Allogeneic BMT Supportive Care guidelines

This guide should be used in conjunction with the Standard Operating Procedures (SOPs), the BMT Febrile Neutropenia Guidelines and BMT Antifungal Guidelines and the patient's individualised protocol. This guide includes prescribing information on:

1. Prophylactic Anti-Infectives

1.1 Antibiotic Prophylaxis

- **Ciprofloxacin**

  For **allogeneic transplants**, start ciprofloxacin prophylaxis once neutrophils <0.5 x10^9/L. Stop when iv antibiotics prescribed or when neutrophils >0.5x10^9/L for 2 consecutive days. Once patient has engrafted, commence penicillin prophylaxis (see below). **Discuss any patient who has a past history of C. diff infection with their consultant before prescribing ciprofloxacin prophylaxis.**

- **Penicillin V** prophylaxis to start once patient has engrafted and intravenous antibiotics stopped. Use erythromycin in penicillin allergic patients. Pneumococcal prophylaxis to continue life long.

Drug & Route	Prophylactic Dose	Notes
Ciprofloxacin PO[1]	**1 month-18 yrs;** 7.5mg/kg (max 500mg) BD	Tablets 250mg, liquid available. Omit if unable to tolerate oral medication
Penicillin V PO	**<1yr;** 62.5mg BD **1-5 yrs;** 125mg BD **5yrs+;** 250mg BD	
Erythromycin PO	**1 month-2yrs;** 125mg twice daily **2-8yrs;** 250mg twice daily **>8yrs;** 250-500mg twice daily	Asplenic adult patients to receive 500mg twice daily

1.2 PCP Prophylaxis

PCP prophylaxis should be commenced at day +28 post transplant and continue for 12 months or longer if patient on immunosuppression or until CD4 count reaches 300.

- **Co-trimoxazole** (standard prophylaxis) to commence post-transplant D+28, when platelet count is >50x10^9/L and neutrophils >1x10^9/L.
- **Folic acid** start D+28, when patient on co-trimoxazole, give once a week on Mondays for paediatric patients or once a week on Saturdays for adult patients.

- **Pentamidine nebules** for patients intolerant of co-trimoxazole. Consider switching back to co-trimoxazole if blood counts have recovered.

- **Atovaquone** Consider only if co-trimoxazole or nebulised pentamidine inappropriate. Discuss with patient's consultant.

- **Dapsone** Consider only if co-trimoxazole or nebulised pentamidine inappropriate as dapsone associated with risk of haemolysis. Discuss with patient's consultant.

Drug & Route	Prophylactic Dose	Notes
Co-trimoxazole PO[2,3]	**1 month -18 yrs;** <0.5m^2; 24mg/kg BD Sat & Sun 0.5-0.75m^2; 240mg BD Sat & Sun 0.76-1m^2; 360mg BD Sat & Sun >1m^2; 480mg BD Sat & Sun **Adults;** 480mg BD on Monday, Wednesday, Friday ONLY	
Folic acid PO	**2-18yrs;** 5mg weekly on Friday **Adults;** 5mg weekly on Saturday	For patients on co-trimoxazole
Pentamidine nebulised	**From 5 yrs;** 300mg every 4 weeks	
Atovaquone PO[2,4]	**1 month -18 yrs;** 30mg/kg (max 1500mg) OD **Adults;** 1500mg OD	See notes above. Take with high fat food to aid absorption
Dapsone PO[2,5]	**1 month -18 yrs;** 2mg/kg (max 100mg) OD **Adults;** 100mg OD	See notes above

1.3 Antifungal Prophylaxis

Consult BMT adult antifungal guidelines and BMT paediatric antifungal guidelines

1.4 Antiviral Prophylaxis

- **Oral aciclovir** from day –4 until six months post-transplant. Switch to **intravenous aciclovir** prophylaxis if oral medication not tolerated. Stop aciclovir prophylaxis whilst patient receiving valganciclovir, ganciclovir or foscarnet.

- Immunoglobulin levels to be checked at work up for both adult and paediatric patients. Adult patients with hypogammaglobulinaemia to receive **intravenous human immunoglobulin (Octagam)** 400mg/kg/dose at day-1 and then every four weeks until 6 months post-transplant. Consult Octagam SOP for further details.

Drug & Route	Prophylactic Dose	Notes
Aciclovir PO[1]	**< 1yr;** 200mg BD **1-12yrs;** 400mg BD **>12yrs;** 400mg TDS	HSV prophylaxis. Consult BNF for dosing in varicella zoster prophylaxis
Aciclovir IV	**3 months -12yrs;** 250mg/m^2 TDS **>12yrs;** 5mg/kg TDS	Use ideal bodyweight for obese patients. See drug labels for treatment dose.

Consult relevant SOPs for ganciclovir and foscarnet for the treatment of CMV infection and the SOP for cidofovir for the treatment of CMV/adenoviral infection.

