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
- Mycobacterium Avium Complex (MAC)
- Latent Tuberculosis
- Cryptosporidiosis
- Microsporidiosis

For guidance on samples to be taken for each infection refer to the lab handbook (available on ICE requesting system) or discuss with Microbiology.
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<tr>
<th>INFECTION</th>
<th>SEVERITY</th>
<th>TREATMENT</th>
<th>FURTHER INFORMATION</th>
<th>PROPHYLAXIS</th>
<th>LICENCE/AVAILABILITY</th>
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<tbody>
<tr>
<td><strong>PNEUMOCYSTIS PNEUMONIA (PCP)</strong> (Pneumocystis jiroveci)</td>
<td>Mild to Moderate</td>
<td>PaO₂ &gt;9.3kpa on room air</td>
<td>Co-trimoxazole oral 1920mg TDS or 90mg/kg/day in 3 divided doses (rounded to nearest 480mg)</td>
<td>Duration: 21 days</td>
<td>*Check G6PD prior to prescribing dapsone or primaquine but do not delay treatment. If significant haemolysis while on other treatment then check G6PD. Atovaquone has poor bioavailability. Presence of food (particularly high fat) increases the absorption 2-3 fold.</td>
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<tr>
<td><strong>Severe</strong></td>
<td>PaO₂ ≤9.3kpa on room air</td>
<td>Co-trimoxazole IV infusion 120mg/kg/day in 3-4 divided doses for 21 days + steroids (see further information box) Switch to oral co-trimoxazole at same dose when appropriate after clinical improvement to complete course.</td>
<td>Option1: Clindamycin IV infusion 600 QDS or 900mg TDS + Primaquine oral 30mg OD</td>
<td>Duration: 21 days</td>
<td>*Check G6PD prior to prescribing dapsone or primaquine but do not delay treatment. If significant haemolysis while on other treatment then check G6PD. If O₂ saturations &lt;92% or PaO₂ ≤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.</td>
</tr>
</tbody>
</table>

Reference: ◦Dose recommended in BNF 2018/CDC guidance 2018/EACS guidance 2018 ●CDC guidance
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</table>
| **CRYPTOCOCCAL MENINGITIS** *(Cryptococcus neoformans)* | **1ST LINE**  
**INDUCTION THERAPY:**  
Liposomal Amphotericin B IV infusion (Ambisome)  
4mg/kg/day  
+  
*Flucytosine* PO/IV infusion  
100mg/kg/day in 4 divided doses  
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 | **2ND LINE**  
For patients who cannot tolerate or are unresponsive to amphotericin consider using:  
**INDUCTION THERAPY:**  
Fluconazole PO/IV infusion  
400mg – 800mg OD (higher dose if life threatening)  
+  
*Flucytosine* PO/IV infusion  
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 >250mmH2O. 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.  
Licensed dose of flucytosine IV is 200mg/kg/day but a lower dose is sufficient in this situation as it is synergistic when co-administered.  
IV flucytosine is available in NW pharmacy and not the night emergency drug cupboard because there is a strict temperature range it must be stored at. |
| **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

#### CEREBRAL TOXOPLASMOSIS

**(Toxoplasma gondii)**

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<th><strong>2ND LINE</strong></th>
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<th><strong>PROPHYLAXIS</strong></th>
<th>** LICENCE / AVAILABILITY**</th>
</tr>
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</table>
| Sulfadiazine PO  
<60kg 1g QDS  
>60kg 1.5g QDS  + | 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)  | 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)  | ** 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. |
| Maintenance Therapy:  
Sulfadiazine PO  
500mg QDS or 1g BD  + | Maintenance Therapy:  
**Clindamycin** PO  
600mg TDS  +  
**Pyrimethamine** PO  
25mg OD  +  
**Folinic Acid** PO  
15mg OD (can be increased up to 45mg OD)  | Duration: minimum 6 weeks  
**Then step down to:**  
Maintenance Therapy:  
**Clindamycin** PO  
600mg QDS  +  
**Pyrimethamine** PO  
25mg OD  +  
**Folinic Acid** PO  
15mg OD (can be increased up to 45mg OD)  | **Secondary prophylaxis:** See maintenance therapy |
| Pyrimethamine PO  
200mg once off then  
<60kg 50mg OD  
≥60kg 75mg OD  + |  | Duration: minimum 6 weeks  
**Then step down to:**  
Maintenance Therapy:  
**Dapsone** PO  
50mg OD  
(or 200mg/week)  
(also covers PCP)  
+  
**Pyrimethamine** PO  
50mg weekly  
+  
**Folinic acid** PO  
15mg OD  | | |
| Folinic Acid PO  
15mg OD (can be increased up to 45mg OD) | See note in further information box re steroids. | | | | |

