
</table>

## Rash

<table>
<thead>
<tr>
<th>CTCAE Grade</th>
<th>Recommended Course</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 or 3</td>
<td>Withhold lenalidomide until rash recovers to ≤ Grade 1. Following recovery, resume lenalidomide at the next lower dose</td>
</tr>
<tr>
<td>4</td>
<td>Discontinue treatment regimen</td>
</tr>
</tbody>
</table>

## Renal Adjustments (CrCl<sub>a</sub>)

<table>
<thead>
<tr>
<th>CrCl&lt;sub&gt;a&lt;/sub&gt;</th>
<th>Dose</th>
<th>Hepatic Adjustments</th>
</tr>
</thead>
<tbody>
<tr>
<td>30 - 50 ml/min</td>
<td>10mg once daily*</td>
<td>No formal studies. No specific dose recommendations</td>
</tr>
<tr>
<td>&lt; 30 ml/min, no dialysis</td>
<td>15 mg every other day**</td>
<td></td>
</tr>
<tr>
<td>&lt; 30 ml/min, requiring dialysis</td>
<td>5 mg once daily***</td>
<td></td>
</tr>
</tbody>
</table>

*Calculation used to estimate creatinine clearance (CrCl<sub>a</sub>) should follow local institutional standard.

* Can increase to 15mg OD if no response and patient tolerating.

** Can increase to 10mg OD if no response and patient tolerating.

*** Administer on dialysis day, timing the dose after dialysis as lenalidomide is most likely dialysed.

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Dexamethasone
There are no specific dose modifications for dexamethasone. Intolerance to steroid side-effects (e.g., insomnia, agitation, indigestion, acid reflux), or a pre-emptive reduction in the elderly, may be managed by a trial of dose reduction to 20 or 10mg depending on the stage of therapy, and possibly lower if stable disease at clinician discretion.

Should there be loss of disease control, steroid dose may be re-escalated.

INVESTIGATIONS (at the beginning of each cycle unless otherwise noted)
- FBC
- U&E, LFTs, Ca**
- TFTs – monitor for hypothyroidism.
- Ig’s, paraprotein, Freelite assay
  - Consider repeat BM aspirate and trephine after 3 cycles in non-secretory myeloma and check result prior to starting cycle 5.
- Blood pressure
- Perform blood glucose monitoring in patients with diabetes and those with signs of glucose intolerance.

EMETIC RISK
Low - moderate risk

EXTRAVASATION RISK:
Carfilzomib - Not a known vesicant. No data is available regarding skin corrosion/irritation.

CONCURRENT MEDICATIONS
- Cycle 1 - Allopurinol 300 mg OD for 7 days.
- Aciclovir 200 mg TDS (consider reducing to 200mg BD if CrCl <10ml/min)
- Fluconazole 50mg OD
- Apixaban 2.5mg BD (unless other risk factors or drug interactions present, always clinically assess - see thromboprophylaxis information in adverse effects section below)
- H2 antagonist - famotidine 40mg OD (unless established on PPI)
- Bone protection as per NSSG Bone Protection protocol MM.3
  - Note patients will need dental review prior to any bisphosphonate treatment.
- Consider prophylactic co-trimoxazole 960mg OD M/W/F, if heavily pre-treated or previous autograft. Reduction to 480mg can be considered if persistent low WCC/neutrophil counts.
- Patients deemed high risk of infection - Consider prophylactic levofloxacin 500mg od for 12 weeks (cycles 1 - 3). Adjust dose for renal function. Beware tendonitis risk.

As and when required:
- Onset of diarrhoea: Consider offering prophylactic loperamide PRN 4mg stat at first loose stool, then 2mg PRN every 4 hours up to maximum of 16mg in 24 hours.
• Suspicion of bile salt malabsorption with lenalidomide: Consider colestyramine sachets 4 g once daily initially (may need to increase to 2-3 times a day) or colesevelam 2g OD (may need to increase to 2-3 times a day) – unlicensed indication. Colestyramine and Colesevelam may delay or reduce the absorption on other drugs: Lenalidomide, Ixazomib and other medication should be taken 1h before or 6h after Colestyramine. Colesevelam should be taken 4 hours before or 4 hours after Lenalidomide, Ixazomib and other medication.
• Nausea/vomiting: Consider metoclopramide 10mg TDS or cyclizine 50mg TDS PRN.

