TREATMENT AND PROPHYLAXIS OF OPPORTUNISTIC INFECTIONS IN HIV

All doses stated should be reviewed for each individual patient and adjusted if they have renal or liver impairment.
Any potential interactions with HIV medicines can be checked at www.hiv-druginteractions.org
Primary care may be requested to prescribe medicines for prophylaxis or maintenance. Unless otherwise requested in hospital discharge or clinic letters monitoring is undertaken by secondary care.

Infections covered by this guidance:

Pneumocystis Pneumonia (PCP/PJP)
Cryptococcal Meningitis
Pulmonary Cryptococcosis
Cerebral Toxoplasmosis
CMV retinitis
CMV colitis
Oropharyngeal Candidiasis
Oesophageal Candidiasis
HSV Oesophagitis
Mycobacterium Avium Complex (MAC)
Latent Tuberculosis
Cryptosporidosis
Microsporidosis

For guidance on samples to be taken for each infection refer to the lab handbook (available on ICE requesting system) or discuss with Microbiology.

INFECTION	TREATMENT			FURTHER INFORMATION	PROPHYLAXIS	LICENCE/ AVAILABILITY
	SEVERITY	1ST LINE	2ND LINE			
PNEUMOCYSTIS PNEUMONIA (PCP) *(Pneumocystis jiroveci)*	**Mild to Moderate** PaO_2 >9.3kpa on room air	**Co-trimoxazole** oral 1920mg TDS or 90mg/kg/day in 3 divided doses (rounded to nearest 480mg) Duration: 21 days	*Option1:* **Clindamycin** oral 600mg tds✧ + **Primaquine*** oral 30mg OD *Option2:* **Dapsone** 100mg oral daily + **Trimethoprim** oral 20mg/kg/day in 3 divided doses rounded to nearest 50mg *Option3:* **Atovaquone** oral 750mg BD, with food (preferably high fat) Duration: 21 days	**<u>*Check G6PD prior to prescribing dapsone or primaquine but do not delay treatment.</u>** Atovaquone has poor bioavailability. Presence of food (particularly high fat) increases the absorption 2-3 fold.	*Secondary prophylaxis:* Essential after first infection. **Co-trimoxazole** 480mg OD or **Dapsone** 100mg OD or **Atovaquone** 750mg BD or 1500mg od (off label) Discontinue secondary prophylaxis when CD4>200 for 3 months *Primary prophylaxis:* For all patients with CD4 count ≤200 or CD4% <14. Treat as per secondary prophylaxis above. Discontinue secondary prophylaxis when CD4 count >200 for >3months.	Primaquine is not licensed in the UK but can be prescribed on a named patient basis – contact pharmacist to order. Atovaquone is only available as a liquid. Use of clindamycin and trimethoprim are off label for treatment of PCP. Use of atovaquone and dapsone are off label for prophylaxis of PCP.
	Severe PaO_2 ≤9.3kpa on room air	**Co-trimoxazole** IV infusion 120mg/kg/day for 3 days then reduce to 90mg/kg/day for 18 days. Daily dose divided into 3-4 doses. **+ steroids** (see further information box) Switch to oral co-trimoxazole at same dose when appropriate after clinical improvement to complete course.	*Option1:* **Clindamycin** IV infusion 600 QDS or 900mg TDS + **Primaquine*** oral 30mg OD *Option2:* ****Pentamidine isetionate** IV infusion 4mg/kg OD in 250ml 5% glucose over at least 60 mins.. ◆Reduce dose to 3mg/kg od if toxicity Caution: hypotension, hypoglycaemia Duration: 21 days	**<u>*Check G6PD prior to prescribing dapsone or primaquine but do not delay treatment.</u>** If O_2 saturations <92% or PaO_2 ≤9.3kpa on room air start steroids at the same time as treatment (or within 72 hours). **Prednisolone** oral 40mg bd for 5 days, 40mg od for 5 days then 20mg daily for 11 days then stop. If IV required use methylprednisolone at 75% of oral prednisolone dose. Pneumothorax is a common complication of severe disease and carries a poor prognosis. CXR required if deterioration and/or chest pain.	*Secondary prophylaxis:* Essential after first infection. **Co-trimoxazole** 480mg OD or **Dapsone** 100mg OD or **Atovaquone** 750mg BD Discontinue secondary prophylaxis when CD4>200 for 3 months *Primary prophylaxis:* As above	Primaquine is not licensed in the UK but can be prescribed on a named patient basis – contact pharmacist to order. Use of atovaquone and dapsone are off label for prophylaxis of PCP. Atovaquone is only available as a liquid. **Pentamidine IV should be made in Pharmacy Aseptic Unit