**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.*

*Primary prophylaxis can be discontinued when CD4 count >200 for 3 months and VL undetectable.*

*Or*  
**Atovaquone**  
1500mg OD (off label)
<table>
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<tr>
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<tbody>
<tr>
<td>CMV RETINITIS (Cytomegalovirus)</td>
<td><strong>INDUCTION</strong></td>
<td><strong>MAINTENANCE</strong></td>
<td><strong>Primary prophylaxis:</strong></td>
<td><strong>Secondary prophylaxis:</strong></td>
</tr>
<tr>
<td>Option 1: Valganciclovir PO 900mg bd for 21 days</td>
<td>Option 1: Valganciclovir PO 900mg OD</td>
<td>Monitor FBC, U&amp;Es, LFTs for all anti-CMV medications.</td>
<td>not indicated</td>
<td>Ganciclovir infusions should ideally be made in pharmacy aseptic department.</td>
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<tr>
<td>Option 2: Ganciclovir IV infusion 5mg/kg bd for 14-21 days</td>
<td>Option 2: Ganciclovir IV infusion 5mg/kg od or 6mg/kg/day for 5 days a week</td>
<td>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.</td>
<td></td>
<td>Foscarnet and Cidofovir are not routinely kept as stock and will require to be ordered in.</td>
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<tr>
<td>Option 3: Foscarnet IV infusion 90mg/kg bd for 14-21 days</td>
<td>Option 3: Foscarnet IV infusion 60mg/kg od then increase if tolerated to 90-120mg/kg od (Ref: BNF/BHIVA)</td>
<td>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.</td>
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<td>Option 4: Cidofovir IV infusion 5mg/kg weekly for 2 weeks</td>
<td>Option 4: Cidofovir IV infusion 5mg/kg given fortnightly</td>
<td>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.</td>
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<td>Maintenance therapy can be stopped when CD4&gt;100 for &gt;3-6 months and VL undetectable. Ophthalmology checks every 3 months until immune system recovery then annually.</td>
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<tr>
<th>CMV COLITIS</th>
<th><strong>INDUCTION</strong></th>
<th><strong>MAINTENANCE</strong></th>
<th><strong>Secondary prophylaxis:</strong></th>
<th><strong>Secondary prophylaxis:</strong></th>
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<tbody>
<tr>
<td>Option 1: Ganciclovir IV infusion 5mg/kg bd for 14-28 days or until symptoms resolved</td>
<td>Not routinely recommended unless patient relapses after induction therapy ceases.</td>
<td>See above for information on ganciclovir and foscarnet.</td>
<td>See maintenance therapy</td>
<td>Foscarnet and valganciclovir are not licensed for this indication.</td>
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<tr>
<td>Option 2: Foscarnet IV infusion 90mg/kg bd for 14-28 days or until symptoms resolved</td>
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<td>Valganciclovir may be considered as a treatment option if symptoms do not interfere with absorption.</td>
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<td>FURTHER INFORMATION</td>
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<td>LICENCE / AVAILABILITY</td>
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<tr>
<td><strong>OROPHARYNGEAL CANDIDIASIS</strong></td>
<td><strong>1ST LINE</strong></td>
<td>Fluconazole PO 100mg OD for 7-14 days</td>
<td>For allazole antifungals check for interactions with other medications.</td>
<td><strong>Primary prophylaxis:</strong> not recommended - promotes resistance.</td>
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<td>Itraconazole liquid PO 100mg BD (10-20ml) for 7-14 days</td>
<td>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.</td>
<td><strong>Secondary prophylaxis:</strong> not recommended - promotes resistance.</td>
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<td><strong>2ND LINE</strong></td>
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<td>Fluconazole PO 100mg OD for 14-21 days</td>
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<td>Itraconazole liquid PO 100-200mg BD (10-20ml) for up to 14 days</td>
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<td><strong>Non-responders to resistant Candida:</strong></td>
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<td>Voriconazole, posaconazole or anidulafungin</td>
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<td><strong>OESOPHAGEAL CANDIDIASIS</strong></td>
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<td><strong>1ST LINE</strong></td>
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<td></td>
<td>Fluconazole PO 100-200mg BD (10-20ml) for up to 14 days</td>
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<td><strong>2ND LINE</strong></td>
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<td><strong>Disseminated MYCOBACTERIUM</strong></td>
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<tr>
<td><strong>AVIUM COMPLEX (DMAC)</strong></td>
