# Carmustine/Etoposide/Cytarabine/Melphalan/Alemtuzumab RIC-SIB/MUD

## INDICATIONS FOR USE:

| INDICATION | ICD10 | Regimen Code | Reimbursement Status |
|---|---|---|---|
| Reduced intensity conditioning for sibling or matched unrelated allogeneic stem cell transplantation in Hodgkins and Non-Hodgkins Lymphoma | C81<br>C85 | 00638a | Hospital |

## TREATMENT:

Conditioning chemotherapy is administered over **6 days**. Stem cells are infused on **day 0**.

Facilities to treat anaphylaxis MUST be present when the conditioning therapy and stem cells are administered.

| Day (time) | Drug | Dose | Route | Diluent & Rate |
|---|---|---|---|---|
| -6 | Carmustine[a,b,c] | 300mg/m$^2$ | IV infusion | 1000ml glucose 5% over 1 hour |
| -5,-4,-3,-2 **(AM dose)** | Cytarabine | 200mg/m$^2$ | IV infusion | 100ml sodium chloride 0.9% over 30 mins |
| -5,-4,-3,-2 | Etoposide | 100mg/m$^2$ | IV infusion | 1000ml sodium chloride 0.9% over 2 hours |
| -5,-4,-3,-2 **(Commence immediately after first etoposide dose has been administered)** | Etoposide | 100mg/m$^2$ | IV infusion | 1000ml sodium chloride 0.9% over 2 hours |
| -5 | Alemtuzumab | 10mg | IV infusion | 100ml sodium chloride 0.9% over (see below)[d] |
| -4,-3,-2,-1 | Alemtuzumab | 10mg | IV infusion | 100ml sodium chloride 0.9% over 4 hours[e] |
| -5,-4,-3,-2 **(PM dose - 12 hours post start of AM dose)** | Cytarabine | 200mg/m$^2$ | IV infusion | 100ml sodium chloride 0.9% over 30 mins |
| -1 | Melphalan[f,g] | 140mg/m$^2$ | IV push | Into side arm of fast flowing sodium chloride 0.9% infusion over 30 mins |
| 0 | Stem Cell Infusion | | | |
| Start +6 **(until ANC > 1.0x10$^9$/L for two consecutive days)** | Filgrastim (GCSF) | 300 mcg | S/C | n/a |

**Dose rounding**
Carmustine doses to the nearest 3.3mg
Etoposide to the nearest 4mg if ≤200mg and nearest 20mg if >200mg
Cytarabine to the nearest 20mg
Melphalan to the nearest 5mg

[a]If carmustine is unavailable, lomustine 200mg/m$^2$ PO day -6 can be substituted. Lomustine is rounded to the nearest 40mg capsule and is contraindicated in patients with coeliac disease/wheat allergy

[b]When reconstituted carmustine has a very short expiry time. **(Refer to local policy for guidance on stability and shelf life to co-ordinate administration with pharmacy compounding)**

[c]Carmustine intravenous solution is unstable in polyvinyl chloride container. The carmustine solution should be administered from PVC free containers only.

[d]10ml/hr for first hour, 20ml/hr for second and third hours, 30ml/hr for subsequent hours

[e]4 hour infusion applicable if tolerated on day -5

[f]When reconstituted melphalan has a very short expiry time. **(Refer to local policy for guidance on stability and shelf life to co-ordinate administration with pharmacy compounding)**



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## ELIGIBILITY:

- Indications as above
- Medical assessment as per SJH BMT assessment form

## EXCLUSIONS:

- Hypersensitivity to carmustine, etoposide, cytarabine, melphalan, alemtuzumab or any of the excipients
- Pregnancy and lactation

## PRESCRIPTIVE AUTHORITY:

- The treatment plan must be initiated by a Haematology Consultant working in the area of stem cell transplantation in a unit suitable for carrying out this treatment.

## TESTS:

- Baseline and regular tests in accordance with SJH Haematopoietic Stem Cell Transplant work-up protocols

**Disease monitoring:**
Disease monitoring should be in line with the patient's treatment plan and any other test/s as directed by the supervising Consultant.

