

Treatment of NTM **Tips & Information**



This informational booklet was developed and led by the Chairs of the NTM Network UK Pharmacist Subgroup with support from the NTM Network UK Pharmacist Subgroup members, Chair of NTM Network UK, NTM Patient Care UK and most importantly our patient stakeholders.



Treatment of NTM

Tips & Information

Not everyone with Non-Tuberculous Mycobacterial (NTM) disease needs to take specific antibiotic treatment. However, if they do, this is often a combination of several drugs taken for months and sometimes years. This leaflet has been written to provide you with information about the treatments for NTM

It also includes top tips to help with taking your medication and manage possible side effects that can occur when on treatment

You will also find links to further information about each of the commonly used drugs, including how to take them, possible interactions with other medication you might use, side effects and any necessary monitoring your clinical team will perform. This information can be found at the NTM Patient Care website (www.ntmpatientcare.uk)

We hope that by providing this information you will feel more informed, more comfortable with the medication and able to speak to others including your health care providers about any concerns that you may have

Please do let us know what you think of this leaflet as we are always looking to improve it!

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How is Non-Tuberculous Mycobacterial disease treated?

- NTM can cause disease anywhere in the body, but most often this is in the lung. Treatment includes both non-antibiotic approaches, such as sputum clearance for NTM lung disease, and antibiotics that target the specific NTM thought to be causing the disease. People will be asked to take several antibiotics together for several months or more. A combination of three or four antibiotics is generally used to treat the NTM bacteria in different ways and prevent the bacteria from becoming resistant to antibiotics
- Your NTM treatment is specific to you. Not all NTM infections are treated the same way, and this is dependent on the species of bug (strain), where in your body it is causing disease, and how badly the illness is affecting you. You may be prescribed, therefore, a different combination of antibiotics to other people with NTM. Most antibiotics are taken by mouth (orally), though in some instances, depending on the specific NTM, you may be offered antibiotics given intravenously (by a drip into the arm), or breathed in through a nebuliser
- As with all medications, some people may experience side effects during treatment. In many instances, these may be mild and/or short-lasting and can be managed easily. In the event of a serious adverse reaction, please notify your clinician immediately. Serious adverse reactions may also be reported to the MHRA (national medicines surveillance group) via a “yellow card” report. The form can be accessed via yellowcard.mhra.gov.uk and will usually be completed by a pharmacist or doctor involved in your care
- Before starting treatment tell your clinician about any medications you are taking including over the counter medicines, herbal medicines, any allergies and if you are pregnant or intending to become pregnant, or breastfeeding

Duration of treatment

- It takes a long time to kill NTM bacteria, so treatment durations are usually for months or years. For example, if you have NTM lung disease, treatment is for at least 12 months after your sputum samples have stopped growing NTM bugs (often called ‘culture conversion’). For NTM skin disease this may be for just a few months. Your NTM team will advise you for how long you need to take your treatment
- It is important that you take your antibiotics regularly as prescribed even if you feel well. This will help to treat the bug, reduce the chance of it coming back, and will also help to prevent it becoming resistant to the drug treatments



Stopping or changing treatment

- Your NTM team will advise you if you need to stop or change treatment
- Your NTM team will advise you when you have completed your course of treatment
- Your NTM team may also change your treatment depending on your response to the prescribed medication
- If you have any serious side effects, your NTM team will be able to provide advice on switching to alternative antibiotics

Monitoring

- For people with NTM Lung Disease, it is really important that you produce regular sputum (phlegm) samples. These will provide your clinical team with more information about the bug growing, which treatment is best and how it is working for you
- Your NTM team should check your sputum (phlegm) every 4–12 weeks during treatment and for 12 months after completing treatment if you are still productive

Staying on track with your treatment

- It is very important that you take your medicines every day or as prescribed by your healthcare team. As you will be taking your NTM medications for a long period of time, here are some suggestions to help you get into a routine:
 - Take your tablets at the same time every day
 - Put your tablets in a weekly dispenser. Medication organisers, e.g. a pillmate® or dosette®, are helpful for some patients and are available from local pharmacies
 - Mark off each day on a calendar once you have taken your medicines
 - Set a reminder on your phone/use a phone app
 - Request support from your NTM clinical team to write a medication card which lists all your NTM medicines along with how and when to take these
 - Ask a friend or relative to help you
 - Use a combination of the above