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|                               |                                          | For treatment failure: 3 drug combination to include at least 2 drugs not previously used. | Patients should have a full ophthalmological examination prior to starting ethambutol. | **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. |
|                               |                                          | 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                                                |                                                                            |                             |
|                               |                                          | **2ND LINE**                                                                         |                                                                            |                             |
|                               |                                          | *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                                                |                                                                            |                             |
|                               |                                          | **FURTHER INFORMATION**                                                             |                                                                            |                             |
|                               |                                          | For allazole 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. |                                                                            |                             |
|                               |                                          | **PROPHYLAXIS**                                                                     |                                                                            |                             |
|                               |                                          | **Primary prophylaxis:** not recommended - promotes resistance.  |                                                                            |                             |
|                               |                                          | **Secondary prophylaxis:** not recommended - promotes resistance.                  |                                                                            |                             |
|                               |                                          | **LICENCE / AVAILABILITY**                                                          |                                                                            |                             |
|                               |                                          | 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. |                             |                             |
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<tr>
<td>LATENT TUBERCULOSIS</td>
<td>Isoniazid 5mg/kg (max 300mg) OD</td>
<td>Duration: 6 months</td>
<td>Should be started if positive IGRA or as based on contact tracing assessment.</td>
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<tr>
<td>INFECTION</td>
<td>+ Pyridoxine 10mg OD</td>
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<tr>
<td>CRYPTOSPORIDOSIS</td>
<td>Initiate or optimise HAART</td>
<td>CONSIDER Nitazoxanide PO 500mg BD for 3 days (can be extended up to 12 weeks)</td>
<td>Nitazoxanide efficacy is limited in severely immunocompromised patients.</td>
<td>Primary prophylaxis: not indicated</td>
</tr>
<tr>
<td>(Cryptosporidium</td>
<td>+ Symptomatic treatment of diarrhoea</td>
<td>+ all elements of 1st line therapy</td>
<td></td>
<td>Nitazoxanide is not licensed in the UK.</td>
</tr>
<tr>
<td>parvum)</td>
<td>+ Adequate hydration</td>
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<td></td>
<td>Available on a named patient basis.</td>
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<td>Contact Pharmacist to order.</td>
</tr>
<tr>
<td>MICROSPORIDOSIS</td>
<td>Initiate or optimise HAART</td>
<td>Consider Albendazole PO 400mg BD for 21 days</td>
<td>Albendazole has poor oral bioavailability so should be taken with fatty food to maximise absorption. Check for drug interactions.</td>
<td>Primary prophylaxis: not indicated</td>
</tr>
<tr>
<td>(Intestinal infection)</td>
<td>+ Symptomatic treatment of diarrhoea</td>
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<td>Albendazole is not licensed in the UK.</td>
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<td>+ Adequate hydration</td>
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<td>Contact Pharmacist to order.</td>
</tr>
<tr>
<td>STIs</td>
<td>Treat as per non HIV patients. Follow NHS Tayside guidance</td>
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</tbody>
</table>

Prepared by: K Hill, HIV/Antimicrobial Pharmacist
Reviewed by: HIV MDT May 2012
Approved by: AMG June 2012
Updated: April 2019
Review: April 2022