# Prophylaxis and Treatment of Pneumocystis Jirovecii Pneumonia (PJP) for Allogeneic and Autologous Blood and Marrow Transplant (BMT) Recipients

## DEFINITION

Pneumocystis jirovecii is a fungal pathogen with a propensity to cause severe pneumonia in immunocompromised patients. Effective prophylaxis should reduce the incidence of infection with pneumocystis jirovecii to <1% but occasional patients will be seen with suspected infection.

## Prophylaxis of Pneumocystis Jirovecii Pneumonia

### Intravenous Pentamidine

**Dose:**

**4 mg/kg (max dose 300 mg) ONCE MONTHLY** in 100 ml sodium chloride 0.9% via intravenous infusion over 1 hour

**Allogeneic recipient Schedule and duration**

Start: Day +1 **and** +30 (Day 30 dose is only needed if not on co-trimoxazole)

Continue monthly if:

- patient is intolerant of co-trimoxazole
- has low blood counts i.e. neutrophils < 1.0 x $10^9$ /L and / or not platelet independent

Stop: when CD4 count exceeds 0.2 x $10^9$ /L

**Autologous recipient Schedule and duration**

Start: Day +1

Continue monthly if:

- patient is intolerant of co-trimoxazole
- has low blood counts i.e. neutrophils < 1.0 x $10^9$ /L and / or not platelet independent

Stop: 3 months post autograft or when peripheral blood lymphocytes > 1 x $10^9$/L

**Monitoring:**

- U&Es, including creatinine – dose reductions only needed if creatinine clearance < 10 ml/min
- LFTs
- FBC
- Blood glucose before and after infusion
- ECG – before, during and immediately after first dose then as required unless suspect /high risk of arrhythmias
- BP, temperature and pulse - first dose: before, during and immediately after infusion. Further doses: before and after, and if patient symptomatic of hypotension
- Amylase – if pancreatitis suspected (e.g. abdominal pain) or

hypoglycaemia

**Side effects:** IV pentamidine can have many toxic effects, but most of these are cumulative effects in daily treatment dosing. These include:
nephrotoxicity (about 20% patients), hepatotoxicity (about 5% patients) pancreatitis, electrolyte disturbance, cardiac arrhythmias
Adverse effects that can occur in both treatment and prophylaxis include: acute hypoglycaemia, electrolyte disturbance, arrhythmias (rare), QT prolongation, severe hypotension.

**Precautions:** Because of potential hypotension, the patient should receive the infusion lying or sitting down

**Oral Co-trimoxazole**

**Dose** **Co-trimoxazole 480 mg OD PO on Mondays, Wednesdays & Fridays only.**
**Escalate to 960 mg OD** (Equivalent to approx.150 mg trimethoprim/$m^2$/day) when counts stable and in the absence of side effects.

**Schedule and duration** **Start**: When neutrophils > 1.0 x$10^9$/L post-transplant & platelet transfusion independent

**Stop:**
**Allogeneic Transplant:**
When immunosuppression stop and CD4 count > 0.2 x$10^9$/L
**Autologous Transplant**: 3 months post autologous transplant or when peripheral blood lymphocytes are > 1 x $10^9$/L

**Side Effects:** Rash, Nausea, Myelosuppression, Stevens-Johnson Syndrome (rare)

**Dapsone** is an alternative to co-trimoxazole and pentamidine. Use should be discussed with a consultant

**Dose** Dapsone 100mg PO daily

**Side Effects and contraindications** Dapsone causes dose related-haemolytic anaemia and methaemoglobinaemia and is **contraindicated for patients with glucose-6-phosphamate dehydrogenase deficiency (G6PD), porphyria or severe anaemia.**
Common side effects include: neutropenia, rash, nausea and a sulfone syndrome (fever, rash, lymphadenopathy, hepatitis and methaemoglobinaemia). It should be noted that a substantial number of patients allergic to co-trimoxazole will also be intolerant of dapsone and

the drug should not be used as an alternative for patients with severe or life-threatening co-trimoxazole related toxicities.