2. Graft versus Host Disease (GvHD) Prophylaxis

- **Ciclosporin** from day-1 pre-transplant intravenously (Sandimmun), converting to oral ciclosporin (Neoral) when able to tolerate oral medication. Refer to ciclosporin SOP and individualised patient protocol for dosing and therapeutic levels. **NB** Start date and required levels of ciclosporin may differ from SOP for patients on clinical trials. Refer to the trial protocol for these patients.

- **Tacrolimus** may be used second line as graft versus host disease prophylaxis although of limited value in ciclosporin intolerance due to similar adverse effect profile. Refer to tacrolimus SOP for dosing and therapeutic levels.

- **Mycophenolate Mofetil** (MMF) may be used in addition to ciclosporin or used as monotherapy post-transplant in ciclosporin intolerance. **NB** Clinical trials may use alternative dose and/or frequency to those stated below.

Drug & Route	Dose	Notes
Mycophenolate Mofetil (MMF) IV/PO[1]	**1 month-18yrs;** 12.5mg/kg BD or 600mg/m^2 BD (max 1 gram BD) **Adults;** 1 gram BD	IV and oral doses equivalent. Tablets/capsules 250mg and 500mg. Liquid available. Use cytotoxic precautions when preparing.

- **Short course methotrexate** prescribed from day +1 post-transplant for full intensity transplants with fully matched related donors where an antibody has not been used as part of the conditioning regimen. May also be used as graft versus host disease prophylaxis for mis-matched unrelated donor transplants, or for myelofibrosis patients receiving Flu/Bu/ATG in addition to an antibody. Refer to low dose methotrexate SOP

- **Alemtuzumab and rabbit anti-thymocyte globulin (ATG)** Refer to conditioning protocols plus alemtuzumab SOP or ATG SOP as appropriate.

3. Veno-Occlusive Disease Treatment/Prophylaxis

- **Ursodeoxycholic acid** prescribed as VOD prophylaxis from admission until day+30 or discharge (whichever is earlier). Indicated in full intensity transplants and in reduced intensity transplants associated with an increased risk of hepatic toxicity (busulfan containing regimen or previous history of abnormal liver function tests).

- **Defibrotide** is indicated in the treatment of VOD. Refer to nursing SOP for VOD for monitoring and nursing care. Note funding approval required.

Drug & Route	Dose	Notes
Ursodeoxycholic acid PO[1]	**From 1 month;** 10mg/kg/day in one or two divided doses	Capsules/tablets 150mg and 250mg. Liquid available
Defibrotide IV[6]	**1 month-18yrs;** 6.25mg/kg-10mg/kg QDS	CIVAS available. Vials 200mg

4. Tumour lysis syndrome prophylaxis

Tumour lysis syndrome prophylaxis is only indicated in a BMT setting for patients with a malignancy that is not in a complete remission or myelofibrosis patients.

- **Allopurinol** first line choice for prophylaxis of tumour lysis syndrome. Start with first day of conditioning chemotherapy and continue until day zero
- **Rasburicase** indicated if allopurinol not tolerated or uric acid elevated despite allopurinol therapy

Drug & Route	Dose	Notes
Allopurinol PO[2]	**1 month-18yrs;** 100mg/m^2 (max 100mg) TDS **>18yrs;** 300mg OD	Tablets 100mg and 300mg. Liquid available
Rasburicase IV	**From 1 month;** 200micrograms/kg OD	

5. Anti-emetics

Anti-emetics should be prescribed by the BMT medical co-ordinator referring to the BMT anti-emetic guide. Regular anti-emetics should be reviewed at day +1 post transplant

6. Supportive Care for Specific Conditioning Agents

Intravenous chemotherapy; If a pre-printed drug label or pre-printed chemotherapy prescription chart is not available, all infusion details for chemotherapy must be written on drug charts i.e. infusion fluid, volume and duration of infusion. This is a requirement even if a hydration sheet is also used.

Hyperhydration; Cyclophosphamide and melphalan require pre and post hyper-hydration. This should be prescribed on the pre-printed hydration charts by the medical co-ordinator as the chemotherapy is prescribed.

Cyclophosphamide/Mesna; For non-trial patients, cyclophosphamide and the initial dose of mesna are combined in the same fluid bag by pharmacy PSU. To calculate the size of sodium chloride 0.9% bag required;

$$\frac{\text{(Cyclophosphamide (mg))}}{20} + \frac{\text{Mesna (mg)}}{100} = \text{volume required in mls (round up to next bag)}$$

Sodium chloride 0.9% bag sizes available; 50ml 100ml 250ml 500ml 1000ml.

Cytarabine (Ara-C) at doses above 1g/m^2 per dose;
Co-prescribe

- Prednisolone eye drops 0.5% every two hours
- Betamethasone eye ointment 0.1% at night (when patient is not awake to use drops)
- Eye drops should be commenced 2 hours before the first dose of cytarabine and continued for 5 days after the last dose of cytarabine.