INTERACTIONS

*Not exhaustive, for full details consult product literature/ reference texts.*

Patients on oral hypoglycaemics may require closer monitoring of blood sugar levels.

Carfilzomib is a P-glycoprotein (P-gp) substrate. Carfilzomib inhibits the efflux transport of digoxin, by 25%. Caution should be observed when carfilzomib is combined with substrates of P-gp (e.g., digoxin, colchicine).

Cases of QT prolongation, alongside cardiac toxicity has been reported with carfilzomib use. Evaluate necessity of any concurrent QT prolonging medicines against baseline ECG and level of risk, particularly if more than 3 agents involved long term.

Agents that may increase the risk of thrombosis, such as HRT should be used with caution in multiple myeloma patients receiving lenalidomide.

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

CARFILZOMIB

**MHRA alert: Risk of reactivation of hepatitis B virus**

Local guidelines can be consulted for prevention & management of reactivation. Note that the UK SACT Board has recently published a [position statement](#) on the subject which is encouraged for local adoption.

**Serious adverse reactions** that may occur during carfilzomib treatment include: cardiac failure, myocardial infarction, cardiac arrest, myocardial ischaemia, interstitial lung disease, pneumonitis, acute respiratory distress syndrome, acute respiratory failure, pulmonary hypertension, dyspnoea, hypertension including hypertensive crises, acute kidney injury, tumour lysis syndrome, infusion related reaction, gastrointestinal haemorrhage, intracranial haemorrhage, pulmonary haemorrhage, thrombocytopenia, hepatic failure, hepatitis B virus reactivation, PRES, thrombotic microangiopathy and TTP/HUS. In clinical studies with carfilzomib, cardiac toxicity and dyspnoea typically occurred early in the course of therapy.

**The most common adverse reactions** (occurring in > 20% of subjects) were: anaemia, fatigue, thrombocytopenia, nausea, diarrhoea, pyrexia, dyspnoea, respiratory tract infection, cough and neutropenia. Reference (carfilzomib SPC)

**Infusion reactions:** Symptoms may include fever, chills, arthralgia, myalgia, facial flushing, facial oedema, vomiting, weakness, shortness of breath, hypotension, syncope, chest tightness, or angina. These reactions can occur immediately following or up to 24 hours after administration. Dexamethasone should be administered prior to carfilzomib to reduce the incidence and severity of reactions.

**Cardiac** and **pulmonary** toxicities have been reported.
**Myeloma group**

**Others:** Tumour lysis syndrome (TLS), acute renal failure, pulmonary hypertension, thrombotic thrombocytopenic purpura (TTP)/haemolytic uremic syndrome (HUS), Posterior reversible encephalopathy syndrome (PRES)

**LENALIDOMIDE**

**Teratogenicity:** The manufacturer's pregnancy prevention programme must be observed for all male and female patients. Prescribing and dispensing of lenalidomide must be in line with the pregnancy prevention programme.

**Diarrhoea:** Diarrhea was reported in 42% of patients requiring use of antidiarrheal medication and supportive care. Bile salt malabsorption occurs in a small % of patients taking lenalidomide and in these cases can consider use of a bile acid sequestrant such as colestyramine.

**Venous thromboembolism (VTE):** There is an increased risk of thrombosis with lenalidomide. Unless the patient is thought to be at particularly low risk of thrombosis or high risk of bleeding, some form of VTE prophylaxis is recommended as follows:

1. Prophylactic low-molecular weight heparin OR
2. Prophylactic apixaban 2.5mg bd (check product specific information)

Aspirin can be appropriate for patients with no additional risk factors for thrombosis. It is not a preference for higher-risk patients with additional risk factors.

If VTE occurs, lenalidomide can be continued and the patient should be fully anticoagulated according to standard local guidelines.