Missed doses

- It is very important that you take your medicines every day to ensure the infection is treated and reduce the risk of antibiotic resistance
- If you don't take your medication regularly the bacteria can become resistant to antibiotics, making the infection more difficult to treat now and in the future
- If you do forget or miss a dose:
 - If a once daily regimen and still the same day, take the dose as soon as you remember. If the day has passed, skip the missed dose and take your next scheduled dose
 - If a twice daily or more frequent dosing regimen, take that dose as soon as you remember and then continue to take your antibiotics as normal. But if it's almost time for the next dose, skip the missed dose and continue your regular dosing schedule
 - Do not take two doses at the same time
- Always let your clinician know if you do not remember to take your tablets
- If possible, bring your tablets with you to your NTM clinic as this can help your healthcare team ensure you are getting the most from your drug therapy

Drug interactions

- Drug interactions should be checked before treatment initiation and when there are any new medication changes
- Please make your NTM team aware of all your prescribed medicines (from your GP, other hospital clinics etc.) and any over-the-counter medicines (including vitamins and supplements). Your NTM team will check for interactions and manage these appropriately. Some of the common interactions can be found in the individual drug information leaflets

Known side effects of medications used in treatments for NTM [* uncommon; ** common]

It is important to report any new symptoms that you experience to your NTM team.

Side effects	Rifampicin/ Rifabutin	Azithromycin/ Clarithromycin	Ethambutol	Clofazimine	Doxycycline/ Minocycline
Gastrointestinal: nausea, vomiting, diarrhoea	**	**		**	**
Reflux	*	*			**
Headache; dizziness	**	**			**
Reduced appetite; altered state	**	**			*
Fatigue; malaise (flu like)	**	*			
Visual impairment (acuity/colour)	Risk of uveitis (inflammation of the middle layer of the eye) with Rifabutin		*	*	
Hearing impairment		*			
Photosensitivity				**	**
Prolongs QTc: i.e. prolongs the time it takes for the heart's electrical system to recharge between beats		*		*	
Discoloration of body fluids e.g. tears, sweat, urine	**			**	
Skin pigmentation				**	*
Side effects	Moxifloxacin/ Ciprofloxacin	Isoniazid	Linezolid	Cotrimoxazole	Nebulised Amikacin
Gastrointestinal: nausea, vomiting, diarrhoea	**	**	**	**	**
Reflux	*		*		
Headache; dizziness	**		**	**	**
Reduced appetite; altered state	*		**	*	**
Fatigue; malaise (flu like)	**	*	*		**
Visual impairment (acuity/colour)			**		
Hearing impairment/ Tinnitus	*		*	*	**
Photosensitivity	**			*	
Prolongs QTc: i.e. prolongs the time it takes for the heart's electrical system to recharge between beats	**				
Sensation of numbness, pins and needles of extremities	*	**	**		
Others	Tendonitis risk and muscle pain	Dry mouth	Affect blood counts such as low platelets, anaemia	Affect blood counts such as low platelets, anaemia	Cough, chest tightness, sore throat and mouth, altered voice, coughing up fresh blood



Managing side effects

- Stomach-related side effects including nausea, vomiting, diarrhoea, bloating and reflux (indigestion) can be common with NTM treatments. In most instances these can usually be easily managed in discussion with your team
- If you're struggling with nausea, consider taking your medicines at night before going to bed
- Ginger sweets or tea can sometimes be helpful to overcome the feeling of nausea. Like all remedies they should be used in moderation
- Peppermint tea can sometimes be helpful to relieve the feeling of bloating
- If your nausea does not resolve using the above methods or if you are vomiting (being physically sick), please contact your NTM clinical team to see whether an antiemetic (anti-sickness tablet) may be appropriate. There are different types of antiemetics available, therefore your NTM team will be able to advise whether there is a suitable antiemetic for you, taking into account any other medical conditions and drug interactions
- More serious symptoms of reflux can be managed with lifestyle changes such as having your last meal of the day much earlier before bedtime, avoiding alcohol, caffeinated drinks and spicy foods and stopping smoking. In some cases, medication such as proton pump inhibitors may also be prescribed. Please speak to your NTM team before starting any new medications
- You may experience diarrhoea or frequent loose stools which occur due to the change in balance of good bacteria in your gut. Ensure you are well-hydrated and consider buying probiotic drinks/yoghurts or supplements. One of the most common live cultures available includes *Lactobacillus acidophilus*. Avoid taking probiotics at the same time as your antibiotics. Tell your NTM team if you have severe persistent diarrhoea or blood in your stools
- Skin rashes or itching may occur. Make your NTM team aware if you experience a rash. Sometimes rashes go away on their own accord or your team can provide you with some medication to help with this
- Thrush is a yeast infection which can commonly occur in the mouth or vagina. This is due to the overgrowth of a fungus. Oral thrush can present as a sore mouth with a white, furry coating on your tongue and back of your throat. Vaginal thrush symptoms include creamy abnormal discharge, itch and irritation of the vulva region and pain on urination. Consult your NTM team if you experience any of these symptoms. In some instances, over-the-counter/pharmacy treatments may be recommended to help resolve the infection

