BRENTUXIMAB VEDOTIN

Brentuximab vedotin is a CD30-directed monoclonal antibody-drug conjugate, with the antibody linked to an antimicrotubule cytotoxic agent

1. An option for treating CD30+ve Hodgkin lymphoma if they have relapsed or refractory disease after autologous stem cell transplant (NICE 2017)
2. An option for relapsed or refractory CD30+ve Hodgkin lymphoma after at least 2 previous therapies and the patient cannot have autologous stem cell transplant or multi-agent chemotherapy
3. Relapsed or refractory systemic anaplastic large cell lymphoma

Blueteq registration is required before treatment may start

Drug/Dose: Brentuximab vedotin 1.8mg/kg (max 180mg) IV Day 1

i.e. if a patient's weight is > 100kg, the dose calculation should use 100kg.

Other Drugs: Allopurinol 300mg po daily, ideally starting 24 hours before treatment - review after 3 weeks.
Co-trimoxazole 480mg od continuous, as PCP prophylaxis

Administration: Doses > 100mg in 250ml sodium chloride 0.9% over 30 minutes
Doses ≤ 100mg in 100ml sodium chloride 0.9% over 30 minutes

Blood pressure, pulse, temperature and O_2 saturation must be measured and recorded at baseline, at end of infusion, and 30 minutes post infusion end.

If a patient suffers an infusion-related reaction, the infusion should be interrupted and appropriate management given. The infusion may be re-started at a slower rate after symptom resolution.
For these patients, all subsequent doses of brentuximab should be pre-medicated with paracetamol 1000mg po, chlorphenamine 10mg IV and hydrocortisone 100mg.

Frequency: Every 3 weeks, to progression or unacceptable toxicity, and with added criteria below:

Anaplastic lymphoma:	Patients who achieve stable disease or better should receive a minimum of 8 cycles, and up to a maximum of 16 cycles.
Hodgkin disease after ASCT:	Maximum 16 cycles. Brentuximab must be discontinued after 4 cycles if CT or PET-CT scans demonstrate a response status of less than a PR or CR.
Hodgkin disease after 2 prior therapies & not suitable for ASCT:	Maximum **10** (ten) cycles. Brentuximab must be discontinued after 4 cycles if CT or PET-CT scans demonstrate a response status of less than a PR or CR.
Re-challenge after ASCT, and used as bridge to allogeneic transplant or DLI:	Maximum 16 cycles. Brentuximab must be discontinued after 4 cycles if CT or PET-CT scans demonstrate a response status of less than a PR or CR.

Reason for Update: indications and Frequency section updated	Approved by Chair of Alliance TSSG: Dr A Laurie
Version: 4	Date: 4.9.17
Supersedes: Version 3	Review date: September 2019
Prepared by: S Taylor	Checked by: C Tucker

Main Toxicities: myelosuppression; risk of infections; peripheral neuropathy; infusion-related reactions; alopecia; pruritis; myalgia; diarrhoea; progressive multifocal leukoencephalopathy (rare but potentially fatal); ovarian failure; infertility

Anti-emetics: mildly emetogenic

Extravasation: non-vesicant

Regular Investigations:

FBC	Day 1
U&Es	Day 1
LFTs	Day 1

Comments: All patients must receive irradiated blood products for all future transfusions - inform patient and blood bank.

Women of childbearing potential should use two methods of effective contraception during treatment and until 6 months after treatment.

Dose Modifications

Haematological Toxicity: If neutrophil count < 1.0 x 10^9/l, delay treatment until neutrophils have recovered to ≥ 1.0 x 10^9/l. Then continue treatment at the same dose, and consider G-CSF support with further cycles.

Neuropathy:

Severity of peripheral sensory or motor neuropathy	Brentuximab
Grade 1 (paraesthesia or loss of reflexes with no loss of function)	Continue with same dose
Grade 2 (interfering with function but not ADL) or Grade 3 (interfering with ADL)	Withhold dose until toxicity resolves to ≤ Grade 1, then re-start treatment at 1.2mg/kg every 3 weeks
Grade 4 (sensory neuropathy which is disabling or motor neuropathy which is life-threatening or leads to paralysis)	Discontinue brentuximab

Renal Impairment: If CrCl < 30ml/min, the recommended starting dose is 1.2 mg/kg every 3 weeks.
Patients with renal impairment should be closely monitored for adverse events

Hepatic Impairment: There is limited data in patients with hepatic impairment, but the liver is a major route of elimination of the active metabolite.
The recommended starting dose in patients with mild, moderate or severe hepatic impairment is 1.2 mg/kg every 3 weeks.
Patients with hepatic impairment should be closely monitored for adverse events.

Patient Information: Brentuximab leaflet available at cancerresearchuk.org

References: Younes, A et al; JCO 2012; 30 (18): 2183 – 2189
Pro, B et al; JCO 2012; 30 (18): 2190 - 2196