## DOSE MODIFICATIONS:

- Any dose modification should be discussed with a Consultant.
- **Chemotherapy dosing in obese adult patients:** For patients with a BMI > 30kg/m$^2$ please refer to 'Chemotherapy Dosing in Obese Adult Stem Cell Transplant Recipients – Guidelines' for guidance on individual drug dosing as per SJH policy available on the SJH intranet.
- **Renal and Hepatic Impairment:**
    - Dose modifications are generally not undertaken in conditioning regimens.
    - Discuss with the consultant if the creatinine clearance is < 50 ml/min or if abnormal hepatic function.
    - Consult the following resources to inform any renal or hepatic dose modification discussions:
        - Summary of product characteristics (SPC) available at http://www.hpra.ie
        - Krens et al Lancet Oncol 2019;20(4) e200-e207 "Dose Recommendations for anticancer drugs in patients with renal or hepatic impairment" available at https://pubmed.ncbi.nlm.nih.gov/30942181/
        - UCHL renal impairment guidelines and hepatic impairment guidelines available on SJH intranet



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## SUPPORTIVE CARE:

### Antiemetics:

**Table 1: Recommended SJH regimen specific anti-emetics**

| Prevention of acute nausea and vomiting | | | Prevention of delayed nausea and vomiting | | | Comment |
|---|---|---|---|---|---|---|
| **Drug** | **Dose** | **Admin Day** | **Drug** | **Dose** | **Admin Day** | |
| Dexamethasone | 6mg PO | -1 | Dexamethasone | 4mg PO | 0, +1, +2 | Dexamethasone with melphalan only |
| Ondansetron | 8mg PO/IV[a] TDS | -6 to -1 | Aprepitant | 80mg PO | 0, +1 | |
| Aprepitant | 125mg PO | -1 | | | | |
| [a]May be administered orally | | | | | | |

### Alemtuzumab Pre-medication:

Prior to alemtuzumab therapy (i.e. 60 minutes pre-therapy), the following should be administered:

- Paracetamol 1g PO
- Chlorphenamine 10mg IV
- Hydrocortisone 100mg IV

### Other pre-medications:

- **Melphalan hydration:** Sodium chloride 0.9% must be given at a rate of 125ml/m$^2$/hour for two hours pre melphalan and for 6 hours post melphalan

### Other Supportive Care:

**Table 2: Other Supportive Medication**

| | | |
|---|---|---|
| **GvHD prophylaxis**<br>Refer to signed off BMT assessment form for confirmed **choice and target level** of immunosuppression | **Ciclosporin**<br>• Ciclosporin 5mg/kg once daily IV over 6 hours from day -1<br>• The equivalent oral dose is: (Total IV dose x 0.67) twice daily PO<br>• Target levels: 100-150micrograms/L | **Tacrolimus**<br>• 0.03mg/kg once daily IV over 22 hours, starting from day -1<br>• The equivalent oral dose is: (Total IV dose) twice daily PO<br>• Target levels: 5-10 nanograms/ml |
| **GvHD and VOD prophylaxis** | • Ursodeoxycholic acid 250mg TDS PO<br>• Continue until day +90 | |



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|---|---|
| **HSV prophylaxis** | All patients should receive the following until CD4 count >200/microlitre:<br>• Valaciclovir 500mg once daily PO<br>**or**<br>• Aciclovir 250mg TDS IV (if oral route not available or ANC < $0.5X10^9$/L)<br><br>Patients with an active herpes infection should receive the following:<br>• Valaciclovir 1g TDS PO<br>**or**<br>• Aciclovir 10mg/kg TDS IV (if oral route not available) |
| **CMV prophylaxis**<br>Prescribe for all CMV seropositive recipients | **Patients receiving CMV prophylaxis with letermovir also require HSV prophylaxis above**<br>• Letermovir 240mg once daily PO/IV, as appropriate, starting Day +1 if patient is receiving ciclosporin immunosuppression<br>• Letermovir 480mg once daily PO/IV, as appropriate, starting Day +1 if patient is receiving tacrolimus immunosuppression<br>• Letermovir via the oral route is first line.<br>• Letermovir IV at the same oral dose should be prescribed only where the patient cannot tolerate oral or where there are concerns around absorption.<br>• CMV prophylaxis is usually continued until day +100<br><br>Patients should bring their oral letermovir supply with them on admission. High tech prescription will have been provided to patient at their counselling appointment pre-admission. Liaise with transplant pharmacist if any supply issues arise.<br><br>When ANC>1.0 x $10^9$/L, pre-emptive monitoring (9mls in EDTA [purple tube] (Tuesday and Fridays) should be carried out for CMV reactivation/infection in *all* patients. |
| **Antifungal prophylaxis**<br>Refer to signed off BMT assessment form for confirmed choice of antifungal prophylaxis | When ANC <$0.5x10^9$/L or if patient on high dose steroids:<br>• Liposomal amphotericin 1mg/kg once daily IV Mon/Wed/Fri<br>**or**<br>• Caspofungin 70mg once daily IV Mon/Wed/Fri<br><br>If at higher risk due to prior possible/probable fungal infection:<br>• Liposomal amphotericin 1mg/kg once daily IV<br>**or**<br>• Caspofungin 70mg once daily IV if >80kg<br>**or**<br>• Caspofungin 70mg once daily IV on day 1 of treatment followed by 50mg once daily IV thereafter if <80kg |