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- While trying to take all your medications at the same time each day may help with remembering to take all your treatments, if you experience side effects, discuss with your NTM team how splitting the timings of some of the antibiotics could help you tolerate them better
 - Some medications can cause less serious side effects including a change in colour to body fluids or skin pigmentation. This may make patients feel more self-conscious and can impact on wellbeing. This can also cause staining to lighter-coloured fabrics e.g. clothes and bedsheets; for drugs which cause changes to body secretions it is suggested to avoid white or pale colour clothing and use darker colour bed sheets
 - Fatigue is common due to both the NTM disease and the medications. We recommend good nutritional intake, adequate hydration and building exercise tolerance to help overcome fatigue
 - A new diagnosis and/or a number of new treatments can cause feelings of worry and anxiousness. If you are finding it hard to cope with your mental health, please speak to your clinical team

You may also find support managing your NTM treatment by discussing with other patients with NTM through the Zoom calls which are held regularly. To attend these Zoom meetings, contact us at info@ntmpatientcare.uk.

Drug monitoring

This table shows the tests and frequency of monitoring that you might expect while on treatment for NTM

Monitoring	Blood tests (Full blood counts, liver and kidney function)	Vision (Visual acuity - Snellen chart and colour differentiation - Ishihara plates)	Heart tracing ECG for QTc measurement	Audiometry
Frequency	Baseline, within 4 weeks of initiation and each clinic	Baseline and each clinic	Baseline, within 4 weeks of initiation and each clinic	Baseline and when needed
Rifampicin/Rifabutin	*	* For Rifabutin		
Azithromycin/Clarithromycin	*		*	*
Doxycycline/Minocycline	*			
Ethambutol	*	*		
Clofazimine	*		*	
Isoniazid	*			
Moxifloxacin/Ciprofloxacin	*		*	
Linezolid	* May need more frequent weekly bloods in the first month	*		
Co-trimoxazole	*			
Nebulised Amikacin	*			*

Further information

Diet

- It is important to ensure a well-balanced diet and good nutritional status during and after treatment completion
- Vitamin and Mineral Supplements: Most vitamin and mineral supplements can be taken safely to help supplement your diet, however, some do interact with several of the antibiotics used to treat NTM. Therefore, if you do take or plan to take any vitamin or mineral supplements, please check in advance with your NTM team that the preparation(s) are compatible with your treatment



Further information

Alcohol

- Alcohol consumption should be limited (or avoided where possible) while taking NTM treatment
- It is recommended that you do not exceed the national guidelines, which is that men and women are advised not to drink more than 14 units a week on a regular basis
- If you are prescribed bedaquiline, alcohol should be avoided

Smoking

- All patients who smoke are encouraged to stop. If you would like help to stop smoking, please speak to your clinical team or GP who can refer you to a local stop smoking programme

Vaccinations

- Please ensure you are up to date with your vaccinations where possible. These include:
 - Flu (influenza) annually
 - Pneumococcal once as an adult (or if repeat boosters have been recommended by your NTM team)
 - Covid-19 vaccinations (as per government guidelines)

Pregnancy and Breastfeeding

- Please make your NTM team aware if you are or plan to become pregnant or plan to breastfeed so they can advise appropriately about the medication you are taking

Myasthenia Gravis

- Please inform your NTM team if you have Myasthenia Gravis (a form of muscle weakness) as some medicines may worsen the Myasthenia Gravis symptoms



Further information

Travelling

- When you travel, plan to keep your antibiotics in your hand luggage in case of lost checked in luggage
- Plan to take extra medications in case of disruption or delays to your travel plans
- Always inform your NTM team of travel plans in advance to allow for clinic appointments and prescriptions to be organised as needed

Costs

If you are finding it difficult to pay for your medication, please speak to your NTM team to see if you qualify for an exemption from prescription costs