**Atovaquone** is another alternative to co-trimoxazole and pentamidine but it is not licenced in the UK for this indication. Use should be discussed with a consultant.

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|---|---|
| **Dose** | Atovaquone 750 mg BD |
| **Side Effects and contraindications** | Anaemia; angioedema; bronchospasm; diarrhoea; headache; hypersensitivity; hyponatraemia; insomnia; nausea; neutropenia; skin reactions; throat tightness; vomiting<br><br>Note metoclopramide, rifampicin both reduce atovaquone concentration |

## Diagnosis of Pneumocystis Jirovecii Pneumonia

- 14-28 day history of breathlessness and cough, which is often non-productive.
- sparse inspiratory crackles in about one third of patients
- tachypnoea and cyanosis may be present
- chest X-ray is usually abnormal with bilateral interstitial infiltrates
- blood gases will reveal hypoxia.
- pneumocystis in lower respiratory secretions
- Beta-D glucan levels <7 make PJP unlikely
- Bronchoscopy samples should be sent for PCR. Negative results have a high predictive value. Interpret low level positive results with caution as it can be a normal commensal organism. Advise to discuss with microbiology.
- If BAL not possible, the PJP PCR can be performed on a physio obtained sputum sample (discuss with ID/micro)

## Investigations

- Chest X-ray
- Bronchoscopy
- Arterial blood gases
- Monitoring of oxygen saturation level

## Treatment of Pneumocystis Jirovecii Pneumonia

## First Line Treatment – Co-trimoxazole (with Prednisolone 40mg od)

**Treatment Dose:** **120 mg/kg/day in 4 divided doses IV infusion over 60-90 minutes** (or PO but only in mild cases and where enteral absorption is not compromised).

**Prescribing Notes**:
120 mg/kg of co-trimoxazole is equivalent to 20 mg/kg of the trimethoprim component. Dose is usually calculated to the nearest 480 mg vial.

**Dosing in renal impairment:** Dose reductions are necessary in renal failure:

| Creatinine clearance (ml/min) | Co-trimoxazole dose |
|---|---|
| > 30 | Dose as in normal renal function |
| 15-30 | 60 mg/kg BD for 3 days then 30 mg/kg BD |
| <15 | 30 mg/kg BD (This should only be given if haemodialysis facilities are available) |

**Treatment duration:** 14-21 days of Co-trimoxazole prescribed with high-dose steroids e.g. oral prednisolone 40 mg daily or IV equivalent. The data for corticosteroid use are not clear in non-HIV related pneumocystis infection. Considering stopping prednisolone after 7 days.

**Monitoring:** Daily weight with IV administration
U&Es, FBC, Blood glucose
ECG – before, during and immediately after first dose then as required unless suspect /high risk of arrhythmias.
BP, temp and pulse - first dose: before, during and immediately after infusion. Further doses: before and after, and if patient symptomatic of hypotension

**Toxicity/ adverse effects:**

- Skin effects: skin rashes with photosensitivity. More severe reactions such as Stevens-Johnson syndrome have occurred rarely (discontinue at the first appearance of a skin rash)
- Allergic reactions: anaphylaxis or less severe asthmatic episodes due to sulphite in injection
- Fluid overload with IV preparation
- Nausea, vomiting, dizziness & confusion are likely symptoms of overdose
- Elevation in serum transaminases and bilirubin
- Bone marrow depression (treat with calcium folinate 15 mg daily)

## Second Line Treatments-

There is limited evidence for second line therapy and should only be considered if patient has proven allergy or intolerance to co-trimoxazole.