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|---|---|
| **PJP prophylaxis** | 1st line therapy:<br>• Co-trimoxazole 960mg BD Mon/Wed/Fri PO<br>• Commence only on engraftment when ANC > 1.0x10$^9$/L if appropriate<br><br>2nd line therapy (if allergic to co-trimoxazole or contraindicated):<br>*PJP Prophylaxis and T. gondii IgG NEGATIVE*:<br>• Pentamidine 300mg nebule and salbutamol 2.5mg nebule pre-pentamidine, every 4 weeks<br>**plus**<br>• Phenoxymethylpenicillin 333mg BD daily PO<br><br>Continue the phenoxymethylpenicillin until patients have been revaccinated and have adequate pneumococcal/Haemophilus titres<br><br>*PJP Prophylaxis and T gondii IgG POSITIVE:*<br>• Atovaquone 750mg BD PO plus<br>• Pyrimethamine 25mg once daily PO plus<br>• Folinic acid 15mg once daily PO plus<br>• Phenoxymethylpenicillin 333mg BD daily PO<br><br>Continue the phenoxymethylpenicillin until patients have been revaccinated and have adequate pneumococcal/Haemophilus titres<br><br>Please note: If a patient is to be discharged on atovaquone, pyrimethamine or folinic acid, please contact pharmacy in advance to arrange supply and funding through a community drugs scheme |
| **Mouthcare** | Mucositis WHO grade < 2:<br>• Sodium chloride 0.9% 10ml QDS mouthwash<br>• Nystatin 1ml QDS PO (use 15 minutes after sodium chloride 0.9% mouthwash)<br><br>Mucositis WHO grade ≥ 2:<br>• Chlorhexidine digluconate 0.12% (Kin®mouthwash) 10mls QDS mouthwash<br>• Nystatin 1ml QDS PO (use 15 minutes after Kin® mouthwash) |
| **Gastroprotection** | • Lansoprazole 30mg / omeprazole 40mg once daily PO<br>**or**<br>• Esomeprazole 40mg once daily IV (if oral route not available) |
| **Folate supplementation** | • Folinic acid 15mg once daily IV is commenced from Day+2 onwards<br>• Switch to folic acid 5mg once daily PO when oral route is available |
| **Vitamin K supplementation** | Beginning on day +2 post stem cell transplant<br>• Vitamin K (phytomenadione) 10mg once weekly IV |
| **Prevention of vaginal bleeding** | If required for menstruating female patients until platelets > 50 x10$^9$/L<br>• Norethisterone 5mg TDS PO if >55Kg<br>• Norethisterone 5mg BD PO if <55kg |
| **Tumour Lysis syndrome** | Consider allopurinol in active disease pre transplant<br>• Allopurinol 300mg once daily PO for 5-7 days and review |



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| | |
|---|---|
| **Hepatitis B prophylaxis/treatment** | A virology screen is completed as part of transplant workup. Hepatitis B prophylaxis or treatment may be initiated in consultation with a Virology Consultant or Hepatology Consultant if required.<br><br>Options may include:<br>• Lamivudine 100mg once daily PO<br>**or**<br>• Entecavir 500mcg once daily PO |
| **Prevention of constipation** | Consider laxatives if appropriate e.g.<br>• Senna two tablets (15mg) nocte PO while on ondansetron |
| **Antibiotic standing order** | Antibiotic standing order should be prescribed for neutropenic sepsis/neutropenic fever based on previous microbiology and renal function<br>• Piptazobactam 4.5g QDS IV<br>**plus**<br>• Amikacin* 15mg/kg once daily IV<br><br>*Ciprofloxacin 400mg BD IV may be considered instead of amikacin in cases of renal impairment<br><br>Refer to Antimicrobial Guidelines in the Prescriber's Capsule for antibiotic choice where a patient is allergic to any of the above |
| **Magnesium and potassium standing order** | Magnesium and potassium standing orders should be prescribed for all transplant patients in accordance with stem cell unit practice as indicated on EPMAR |
| **VTE prophylaxis** | Consider VTE prophylaxis in accordance with SJH policy |
| **Bone Health** | Consider calcium and vitamin D supplementation prior to discharge for patients who are on high dose steroids. Other medications for maintenance of bone health may need to be considered as appropriate.<br>• Calcium carbonate and colecalciferol (Caltrate® 600mg/400unit)<br>One tablet BD |

## ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS:

- Please refer to the relevant Summary of Product Characteristics and SJH Stem Cell Transplant Programme PPGs for full details.

## DRUG INTERACTIONS:

- The relevant Summary of Product Characteristics and current drug interaction databases should be consulted.



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| Version | Date | Amendment | Approved By |
|---|---|---|---|
| 1 | 06/08/2021 | | SJH Stem Cell Transplant Group |

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.



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