For patients who are not exempt, you can purchase a prepayment certificate (PPC) for 3 or 12 months. This works out that if you require 4 or more prescriptions in 3 months, or 12 or more prescriptions in 12 months, it may be cheaper to buy a PPC

There is also the option to pay in 10 monthly instalments if you buy a 12-month PPC

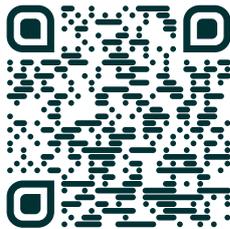
This can be accessed via: <https://www.gov.uk/get-a-ppc>



PLEASE NOTE:

We do hope the information provided in this leaflet is useful to both NTM patients and their wider care community, however we should highlight that this information is provided for guidance only. Please be aware that each person's NTM treatment journey may differ, with treatment usually tailored to the individual patient. However, if you are concerned that any information we have provided here is different to that which has been recommended to you, please speak to your NTM team

More specific information on the most widely prescribed NTM treatments (detailed in the appendices list below) can be found at the NTM Patient Care UK website at the following link: www.ntmpatientcare.uk/coping-with-the-medicines or by using the QR code shown here



Appendices

- Appendix 1:** The Big Three (Azithromycin or Clarithromycin, together with Rifampicin/Rifabutin and Ethambutol)
- Appendix 2:** Clofazamine
- Appendix 3:** Ciprofloxacin & Moxifloxacin
- Appendix 4:** Co-trimoxazole
- Appendix 5:** Doxycycline & Minocycline
- Appendix 6:** Isoniazid
- Appendix 7:** Linezolid
- Appendix 8:** Nebulised Amikacin (using the intravenous preparation as the inhaled drug)
- Appendix 9:** Nebulised Liposomal Amikacin (Arikayce®)

References

- British National Formulary. <https://bnf.nice.org.uk/> Accessed 2022
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- Summary of Product Characteristics (SmPC) Electronic Medicines Compendium. <https://www.medicines.org.uk/> Accessed 2022
- TB Drugs Monographs. <http://www.tbdrugmonographs.co.uk/> Accessed 2022
- Antibiotics - NHS (www.nhs.uk) Accessed 2022



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?

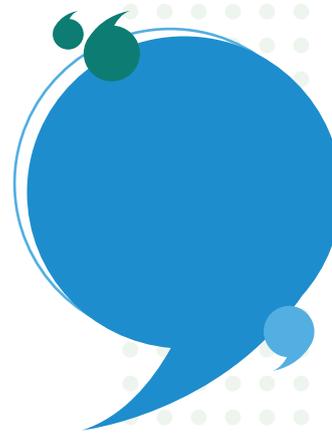
- Tablets can be taken with/without food
- Do not take indigestion remedies (for example Gaviscon® or Rennie®) 2 hours before or after you take azithromycin
- Azithromycin should be used with caution in patients with Myasthenia Gravis

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?

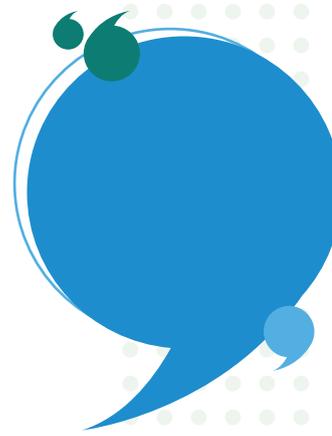
- Ethambutol may also cause side effects. You should make your NTM team aware if you experience any of the following side effects:
 - Any change in vision or visual disturbance (blurred vision or loss of intensity of bright colours)

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



Appendix 2

Clofazimine

How do I take?

- Take clofazimine with meals or with a glass of milk to maximise absorption and reduce stomach upset. Clofazimine capsules contain soybean oil therefore make your NTM team aware if you are allergic or sensitive to peanuts or soya

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

Is there anything I need to look out for?

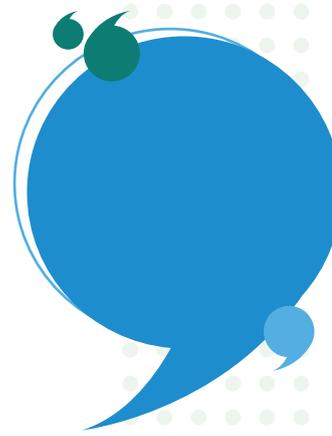
- Clofazimine may cause side effects. You should make your NTM team aware if you experience any of the following side effects:
 - Persistent abdominal pain and diarrhoea
 - Any change in eye colour (pigmentation), change in vision, dry eyes, burning or other eye irritation
 - Clofazimine may make your skin more sensitive to sunlight, causing a rash or severe sunburn. You should avoid strong sunlight and wear sunscreen
 - If you feel your heart beating in your chest or have an abnormal heartbeat

What other side effects might I experience?