Reference: ✧Dose recommended in BNF 2020 ◆CDC guidance

INFECTION	TREATMENT		FURTHER INFORMATION	PROPHYLAXIS	LICENCE / AVAILABILITY
	1ST LINE	2ND LINE			
CRYPTOCOCCAL MENINGITIS *(Cryptococcus neoformans)*	**INDUCTION THERAPY:** **Liposomal Amphoteracin B** IV infusion (Ambisome) 4mg/kg/day + ***Flucytosine** PO 100mg/kg/day in 4 divided doses (or PO not available or oral route not suitable use IV Fluconazole 800mg OD) Duration: 14 days or consider extending duration until negative CSF culture on repeat LP for patients with poor prognosis at baseline or a poor initial clinical response to induction therapy. **MAINTENANCE THERAPY:** *Then step down to:* **Fluconazole** PO 800mg OD for 1 dose then 400mg OD for 8 weeks (EACS guidance) *Then:* Chronic maintenance therapy for 1 year of Fluconazole 200mg OD	For patients who cannot tolerate or are unresponsive to amphoteracin consider using: **INDUCTION THERAPY:** **Fluconazole** PO/IV infusion 800mg OD + ***Flucytosine** PO 100-150mg/kg/day in 4 divided doses Duration: 14 days or until negative CSP culture on repeat LP **MAINTENANCE THERAPY:** *Then step down to:* **Fluconazole** PO 800mg OD for 1 dose then 400mg OD for 8 weeks (EACS guidance) *Then:* Chronic maintenance therapy for 1 year of Fluconazole 200mg OD	A test dose of Ambisome should be given at start of course – 1mg over 10 mins then patient observed for 30 mins for signs of allergic reaction. CSF manometry should be performed on all patients at baseline or if any signs of neurological deterioration occur. Serial lumbar punctures or neurosurgical procedures are indicated for individuals with an opening pressure >250mmH_2O. Corticosteroids, mannitol and acetazolamide have not been shown to be of any benefit. 1st line combination therapy has more rapid CSF sterilisation and decreased incidence of relapse.. Monitor U&Es, Mg, LFTs, FBC daily. Monitor flucytosine trough levels pre 5th dose. Aim for 20-40mg/L (as per Bristol TDM lab guidance) For azole anti-fungals consider interactions with other medicines.	**Primary prophylaxis:** not indicated **Secondary prophylaxis:** **Fluconazole** PO 200mg OD if CD4 drops <100 Other options for prophylaxis: **Ambisome** 4mg/kg/weekly **Itraconazole** is inferior to fluconazole and should not be used Discontinue prophylaxis when CD4 count is >100 for at least 3 months and viral load undetectable and completed 1 year of chronic maintenance therapy.	*Oral flucytosine is not licensed in the UK but can be prescribed on a named patient basis – contact pharmacist to order. IV flucytosine is no longer available in the UK.
PULMONARY CRYPTOCOCCOSIS *(Cryptococcus neoformans)*	As per cryptococcal meningitis	As per cryptococcal meningitis	If CSF exam is negative and • there is no other evidence of dissemination and • radiological infiltrates are focal and • there is no hypoxia **Fluconazole** PO 400mg OD for 10 weeks then 200mg OD thereafter is an alternative strategy.	As per cryptococcal meningitis	