**Myelosuppression**

**Drowsiness, somnolence and sedation:** Dose best taken at night time.

**Peripheral neuropathy:** Lenalidomide is structurally related to thalidomide, which is known to induce neuropathy. However, published data suggests that significant toxicity is uncommon. Patients should be advised to report pricking, numbness and paraesthesia.

**Dizziness and orthostatic hypotension**

**Other warnings:** Patients should be informed not to donate blood or semen during or within 8 weeks of stopping lenalidomide treatment.

**There is an MHRA alert on an increased risk of secondary malignancies in three large trials of lenalidomide treatment.** The MHRA recommend vigilance in reporting such events promptly. Quoted incidence is 3 to 4% per annum.

**Hypothyroidism** has been reported in patients on lenalidomide. Baseline assessment of thyroid function and ongoing monitoring is recommended.

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**TREATMENT RELATED MORTALITY**

<5%

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**REFERENCES**

2. Kryprolis Summary of Product Characteristics. eMC. Last updated April 2022
3. eMC UK Summary of Product Characteristics for Revlimid 25mg, Celgene, last updated November 2021

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<td>1.0</td>
<td>May 2018</td>
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<td>Faouzi Djebbari Haematology Pharmacist</td>
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Nursing Care Plan Carfilzomib Lenalidomide Dexamethasone

Indication: Relapsed Myeloma.
Frequency: 28 day cycles until disease progression or unacceptable toxicity.
Alopecia: No

CARFILZOMIB: Proteasome inhibitor
Administered as IV infusion on days 1, 2, 8, 9, 15, 16 for cycles 1-12, and days 1, 2, 15, 16 for cycles 13-18. Carfilzomib is infused over 10 minutes. Carfilzomib comes in 5% glucose bags but is compatible to be flushed with 0.9% normal saline.

On cycle 1 and cycle 2 day 1 patients will have pre and post hydration either side of the Carfilzomib infusion (500mls 0.9% normal saline over 1 hour pre and post).

After cycle 2 day 1 pre and post hydration (at least 1 litre) can be taken orally as long as the patient’s biochemistry profile is stable and there is no risk of TLS.

Classification of extravasation: Not vesicant (There is no data available regarding skin corrosion/irritation or extravasation).

Emetic risk: low.

Side effects: anaemia, thrombocytopenia, neutropenia, hypertension, peripheral oedema, upper respiratory tract infections, diarrhoea, fatigue, pyrexia, dyspnoea, cough, upper respiratory tract infection, pneumonia and hypokalaemia.

Dosing reaction: fever, chills, arthralgia, myalgia, facial flushing, facial oedema, vomiting, weakness, shortness of breath, hypotension, syncope, chest tightness, or angina. These reactions can occur immediately following or up to 24 hours after administration.

LENALIDOMIDE: Immunomodulator and angiogenesis inhibitor.
Administered orally on days 1-21.

Emetic risk: minimal.

Side effects: neutropenia, peripheral neuropathy, diarrhoea, constipation, flu like syndrome, infections, fatigue, muscle cramps, rash/itching, venous thromboembolism, bone marrow depression, drowsiness/sedation (recommended taking at night time).

DEXAMETHASONE: Corticosteroid tablets
Administered orally on days 1, 8, 15, 22. Taken with or after food preferably at breakfast. Carfilzomib is given at least 30 minutes pre Carfilzomib infusion.

Side effects: restlessness, insomnia, mood changes, gastritis, hyperglycaemia, increased appetite, fluid retention, weight gain, immunosuppression.

Regime Specific Considerations:
Baseline lying and standing blood pressure should be recorded prior to administration of cycle #1. Ensure BP well controlled prior to starting therapy and throughout. Baseline ECG required.

Patients should attempt to drink 3 litres of water a day.

Bloods are required at the start of each cycle. Patients with unstable blood counts may require more frequent monitoring. Random glucose monitoring required due to dexamethasone (unless patient is diabetic, then tighter blood glucose control is required).

Pregnancy test for pre-menopausal women under the age of 55 before the start of each cycle (due to the teratogenic effect of lenalidomide).