- Other side effects include (but not limited to):
 - Gastrointestinal: abdominal pain, nausea, vomiting, diarrhoea and weight loss.
 - Pink to brownish-black skin discolouration (resembling sun-tanning) within 1–4 weeks; it disappears within 6–12 months after stopping treatment
 - Thickening, dry and/or itchy skin
 - Rash
 - Discolouration of soft contact lenses
 - May discolour urine red
- Please see patient information insert provided with medication for full list of side effects

How will I be monitored?

- 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



Appendix 3

Ciprofloxacin & Moxifloxacin

How do I take?

- Tablets can be taken with/without food
- Do not take with dairy products e.g. milk/yoghurt, indigestion remedies (for example Gaviscon® or Rennie®), or medicines containing iron, calcium, magnesium or zinc, 2 hours before or after you take this medicine
- Ciprofloxacin and moxifloxacin should be used with caution in patients with Myasthenia Gravis

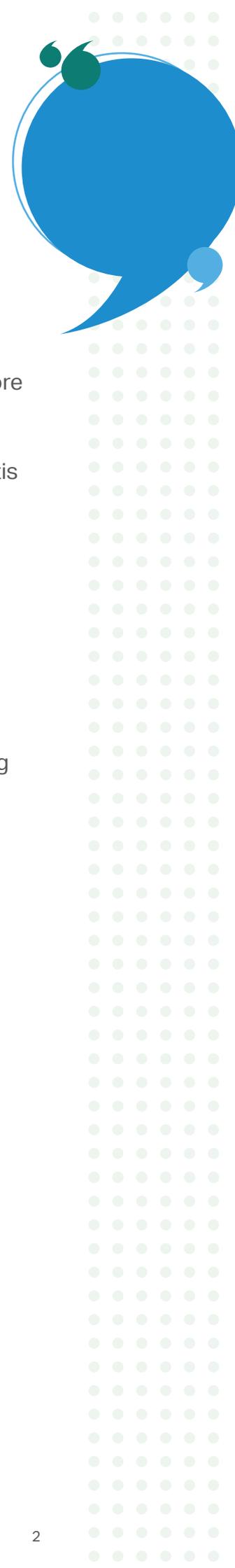
Will there be any interactions with any of my other medicines?

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 ciprofloxacin and moxifloxacin interact with include (but not limited to):

- Amiodarone
- Non-steroidal anti-inflammatory drugs (NSAIDs) e.g. ibuprofen, naproxen
- Theophylline
- Ondansetron
- Warfarin

Is there anything I need to look out for?

- Before taking ciprofloxacin/moxifloxacin, tell your clinician if you have experienced previous tendon damage as these medicines have been linked to very rare but serious side effects involving tendons, muscles, joints and nerves. In some patients, these effects may lead to long-lasting or permanent disability. Tell your clinician if you take corticosteroid medication (such as prednisolone or hydrocortisone) as the risk of tendon problems is greater
- Stop taking ciprofloxacin/moxifloxacin immediately and tell your clinician at the first signs of tendon swelling or tendon rupture, muscle pain, muscle weakness, joint pain, joint swelling or persistent pins and needles/numbness in any part of the body. These symptoms are rarely reported but damage or rupture may occur within 48 hours of treatment and several months after stopping treatment
- Before taking ciprofloxacin/moxifloxacin tell your clinician if you have epilepsy or previous history of convulsions (seizures). Avoid taking non-steroidal anti-inflammatory medicines (NSAIDs e.g. ibuprofen, naproxen, diclofenac) at the same time as this may also induce them



Is there anything I need to look out for? (continued)

- Rarely, events of aortic aneurysm and dissection may occur. Seek medical attention immediately if you develop sudden-onset severe abdominal, chest, or back pain. Inform your clinician if you have a history of vascular disease
- Ciprofloxacin/moxifloxacin has been associated with an increased risk of heart valve regurgitation (leaking from a valve that does not close all the way) therefore tell your clinician if you have congenital or pre-existing heart valve disease, a connective tissue disorder, or any risk factors including hypertension, Turner's syndrome, Behcet's disease, rheumatoid arthritis, infective endocarditis
- If you experience any of the following after starting ciprofloxacin/ moxifloxacin; a rapid onset of shortness of breath (especially when lying down flat in bed), swelling of the ankles, feet, or abdomen, or new-onset heart palpitations, seek immediate medical attention

What other side effects might I experience?