## If patient can take oral medications, and without G6PD deficiency:

**Treatment Dose:** **Clindamycin 600 mg PO/IV QDS**
**Primaquine 30 mg PO OD**

**Treatment duration:** 14 to 21 days

**Precautions:** **Primaquine should be used with caution in patients with G6PD deficiency**.

**Monitoring:**
- Daily FBC
- Weekly U&E, Creatinine. No dose reduction is required for renal impairment.
- LFTs – bilirubin, alk phos and AST/ ALT –Baseline, then weekly, unless increased, then twice a week

**Side Effects:**
- Nausea and vomiting
- Neutropenia
- Clostridium difficile associated diarrhoea
- Haemolysis in patient with G6PD deficiency

## If patient can take oral medications, with G6PD deficiency or unable to confirm G6PD status:

**Treatment Dose:** **Atovaquone 750 mg PO BD**

**Treatment duration:** 14 to 21 days

**Administration:** Take with high fat food.

**Side Effects:**
- Nausea and vomiting
- Rash
- Anaemia and neutropenia
- Hyponatraemia
- Elevated liver enzymes levels

**Monitoring:**
- Daily FBC
- Weekly U&E, Creatinine. No dose reduction for renal impairment is required but use with caution if CrCl <10 mL/min
- LFTs – bilirubin, alk phos and AST/ ALT –Baseline, then weekly, unless increased, then twice a week

## If patient cannot take oral medication: Pentamidine

Treatment Dose: **4 mg/kg/day (300mg max dose)** in 100ml sodium chloride 0.9% IV infusion over 1 hour

**Dosing in renal impairment:**

| Creatinine clearance (ml/min) | Pentamidine dose |
|---|---|
| >10 | Dose as in normal renal function |
| <10 | Depending on severity of infection:<br>4 mg/kg/day IV for 7-10 days, then on alternate days to complete minimum 14 doses, *or* 4 mg/kg on alternate days to complete minimum of 14 doses |

Treatment Duration: 14 to 21 days
Usually co-prescribed with high-dose steroids e.g. oral prednisolone 40mg daily or iv equivalent

Precautions: Because of potential hypotension, the patient should receive the infusion lying or sitting down

Monitoring:

- Daily U&Es, including creatinine – dose reductions only needed if creatinine clearance < 10ml/min
- Weekly serum calcium, magnesium and phosphorus
- Daily FBC
- Blood glucose before and after infusion
- LFTs – bilirubin, alk phos and AST/ ALT – Baseline, then weekly, unless increased, then twice a week
- ECG – before, during and immediately after first dose then twice a week, unless suspect/ high risk of arrhythmias perform daily with each dose
- BP, temp and pulse - first dose: before, during and immediately after infusion. Further doses: before and after, and if patient symptomatic of hypotension
- Amylase – if pancreatitis suspected (e.g. abdo pain) or hypoglycaemia

## REFERENCES

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## Audit
These processes are subject to the OxBMT/IEC audit programme.

## Author
E. Rawlings, SDU Manager, Version 1 & 2, 2004
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## Circulation
NSSG Haematology Website

**Review**

| Name | Revision | Date | Version | Review date |
|---|---|---|---|---|
| Dr Tim Littlewood | Updating | July 2102 | 4.0 | July 2014 |
| Dr Andy Peniket,<br>Julia Wong Pharmacist | Update Pentamidine dose | Oct 2014 | 4.1 | Oct 2016 |
| Cheuk-Kie Cheung, Specialist Cancer Pharmacist<br><br>Paolo Polzella, Specialist Haematology Registrar | Minor drug amendments, clarity of instruction, references<br>No changes | Feb 2017 | 4.2 | Feb 2019 |
| Cheuk-Kie Cheung, Specialist Cancer Pharmacist | Addition of atovaquone and clindamycin/ primaquine as alternative treatment agents | June 2017 | 4.3 | Feb 2019 |
| Dr James Davies, BMT consultant<br>Nadjoua Maouche, Lead Haematology pharmacist | Diagnosis information. Reformatting and restructuring of information. New references added | July 2019 | 5.0 | July 2021 |
| Dr James Davies, BMT consultant | Minor changes only | Apr 2022 | 5.1 | Apr 2024 |
| Dr James Davies, BMT consultant<br>Yen Lim, Lead Haematology Pharmacist | Minor changes only | Oct 2024 | 5.2 | Oct 2026 |