Anti-epileptic prophylaxis for busulfan;

- Clonazepam, starting 24 hours before first busulfan dose, continuing until 24 hours after last busulfan dose

Drug & Route	Dose	Notes
Clonazepam PO[1,7]	**1 month-12yrs;** 12.5micrograms/kg (max 500 micrograms) BD **>12yrs;** 500 micrograms BD	Tablets 500 micrograms. Liquid available. Doses may be increased – consult pharmacist.

Cover;
Consult BNF/BNFc for dosing of chlorphenamine and paracetamol

Drug & Route	Dose	Notes
Pethidine IV[8]	**1month-12yrs;** 0.5-1mg/kg (max 50mg) max four hourly **>12yrs;** 25-50mg max four hourly	
Hydrocortisone IV (as sodium succinate)	**From 1 month;** 2-4mg/kg (max 100mg) 6 hourly	For cover. For replacement oral doses, consult BNF/BNFc

Miscellaneous drug dosing;

Doses detailed below are those used in common practice on the BMT unit, but are not detailed in the BNF for Children, BNF or on the manufacturers SPC.

Drug & Route	Dose	Notes
Dihydrocodeine PO/IV	**1-4yrs;** 0.5mg/kg QDS PO/IV **4-12yrs;** 0.5-1mg/kg (max 30mg) QDS PO/IV **>12yrs;** 30mg QDS PO or 50mg QDS IV	Intravenous route unlicensed
Lenograstim SC/IV (G-CSF)	0.64 MIU/kg once daily (max 33.6 MIU)	Equivalent to 5micrograms/kg/dose. CIVAs available for part vial doses. Higher doses used for donors. See lenograstim SOP
Pantoprazole IV	**From 1 month;** 1mg/kg (max 40mg) once daily	
Tramadol PO/IV	**>1yr-12yrs;** 1mg/kg (max 100mg) QDS **>12yrs;** 50-100mg QDS	Available as 100mg vial, 50mg capsules or 50mg soluble tablets

3. Possible adverse effects of commonly used chemotherapeutic agents

This is **not a comprehensive list**. Refer to the 'Summary of Product Characteristics' (SPC), for a more detailed list of adverse effects. However, the **more common side effects** to monitor for are:

Busulfan
Irreversible pulmonary fibrosis
Gynaecomastia/Amenorrhoea/Azospermia/Impotence
Skin pigmentation
Potentially teratogenic
Hyperuricaemia

Cyclophosphamide:
Severe myelosuppression
Alopecia
Moderate - severe mucositis/diarrhoea.
Haemorrhagic cystitis - check urine DipStix for haematuria at least 6 hourly.
Pulmonary toxicity
Xerostomia/parotitis
Nausea and vomiting at high doses (500mg/m^2 and above)
Potentiation of cardiotoxicity
Skin erythema
Metallic taste, nasal stuffiness
Amenorrhoea/testicular atrophy/sterility

Melphalan
Anaphylaxis- very rare
Nausea and vomiting
Alopecia
Pulmonary fibrosis
Dermatitis
Acute leukaemia with long tem therapy

Fludarabine
Mild nausea and vomiting
Fatigue and anorexia
Neurological effects with higher doses (weakness, visual disturbances)
Haemolytic anaemia (rare)
Tumour lysis syndrome

Alemtuzumab (Campath)
Infusion related reactions (due to cytokine release) are common with doses 1 and 2. Typical reactions include fever, tachycardia and tachypnoea.
Other possible side effects are:
Headache

Nausea/vomiting/diarrhoea
Back and skeletal pain
Urticaria/rash
Hypotension or hypertension
Long term- infection

Etoposide
Severe hypotension if infused in less than 30 minutes
Nausea and vomiting
Alopecia
Peripheral neuropathy
Hyperbilirubinaemia

Cytarabine
Nausea and vomiting
Flu like syndrome (transient) - fever, arthralgia
Bone marrow depression
Conjunctivitis
Hyperuricaemia
Hepatotoxicity (rare)
Lethargy

Carmustine
Severe nausea and vomiting
Intense venous pain if given rapidly (peripheral)
Facial flushing
Bone marrow depression
Gynaecomastia
Nephrotoxicity (rare)
Hepatotoxicity (rare)

TBI
Myelosuppression
Nausea/vomitting
Headaches
Erythema
Mucositis
Pulmonary toxicity
Secondary malignancy

References

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Supportive Care Guidelines updated February 2013: [redacted], BMT Pharmacist			
Checked by:			
Quality Lead **Bristol SCT**	**Checking** **Pharmacist**		
Name: Signature: Date:	Name: [redacted] Signature: Date:		
Authorised by:			
Programme Director	**Effective date:**	**Review date:**	**Obsolete Date:**
Name: Signature: Date:			