- Other side effects include (but not limited to):
 - Decreased appetite and/or altered taste
 - Diarrhoea, constipation, abdominal pain, flatulence (wind), nausea, vomiting
 - Headache
 - Rash
 - Fatigue
 - Joint/ muscle pain
- Please see patient information insert provided with medication for full list of side effects

How will I be monitored?

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.



Appendix 4

Co-trimoxazole

This is sometimes used as part of a combination regimen for *M. Abscessus* treatment.

How do I take?

- Take co-trimoxazole with food
- Co-trimoxazole is a combination of two antibiotics - sulfamethoxazole and trimethoprim, hence should be avoided if you have experienced adverse reactions to either of these. It should also be avoided if you are known to have acute porphyria or Glucose 6-phosphate dehydrogenase (G6PD) deficiency

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 medications you take and any over the counter medications.

- Medicines that co-trimoxazole interacts with include (but not limited to):
 - Ciclosporin
 - Warfarin
 - Phenytoin
 - Digoxin
 - Methotrexate
 - Some diuretics (water tablets)
 - Pyrimethamine

Is there anything I need to look out for?

- Co-trimoxazole may cause side effects. You should make your NTM team aware if you experience any of the following side effects:
 - Skin reactions such as rash with blisters, peeling skin with or without fever
 - Sore throat, fever, chills, mouth ulcers or cold sores
 - Unusual bruising or bleeding
 - Unusual tiredness or weakness
 - Unexpected worsening of cough and shortness of breath
 - Stomach pains with blood in your stools
 - Palpitations (feeling of having a fast heartbeat). This may suggest a rise in potassium

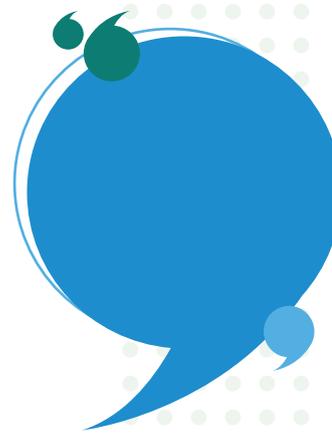


What other side effects might I experience?

- Other side effects include (but not limited to):
 - Headaches
 - Muscle cramps, weakness
 - Nausea
 - Co-trimoxazole may make your skin more sensitive to sunlight, causing a rash or severe sunburn. You should avoid strong sunlight and wear sunscreen
 - Ringing in your ears
- 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 full blood count, liver and kidney function before you start treatment and regularly throughout your treatment
- Monthly full blood count including folate levels should be monitored while on long courses of co-trimoxazole. You may be prescribed folic acid supplements to prevent or treat anaemia



Appendix 5

Doxycycline & Minocycline

These are sometimes used as part of a combination regimen for M. Abscessus treatment.

How do I take?

- Take with a full glass of water, during meals while sitting or standing. It is important not to lie down for at least 30 minutes after taking, to reduce the risk of throat irritation
- Do not take indigestion remedies (for example Gaviscon® or Rennie®) or medicines containing iron, calcium, magnesium or zinc, 2 hours before or after you take this medicine

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 doxycycline and minocycline interact with include (but not limited to):

- Warfarin
- Medicines for epilepsy, including phenytoin and carbamazepine
- Lithium
- Rifampicin

Is there anything I need to look out for?

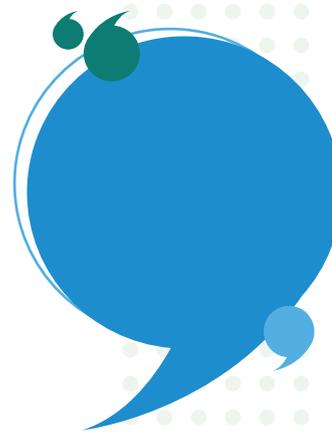
Your skin may be more sensitive to sunburn. Protect your skin from sunlight and wear sunscreen, even on a bright but cloudy day. Do not use sunbeds.

What other side effects might I experience?