INFECTION	TREATMENT		FURTHER INFORMATION	PROPHYLAXIS	LICENCE / AVAILABILITY
	1ST LINE	2ND LINE			
CEREBRAL TOXOPLASMOSIS *(Toxoplasma gondii)*	**Sulfadiazine** PO <60kg 1g QDS >60kg 1.5g QDS + **Pyrimethamine** PO 200mg once off then <60kg 50mg OD ≥60kg 75mg OD + **Folinic Acid** PO 15mg OD (can be increased up to 45mg OD) **See note in further information box re steroids.** Duration: minimum 6 weeks *Then step down to:* Maintenance Therapy: **Sulfadiazine** PO 500mg QDS or 1g BD + **Pyrimethamine** PO 25mg OD + **Folinic Acid** PO 15mg OD (additional PCP prophylaxis not required) Maintenance therapy can be discontinued when CD4 >200 for 6 months and VL undetectable.	**Clindamycin** PO/IV infusion 600mg QDS + **Pyrimethamine** PO 200mg once off then <60kg 50mg OD ≥60kg 75mg OD + **Folinic Acid** PO 15mg OD (can be increased up to 45mg OD) **See note in further information box re steroids.** Duration: minimum 6 weeks *Then step down to:* Maintenance Therapy: **Clindamycin** PO 600mg TDS + **Pyrimethamine** PO 25mg OD + **Folinic Acid** PO 15mg OD (additional PCP prophylaxis is required) Maintenance therapy can be discontinued when CD4 >200 for 6 months and VL undetectable.	If need IV therapy use 2nd line option. IV sulfadiazine is no longer available. With sulfadiazine a fluid output of >1200ml/day should be maintained to prevent crystalluria. If this does occur stop treatment and alkalise urine using bicarbonate. Lack of response to 2 weeks of treatment, clinical deterioration of features that are not typical should lead to consideration of a brain biopsy. Sulfadiazine and clindamycin have good bioavailability so the oral route is preferred. Corticosteroids should ***NOT be used routinely*** as they cloud the diagnostic therapeutic trial. They are ONLY indicated in patients with symptoms and signs of raised intracranial pressure such as headache, vomiting, drowsiness and papilloedema. When indicated dexamethasone 4mg QDS, gradually reducing, is the treatment of choice. (Ref: BHIVA Guidelines 2011)	*Primary prophylaxis:* all patients with CD4 <200 and positive toxoplasma serology. **Co-trimoxazole** PO 480mg OD (also covers PCP) or **Dapsone** PO 50mg OD (or 200mg/week) (also covers PCP) + **Pyrimethamine** PO 50mg weekly + **Folinic acid** PO 15mg OD Or **Atovaquone** 1500mg OD (off label) Primary prophylaxis can be discontinued when CD4 count >200 for 3months and VL undetectable. *Secondary prophylaxis:* See maintenance therapy	IV sulfadiazine – no longer available. Alternative name for folinic acid is calcium folinate (Pharmacy Ascribe Code TAY015C). Oral sulfadiazine is available in the NW night emergency drug cupboard.

