Ofatumumab

Indication

Relapsed Chronic Lymphocytic Leukaemia (CLL) 2nd or 3rd line, for patients refractory to fludarabine and/or alemtuzumab or where these are contraindicated.

(Funding via CDF)

ICD-10 codes

Codes with a prefix C91.1

Regimen details

Day	Drug	Dose	Route
1 (first dose)	Ofatumumab	300mg	IV
8 and subsequent doses	Ofatumumab	2000mg	IV

Cycle frequency :

Weekly for 8 weeks followed by a 4-5 week break. Then 4 weekly for 4 doses.

Number of cycles:

Maximum of 12 doses (see above)

Administration:

Ofatumumab is administered in 1000mL sodium chloride 0.9%, via a PVC-free giving set with a 0.2 micron in-line filter.

Infusions 1 and 2:

Initiate the infusion at a rate of 12mL/hour for 30 minutes. Then increase the infusion rate to 25mL/hour for 30 minutes. If this is tolerated double the infusion rate every 30 minutes to a maximum of 200mL/hour (see table below).

Infusion time (minutes)	Rate (mL/hr)
0-30	12
31-60	25
61-90	50
91-120	100
121+	200

Monitor patient's vital signs at baseline and then every 15 minutes (including before each increase in infusion rate) until 1 hour after the end of infusion.

Infusions 3 – 12:

If the 2nd infusion was completed (as above) without a severe reaction, from infusion 3 onwards initiate the infusion at a rate of 25mL/hour for 30 minutes. Then double the infusion rate every 30 minutes to a maximum of 400mL/hour (see table below).

Infusion time (minutes)	**Rate** (mL/hr)
0-30	25
31-60	50
61-90	100
91-120	200
121+	400

Monitor patient's vital signs at baseline and then every 30 minutes (before each increase in infusion rate) until end of infusion.

In the event of a mild or moderate infusion-related reaction, the infusion should be interrupted and, when the patient is stable, re-started at half the infusion rate at the time of interruption. The infusion rate can then be increased according to patient tolerance, but should not exceed doubling the rate every 30 minutes. (If the reaction occurred when the infusion rate was 12mL/hr, then re-start at 12mL/hr).

In the event of a severe infusion-related reaction, the infusion should be interrupted and, when the patient is stable, re-started at 12mL/hour. The infusion rate can then be increased according to patient tolerance, but not to exceed doubling the rate every 30 minutes. If in doubt, check with the consultant.

Pre-medication :

30-120 minutes prior to infusion:

- Paracetamol PO 1g
- Chlorphenamine 10mg iv
- Dexamethasone 8-16mg iv

If the 1st and 2nd infusions are administered without a serious reaction, the dexamethasone dose may be reduced for the remaining weekly doses.
The dexamethasone dose must be increased back to 16mg IV for the first 4-weekly infusion (i.e. the 9th dose). If the 9th dose is administered without a serious reaction, the dexamethasone dose may be reduced to 8mg IV for the remaining 4-weekly doses.

Emetogenicity:

This regimen is mildly emetogenic – routine anti emetics are not usually required.

Additional supportive medication:

Allopurinol 300mg OD (or 100mg OD if creatinine clearance <20mL/min) for the first 28 days.
PCP prophylaxis according to local policy, continue during treatment and for up to 12 months after.

Extravasation:

Ofatumumab is neutral (Group 1)

Investigations – pre first cycle

Investigation	**Validity period** (or as per local policy)
FBC	14 days
U+E (including creatinine)	14 days
LFTs	14 days

Hepatitis B and C and HIV screening is also required.

Investigations – pre subsequent cycles

Investigation	**Validity period** (or as per local policy)
FBC	Weekly on day of treatment, then as clinically indicated
U+E (including creatinine)	Monthly, or as clinically indicated
LFTs	Monthly, or as clinically indicated

Standard limits for administration to go ahead

If blood results not within range, authorisation to administer **must** be given by prescriber/ consultant

Investigation	**Limit**
Neutrophils	≥ 0.5 x 10^9/L
Platelets	≥ 25 x 10^9/L
CrCl	≥ 30mL/min

Dose modifications

- **Haematological toxicity**

If neutrophils < 0.5 x 10^9/L and/or platelets < 25 x 10^9/L, delay ofatumumab until counts have recovered, then continue with full dose.

- **Renal impairment**

There is no data for use in patients with CrCl <30mL/min - use with caution (consultant decision).

- **Hepatic impairment**

There are no studies of ofatumumab in patients with hepatic impairment, however, patients with hepatic impairment are unlikely to require dose modification.

- **Other toxicities**

For management of infusion related reactions, see above.

Adverse effects - for full details consult product literature/ reference texts

- **Serious side effects**

Infusion- related reactions
Myelosuppression
Hepatitis B reactivation
Progressive Multi focal Leukoencephalopathy (PML)
Tumour lysis syndrome
Cardiac arrhythmias
Bowel obstruction

- **Frequently occurring side effects**

Infusion - related reactions
Myelosuppression
Nausea and vomiting
Diarrhoea

- **Other side effects**

Rash
Back pain

Significant drug interactions – for full details consult product literature/ reference texts

No known clinically significant interactions with other medicinal products.

Additional comments

References:

- Summary of Product Characteristics Ofatumumab (GSK) accessed via www.medicines.org.uk (18 Feb 2015)
- NHS England Cancer Drug Fund List. Accessed 18 Feb 2015 via www.england.nhs.uk
- RIAltO clinical trial protocol
- Coiffier, B., et al. A multicentre, phase II trial of ofatumumab monotherapy in relapsed/progressive diffuse large B-cell lymphoma. Br. J. Haematol. 2013; 163(3) 334-42.

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Date: February 2015