- Other side effects include (but not limited to):
 - Swelling of eyelids, face or lips
 - Headache
 - Skin reaction/rash
 - Nausea, vomiting, diarrhoea
- Please see patient information insert provided with medication for full list of side effects

How will I be monitored?

No specific monitoring is required for doxycycline or minocycline; however, it is likely additional antibiotics you are prescribed will require monitoring.



Appendix 6

Isoniazid

How do I take?

Take isoniazid on an empty stomach, 30 minutes before a meal or at least 2 hours after.

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 medications you take and any over the counter medications.

- Medicines that isoniazid interacts with include (but not limited to):
 - Aminophylline/theophylline
 - Carbamazepine
 - Benzodiazepines
 - Disulfiram
 - Antifungal agents e.g. itraconazole
 - Ethambutol
 - Food rich in histamine and tyramine in excessive amounts e.g. cured meats, mature cheeses, wine, beer and certain fish like tuna, mackerel and salmon. Isoniazid affects the metabolism (break down) of tyramine and histamine; hence the build-up of histamine and tyramine can cause symptoms such as headaches, sweating, palpitations, flushing and low blood pressure. Dietary restrictions are not usually necessary unless symptoms are experienced

Is there anything I need to look out for?

- Isoniazid 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
 - Symptoms suggestive of peripheral neuropathy such as sensations of 'pins and needles' of extremities, some describe as burning sensations or numbness. Your NTM team will usually co-prescribe vitamin B6 (also known as pyridoxine) to reduce this side effect risk.
 - Mood or sleep disturbances

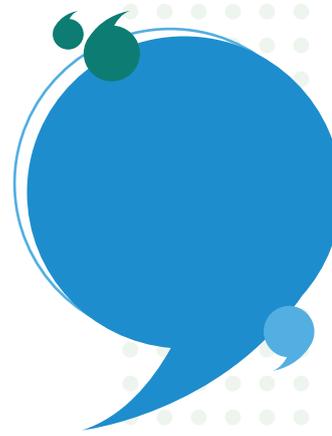


What other side effects might I experience?

- Other side effects include (but not limited to):
 - Diarrhoea, stomach upset, nausea
 - Loss of appetite
 - Constipation
 - Dry mouth
- 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 full blood count and liver function before you start treatment and regularly throughout your treatment
- Nerve conduction tests may be arranged if you report symptoms suggestive of peripheral neuropathy
- If you are diabetic, do keep up with regular blood glucose monitoring as isoniazid can affect blood sugar control



Appendix 7

Linezolid

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 medications you take and any over the counter medications.

- Medicines that linezolid interacts with include (but not limited to):
 - Monoamine oxidase inhibitors (e.g. phenelzine, isocarboxazid, selegiline, moclobemide). Linezolid is recommended not to be used within 2 weeks of taking them
 - Some antibiotics, e.g. clarithromycin or rifampicin, can increase or decrease the levels of linezolid. In this case, your clinical team may consider monitoring linezolid levels, and advise on dosage adjustment
 - Some antidepressants such as tricyclic antidepressants (e.g. amitriptyline) and selective serotonin reuptake inhibitors (SSRIs) (e.g. sertraline, citalopram, fluoxetine)
 - 5HT1 agonists (e.g. sumatriptan)
 - Avoid large amounts of tyramine-rich food (mature cheese, yeast extracts, alcohol – especially draught beers and wine, and fermented soya bean products like soy sauce) because they can cause blood pressure to become dangerously elevated

Is there anything I need to look out for?

- Linezolid may cause side effects. You should make your NTM team aware if you experience any of the following side effects:
 - Symptoms suggestive of peripheral neuropathy such as sensations of 'pins and needles' of extremities, some describe as burning sensations or numbness. Your NTM team may prescribe you a vitamin (pyridoxine - vitamin B6) to reduce this side effect risk
 - Any symptoms of visual impairment
 - Metallic or altered taste
 - If started on potential interacting drugs, report signs suggestive of serotonin syndrome which includes throbbing headache after eating or drinking, extreme high blood pressure, confusion, agitation and loss of usual muscle coordination
 - Abdominal pain

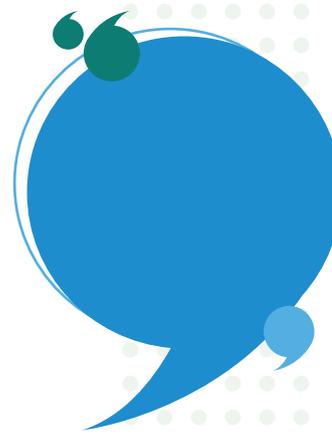


What other side effects might I experience?