INFECTION	TREATMENT		FURTHER INFORMATION	PROPHYLAXIS	LICENCE / AVAILABILITY
	INDUCTION	MAINTENANCE			
CMV RETINITIS (Cytomegalovirus)	*Option 1*: **Valganciclovir** PO 900mg bd for 21 days *Option 2:* **Ganciclovir** IV infusion 5mg/kg bd for 14-21 days *Option 3:* **Foscarnet** IV infusion 90mg/kg bd for 14-21 days *Option 4*: **Cidofovir** IV infusion 5mg/kg weekly for 2 weeks	*Option1:* **Valganciclovir** PO 900mg OD *Option 2:* **Ganciclovir** IV infusion 5mg/kg od or 6mg/kg/day for 5 days a week *Option 3:* **Foscarnet** IV infusion 60mg/kg od then increase if tolerated to 90-120mg/kg od (Ref: BNF/BHIVA) *Option 4:* **Cidofovir** IV infusion 5mg/kg given fortnightly Maintenance therapy can be stopped when CD4>100 for >3-6 months and VL undetectable. Opthalmology checks every 3 months until immune system recovery then annually.	Monitor FBC, U&Es, LFTs for all anti-CMV medications. Valganciclovir should be taken with food. Valganciclovir/ganciclovir are considered potential teratogens and carcinogens in humans. Avoid direct contact of broken or crushed tablets, infusion powder or solution with skin or mucous membranes. If such contact occurs, wash thoroughly with soap and water or rinse eyes thoroughly with sterile water, or plain water if sterile water is unavailable. Foscarnet should be administered via a central line or must be diluted in pharmacy aseptic department to be given peripherally. Slower infusion rates may reduce rates of electrolyte disturbances. Patients should be encouraged to maintain a high level of hygiene to avoid genital ulceration. Cidofovir requires to be administered with IV hydration and probenecid tablets. See SmPC for details. Note: Patients allergic to sulfa-containing medicines should not be given probenecid.	*Primary prophylaxis:* not indicated *Secondary prophylaxis:* See maintenance therapy	Ganciclovir infusions should ideally be made in pharmacy aseptic department. Foscarnet and Cidofovir are not routinely kept as stock and will require to be ordered in.
CMV COLITIS	*Option 1:* **Ganciclovir** IV infusion 5mg/kg bd for 14-28 days or until symptoms resolved *Option 2:* **Foscarnet** IV infusion 90mg/kg bd for 14-28 days or until symptoms resolved	Not routinely recommended unless patient relapses after induction therapy ceases.	See above for information on ganciclovr and foscarnet. **Valganciclovir** may be considered as a treatment option for all or part of the treatment course if symptoms are not severe enough to interfere with swallowing and oral absorption. For mild case, if ART can be initiated without delay, consider withholding CMV therapy.	*Secondary prophylaxis:* See maintenance therapy	Foscarnet and valganciclovir are not licensed for this indication.

INFECTION	TREATMENT		FURTHER INFORMATION	PROPHYLAXIS	LICENCE / AVAILABILITY
	1ST LINE	2ND LINE			
OROPHARYNGEAL CANDIDIASIS	**Fluconazole** PO 100mg OD for 7-14 days In severe disease: up to 200mg OD	**Itraconazole** liquid PO 100mg BD (10-20ml) for 7-14 days	For all azole antifungals check for interactions with other medications. Itraconazole liquid has increased oral bioavailability and it may also have some local effect. The liquid should be taken 1 hour before food or on an empty stomach.	*Primary prophylaxis:* not recommended - promotes resistance. *Secondary prophylaxis*: not recommended - promotes resistance.	
OESOPHAGEAL CANDIDIASIS	**Fluconazole** PO 200mg OD for 14-21 days In severe disease: up to 400mg OD or 200mg BD	**Itraconazole** liquid PO 100-200mg BD (10-20ml) for up to 14 days Non-responders to resistant Candida: **Voriconazole**, **posaconazole** or **anidulafungin**	For all azole antifungals check for interactions with other medications. Itraconazole liquid has increased oral bioavailability and it may also have some local effect so is the preferred formulation. The liquid should be taken 1 hour before food or on an empty stomach. The dose should be swished around the mouth and swallowed without rinsing. **CSM warning: itraconazole** is contra-indicated in patients with evidence of or history of congestive heart failure	*Primary prophylaxis:* not recommended - promotes resistance. *Secondary prophylaxis*: not recommended - promotes resistance.	
HSV OESOPHAGITIS	**Aciclovir** IV 5-10mg/kg tds followed by valaciclovir PO 1g bd for a total of 14 days or until healing is complete			*Not recommended*	
CRYPTOSPORIDOSIS ***(Cryptosporidium parvum)***	Initiate or optimise HAART + Symptomatic treatment of diarrhoea + Adequate hydration	CONSIDER **Nitazoxanide** PO 500mg BD for 3 days (can be extended up to 12 weeks) + all elements of 1st line therapy	Nitazoxanide efficacy is limited in severely immunocompromised patients.	Primary prophylaxis: not indicated	Nitazoxanide is not licensed in the UK. Available on a named patient basis. Contact Pharmacist to order.
MICROSPORIDOSIS (Intestinal infection)	Initiate or optimise HAART + Symptomatic treatment of diarrhoea + Adequate hydration	Consider **Albendazole** PO 400mg BD for 14 days	Albendazole has poor oral bioavailability so should be taken with fatty food to maximise absorption. Check for drug interactions.	Primary prophylaxis: not indicated	Albendazole is not licensed in the UK. Available on a named patient basis. Contact Pharmacist to order.

