



## Appendix 1: “The Big Three”

(azithromycin or clarithromycin, together with rifampicin or rifabutin, and ethambutol)

**The ‘Big Three’** - Most people diagnosed with NTM and who start treatment, take three antibiotics. These are usually azithromycin or clarithromycin, together with rifampicin or rifabutin, and ethambutol.

### Azithromycin & Clarithromycin

#### How do I take?

- Tablets can be taken with/without food
- Do not take indigestion remedies (for example Gaviscon® or Rennie®) 2 hours before or after you take azithromycin
- Azithromycin should be used with caution in patients with Myasthenia Gravis

#### Will there be any interactions with any of my other medicines?

- Your NTM team will check for any interactions. Please ensure you make your NTM team aware of all prescribed medication you take and any over the counter preparations. Medicines that azithromycin and clarithromycin interact with include (but not limited to):
  - Amiodarone
  - Digoxin
  - Methadone
  - Warfarin
  - Ondansetron
  - Colchicine
  - Statins with clarithromycin

#### Is there anything I need to look out for?

- You should make your NTM team aware if you experience any of the following side effects caused by azithromycin and clarithromycin:
  - Any change or loss in hearing
  - If you feel your heart beating in your chest or have an abnormal heartbeat
  - If you develop severe, persistent diarrhoea
  - Yellowing of skin or whites of the eyes



### **What other side effects might I experience?**

- The most common side effects include (but not limited to):
  - Dizziness, headache
  - Burning or prickling sensation
  - Change in taste
  - Visual impairment
  - Vomiting, dyspepsia
  - Rash/ itchy skin
  - Joint stiffness/ pain
  - Tiredness/ lack of energy
  - Diarrhoea, abdominal pain, flatulence (wind), nausea
- Please see patient information insert provided with medication for full list of side effects

### **How will I be monitored?**

- Your NTM team will check your liver function at the beginning of treatment and throughout treatment
- Your NTM team may check your heart trace (ECG) at the beginning of treatment; in some instances, your heart trace may be rechecked after 2 weeks and/or after the addition of any new medication that may also affect your heart trace
- Your NTM team may also check your hearing (audiometry) at the beginning of treatment and intermittently during treatment depending on any risks of hearing changes and symptoms. In addition, if you experience any hearing changes including tinnitus (ringing in the ear) or if you notice you have needed to turn the volume up on your radio or TV for no obvious reason then make your NTM team aware



## Rifampicin & Rifabutin

### How do I take?

- Rifampicin should be taken on an empty stomach, which for most people means first thing on waking and waiting at least 30–60 minutes before their first meal of the day or leaving at least 2 hours after food

### Will there be any interactions with any of my other medicines?

- Your NTM team will check for any interactions. Please ensure you make your NTM team aware of all prescribed medication you take and any over the counter preparations
- Medicines that rifampicin interacts with include (but not limited to):
  - Anticoagulants
  - Some antiepileptics (lamotrigine, phenytoin, phenobarbital)
  - Some oral anti-diabetics
  - Calcium-channel blockers (used for blood pressure) (diltiazem, nifedipine, nimodipine and verapamil)
  - Contraceptives
  - Hormone replacement therapy (HRT)
  - Opioids (codeine, fentanyl, methadone, morphine and possibly oxycodone)
- Medicines that rifabutin interacts with include (but not limited to):
  - Anticoagulants
  - Some oral anti-diabetics
  - Some antiepileptics (carbamazepine and phenytoin)
  - Some antipsychotics (aripiprazole)
  - Contraceptives
  - Corticosteroids
  - Hormone Replacement Therapy (HRT)

### Is there anything I need to look out for?

- Rifampicin and rifabutin may cause side effects. You should make your NTM team aware if you experience any of the following side effects:
  - Symptoms of changes in liver function which includes loss of appetite, upset stomach, tiredness, pain in the right upper belly, vomiting, dark urine, and/or yellowing of the eyes or skin
  - Any unexplained bruising or bleeding



### **What other side effects might I experience?**

- Other side effects include (but not limited to):
  - Reddish discolouration of urine, sweat, sputum, tears (note also discolours soft contact lenses)
  - Nausea
  - Vomiting
  - Heartburn
  - Visual disturbance
- Please see patient information insert provided with medication for full list of side effects

### **How will I be monitored?**

- Your NTM team will check your liver function, blood count and kidney function before you start treatment and throughout your treatment
- Eyesight checks will also be done with rifabutin use



## Ethambutol

### How do I take?

- Tablets can be taken with/without food

### Will there be any interactions with any of my other medicines?

- Your NTM team will check for any interactions. Please ensure you make your NTM team aware of all prescribed medication you take and any over the counter preparations. Medicines that ethambutol interacts with include (but not limited to):
  - Isoniazid

### Is there anything I need to look out for?

- Ethambutol may also cause side effects. You should make your NTM team aware if you experience any of the following side effects:
  - Any change in vision or visual disturbance (blurred vision or loss of intensity of bright colours)

### What other side effects might I experience?

- The most common side effects include (but not limited to):
  - Rash/ itchy skin
  - Nerve disorders
- Please see patient information insert provided with medication for full list of side effects

### How will I be monitored?

- Before taking ethambutol tell your clinician if you have colour blindness or visual disturbances
- Your NTM team will ask you to complete an eye test (to check your visual acuity and colour discrimination) before starting treatment. In some instances, the eye test might be repeated during treatment