- Other side effects include (but not limited to):
 - Diarrhoea, vomiting, nausea
 - Headaches
 - Oral/vaginal thrush
- 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 full blood count and liver function before you start treatment and regularly throughout your treatment
- Before taking linezolid 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 and at appropriate regular time points
- Nerve conduction tests may be arranged if you report symptoms suggestive of peripheral neuropathy



Appendix 8

Nebulised Amikacin (using the intravenous preparation as the inhaled drug)

How do I take?

- You will be taught how to administer amikacin solution via the nebuliser provided by your hospital
- Amikacin is suitable for nebulisation using a jet nebuliser and compressors. A filter will be needed. It is also compatible for use via a vibrating mesh nebuliser like the E-Flow nebuliser machine, but the time taken might be slower. It is not compatible for use with the I-Neb nebuliser machine
- The prescribed dose will be drawn up, usually diluted with sodium chloride 0.9% solution and added to your nebuliser for use
- Amikacin should not be used in people diagnosed with Myasthenia Gravis

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

There are currently no clinical drug interaction studies done with nebulised amikacin. Your NTM team will however still check all prescribed medications you take and any over the counter medications so as to be aware of any drugs that can potentially increase the risk of amikacin toxicity.

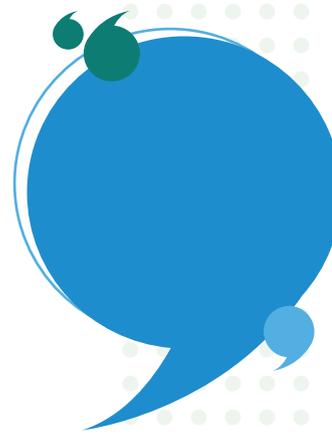
Is there anything I need to look out for?

- Amikacin may cause side effects. You should make your NTM team aware if you experience any of the following side effects:
 - Bronchoconstriction (chest tightness)
 - Cough
 - Sore throat and mouth
 - Hoarseness and/or altered voice
 - Tinnitus (ringing in your ears)
 - Hearing loss
 - Coughing up of fresh blood (haemoptysis)
- Inform your NTM team if you know you have a mitochondrial genetic mutation or are aware of any history of deafness on your mother's side, including deafness in mother, mother's siblings or mother's parents
- Please see patient information insert provided with medication for full lists of side effects



How will I be monitored?

- Before starting treatment, a test dose will be given to check that you can tolerate the nebulised amikacin. You may be asked to use a reliever medicine such as salbutamol before using nebulised amikacin to prevent bronchoconstriction (chest tightness)
- 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
- Your NTM team will also check your kidney function via blood tests regularly throughout treatment



Appendix 9

Nebulised Liposomal Amikacin (Arikayce®)

How do I take?

- You will be taught how to administer amikacin solution via the provided Lamira® Nebuliser System that includes the nebuliser handset, aerosol head and controller
- Liposomal amikacin (Arikayce) contains soy therefore make your NTM team aware if you are allergic or sensitive to soya
- Arikayce should not be used in people diagnosed with Myasthenia Gravis

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

There are currently no clinical drug interaction studies done with nebulised amikacin. Your NTM team will however still check all prescribed medications you take and any over the counter medications so as to be aware of any drugs that can potentially increase the risk of amikacin toxicity.

Is there anything I need to look out for?

- Amikacin may cause side effects. You should make your NTM team aware if you experience any of the following side effects:
 - Shortness of breath (chest tightness)
 - Sore throat and mouth
 - Hoarseness and/or altered voice
 - Haemoptysis (coughing up fresh blood)
 - Tinnitus (ringing in your ears)
 - Hearing loss
 - Muscle weakness
 - Balance disorder
- Inform your NTM team if you know you have a mitochondrial genetic mutation or are aware of any history of deafness on your mother's side, including deafness in mother, mother's siblings or mother's parents
- Please see patient information insert provided with medication for full lists of side effects



How will I be monitored?

- Before starting treatment, a test dose will be given to check that you can tolerate the nebulised amikacin. You may be asked to use a reliever medicine such as salbutamol before using nebulised amikacin to prevent bronchoconstriction (chest tightness)
- 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
- Your NTM team will also check your kidney function via blood tests regularly throughout treatment