Brentuximab Vedotin – Systemic Anaplastic Lymphoma or Relapsed / Refractory CD30+ Hodgkin Lymphoma

DRUG ADMINISTRATION SCHEDULE

<table>
<thead>
<tr>
<th>Day</th>
<th>Drug</th>
<th>Daily Dose</th>
<th>Route</th>
<th>Diluent and rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1</td>
<td>Brentuximab Vedotin</td>
<td>1.8mg/kg</td>
<td>Intravenous</td>
<td>0.9% Sodium Chloride 100-250ml (see below) over 30mins</td>
</tr>
</tbody>
</table>

NUMBER OF DAYS PER CYCLE

21 days until disease progression (maximum 16 cycles) or unacceptable toxicity. Patients who achieve stable disease or better should receive a minimum of 8 cycles, and up to a maximum of 16 cycles.

Approved for use on the National Cancer Drug Fund List for patients who meet the following criteria:

1. Application made by and first cycle of systemic anti-cancer therapy to be prescribed by a consultant specialist specifically trained and accredited in the use of systemic anti-cancer therapy
2. Either:
   a. Relapsed or refractory systemic anaplastic large cell lymphoma, as a bridge to transplant where no other salvage treatment is available
   b. Relapsed or refractory CD30+ Hodgkin Lymphoma, following at least two prior therapies when ASCT or multi-agent chemotherapy is not a treatment option

No treatment breaks of more than 7 weeks are allowed. Should treatment breaks be required, then an Individual Funding Request must be submitted as per CDF processes.

PREMEDICATION

None required, unless patient has had a previous reaction to brentuximab.

RECOMMENDED TAKE HOME MEDICATION

Allopurinol 300mg once daily, usually for the first 21 days, ideally starting the night before treatment.
Co-trimoxazole 960mg three times a week as PCP prophylaxis.
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INVESTIGATIONS / MONITORING REQUIRED
FBC, LFTs & U&Es prior to each cycle.

ASSESSMENT OF RESPONSE
Assessed radiologically after 4th cycle

ELIGIABILITY CRITERIA
As stated above

REVIEW BY CLINICIAN
Before each cycle as appropriate

NURSE / PHARMACIST LED REVIEW
On cycles where not seen by clinician

ADMINISTRATION NOTES
- Brentuximab vedotin is a cytotoxic conjugated to a mono-clonal antibody. It should be handled as a cytotoxic agent as well as a mono-clonal antibody.
- Brentuximab vedotin will normally be mixed in 250ml Sodium Chloride 0.9%, however for doses ≤ 100mg, 100ml Sodium Chloride 0.9% is used.
- If patient suffers an infusion related reaction, the infusion should be interrupted and appropriate management given. The infusion may be restarted at a slower rate after symptom resolution
- For these patients, all subsequent doses of brentuximab should be pre-medicated with paracetamol 1000mg orally, chlorphenamine 10mg IV and hydrocortisone 100mg.
- All patients must receive irradiated blood products for all future transfusions – Inform patient and blood bank.

No treatment breaks of more than 7 weeks from the start of the previous cycle are allowed. Should treatment breaks be required, then an Individual Funding Request must be submitted as per CDF processes.

EXTRAVASATION
Brentuximab vedotin is cytotoxic and should be treated as a Non-Vesicant in the event of extravasation.
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TOXICITIES
- Myelosuppression
- Risk of infections
- Peripheral neuropathy
- Infusion-related reactions
- Alopecia
- Pruritis
- Myalgia
- Diarrhoea
- Progressive multifocal leukoencephalopathy (rare but potentially fatal)
- Ovarian failure
- Infertility

DOSE MODIFICATION

Haematological Toxicity:
- If neutrophil count < 1.0 x 10⁹, delay treatment until neutrophils have recovered to ≥ 1.0 x 10⁹/l. Then continue treatment at the same dose, and consider GCSF support with further cycles.
- PLT should normally be > 100 x 10⁹ prior to each cycle of treatment.

Neuropathy:

<table>
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<tr>
<th>Severity of peripheral sensory or motor neuropathy</th>
<th>Brentuximab</th>
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<tr>
<td>Grade 1 (paraesthesia or loss of reflexes with no loss of function)</td>
<td>Continue with same dose</td>
</tr>
<tr>
<td>Grade 2 (interfering with function but not ADL) or Grade 3 (interfering with ADL)</td>
<td>Withhold dose until toxicity resolves to ≤ Grade 1, then re-start treatment at 1.2mg/kg every 3 weeks</td>
</tr>
<tr>
<td>Grade 4 (sensory neuropathy which is disabling or motor neuropathy which is life threatening or leads to paralysis)</td>
<td>Discontinue Brentuximab</td>
</tr>
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Renal impairment:
- Pharmacokinetic data shows that clearance of the active metabolite was reduced about 2-fold in patients with CrCl < 30ml/min. Use with extra caution in these patients, and monitor the patients carefully.

Hepatic impairment:
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There is limited data in patients with hepatic impairment, but the liver is a major route of elimination of the active metabolite

**TREATMENT LOCATION**

Cancer Unit where there is a Haematologist with a specialism haemato-oncology patients as appropriate.

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<td>Document No:</td>
<td>NCDF</td>
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</table>
| Author:         | Mandy Nagra  
NHS England CNTW Area | Current Version: 1.0 |
| Reviewed by:    | Calum Polwart  
Area Team Cancer Pharmacist |
| Approved by:    | Anne Lennard, Consultant Haematologist  
Date Approved: 03 April 2014 |
| Due for Review: | March 2016 |
| Summary of Changes | **|