INFECTION	TREATMENT		FURTHER INFORMATION	PROPHYLAXIS	LICENCE / AVAILABILITY
	1st LINE	2nd LINE			
Disseminated MYCOBACTERIUM AVIUM COMPLEX (DMAC)	***Clarithromycin** PO 500mg BD (or ***Azithromycin** 500mg OD) + **Ethambutol** PO 15mg/kg (rounded to nearest 100mg) +/- **Rifabutin** PO 300mg OD (see further information) Treatment can be stopped when CD4 >100 for 2 results at least 3 months apart, clinical response to MAC treatment for at least 3 months and undetectable VL.	For treatment failure: 3 drug combination to include at least 2 drugs not previously used. Options include: **Rifabutin** – if not used 1st line **Ethambutol** – can be continued as it facilitates the penetration of other agents in mycobacteria **Ciprofloxacin** PO 500-750mg BD **Moxifloxacin** 400mg OD **Levofloxacin** 500mg OD **Amikacin** IV 7.5mg/kg BD or 15mg/kg OD (maximum 1.5g/day) for 10 days maximum. **Linezolid, Cycloserine, Prothionamide**	Patients should have a full ophthalmological examination prior to starting ethambutol. Rifabutin should be added if CD4<25 or markedly symptomatic DMAC features and/or laboratory parameters or if effective HAART regime cannot be given. Rifabutin dose requires adjustment for HAART interactions. Amikacin serum level monitoring is required. If treatment is to exceed 10 days an audiogram should be performed and repeated during therapy. Therapy should be stopped if tinnitus or subjective hearing loss develops. Focal MAC treatment normally treated for at least 12 months.	Primary prophylaxis: Consider if CD4 <50 ***Azithromycin** PO 1250mg weekly Follow food /antacid administration instructions for formulation dispensed. Prophylaxis can be stopped if CD4 >100 for at least 3 months.	Unlicensed indication for clarithromycin, azithromycin, ciprofloxacin, amikacin, linezolid. Rifabutin, Cycloserine and prothionamide are not routinely kept as stock and will ordered. *Macrolides consider interactions and prolonged QT interval.
LATENT TUBERCULOSIS INFECTION	**Isoniazid** 5mg/kg (max 300mg) OD + **Pyridoxine** 10mg OD Duration: 6 months		Should be started if positive IGRA or as based on contact tracing assessment.		
OTHER GI INFECTIONS	Refer to BHIVA guidelines				
STIs	Treat as per non HIV patients. Follow NHS Tayside guidance				

Adapted from: BHIVA 2018 Candidiasis Guidelines/BHIVA 2020 GI infections/IDSA 2018 Guidelines Treatment and Prevention of OIs/ BHIVA Guidelines 2011/EACS Guidelines 2020

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Approved by: AMG June 2012

Updated: Nov 2020

Review: Nov 2023