

Treating Mycobacterial infections in Cats – Drugs, Doses & Costs

Approximate costs for 6 month Tx for a 4kg cat.

Details of reformulation laboratory addresses at the end of the document.

RIFAMPICIN

Capsules: @ 10-15*mg/kg po q24h = please contact BOVA laboratories directly who make a Rifampicin/Azithromycin capsule (see below).

*Advise 10mg/kg as higher tends to causes too many side effects.

Liquid 100mg/5ml: @10mg/kg = 40mg/cat = 2.0ml/cat/day: 120ml bottle lasts 60 days @ £15.00, so for 6 months x3 = **£51.00 + dispensing fee**

Rifampicin + Azithromycin combination from BOVA UK

Capsules 35mg rifampicin + 30mg azithromycin^α: 10-15mg/kg po q24h = 1 capsule/day @ £3.24: 1 pot of 100 capsules lasts 100 days so £323.75/3 months, so for 6 months = **£647.50 + dispensing fee**

^α Suitable for weight range 2.5-6kg; for a 4kg cat provides 8.75mg/kg rifampicin + 7.5mg/kg azithromycin. However, if the infection is severe and extensive, especially if involving bone, then consider giving 1 capsule 1 day, 2 the next, then 1 the following, 2 the next, repeated, while also giving NAC or SAME (see below).

Rifampicin is an essential part of treatment as it can kill non-replicating Mycobacteria; the only other drugs that can also do this are Isoniazid and Ethambutol.

Side effects are common (~30% of cases), including poor palatability (very common), hyporexia, nausea, vomiting, raised liver enzymes, jaundice, liver failure; skin discolouration (to red/orange), pruritus, skin oedema, erythema, hyperaesthesia; anaphylaxis (one 1 case). Chlorphenamine, topical hydrocortisone aceponate spray, SAME and/or N-Acetylcysteine (NAC) may help to reduce side effects, helping the cat to stay on Rifampicin (see below).

AZITHROMYCIN

Capsules 5-15[¥]mg/kg po q24h = please contact BOVA laboratories directly who make a Rifampicin/Azithromycin capsule (see below). Alternatively consider tablets which can be quartered, or liquid formulations.

Tablets 250mg : 5-15[¥]mg/kg po q24h = 40-60mg/day = ~1/6-1/4 tablet /day so ~ 1 tablet @ £2.00 lasts ~5 days so £5.00/10 days so £15.00/month: so for 6 months x6 = **£90.00 + dispensing fee**

Liquid 200mg/5ml: @5-15mg/kg po q24h = 40-60mg/day so ~1-1.5ml/day: 15ml bottle^β @£13.00: 1 bottle lasts 10-15 days so x1 month =£26.00-39.00 and x6 months = **£150.00-230.00 + dispensing fee**

[¥]For TB Tx use a higher dose if possible.

^βAfter reconstitution the liquid should be disposed of after 10 days. Perhaps divide the powder into 2 aliquots and reconstitute as needed?

Side effects are uncommon, and usually GI dysfunction.

PRADOFLOXACIN*

Tablets 15 & 60mg: 3-5^ymg/kg po q24h = 15mg i.e. 1 tablet/day = £1.34 so x30 = £40.20/month and x6 = **£241.00 + dispensing fee**

Liquid 25mg/ml: 5-7.5^ymg/kg po q24h = 20mg/day = 0.8ml/day: 15ml bottle so lasts 18 days @ £24.00 = £1.33/day x30 = £40/month x6 = **£240.00 + dispensing fee**

^y Note: the dose of liquid is higher than for the tablets.

Side effects are seen with high doses and long courses which cause neutropenia.

***2021 supply problems** – so use **Moxifloxacin** 50mg/cat po q24h; comes as 400mg tablets or 250ml bags (Avelox™) containing 400mg moxifloxacin in 0.8% saline.

Totals:

Rifampicin + azithromycin + pradofloxacin = ~£390-£840

Rifampicin-azithromycin (combined capsule) + pradofloxacin = ~£800-1000 (no further reformulation cost)

If using CLARITHROMYCIN instead of Azithromycin

Liquid 125mg/5ml: @7-15mg/kg q12h = 40mg/q12h so ~1.6ml/q12h: 70ml bottle@£17.00: 1 bottle lasts 21 days so x6 months = ~**£150.00**^a

^a Price to be checked with supplier

PROPHYLAXIS AGAINST TB

ISONIAZID for 6 months

Capsule 50mg: @ 10-20mg/kg q24h = 50mg/cat so 1 capsule a day @ £0.25/capsule, so for 4 weeks = £7.50, and for 6 months = **£45.00**^a

Liquid: available only on special order from the manufacturer.

Side effects – see below.

^a Price to be checked with supplier

SUPPORTIVE THERAPY

Cats may suffer side effects while on treatment for mycobacterial infections, especially with **RIFAMPICIN**. While they can be concerning to owners and vets, this drug is essential for optimising the outcome of treating cats with TB, and it is the only drug in our 'triple therapy' approach which has activity against non-replicating bacteria.

To help manage dermatological side effects such as pruritus, oedema and erythema we advise using **chlorphenamine** (2-4mg/cat po q8-12h). Focal pruritic lesions can also be managed with topical **hydrocortisone aceponate** spray.

Hepatotoxicity is another possible side effect of rifampicin, which may manifest clinically as hyporexia, nausea or vomiting, or may be identified with increased enzymes on serum biochemistry. **S-Adenosylmethionine (S-AdoMet)** (20mg/kg po q24h) is one hepato-protectant agent that is widely used in cases of drug-induced liver toxicity, as well as in cases of liver disease.

An intriguing alternative agent is **N-Acetylcysteine (NAC)** (600mg/cat po q12h); while pharmacological data is lacking for its use in cats, it is safe and well tolerated, although it has a bad taste and smell, hence giving whole capsules is usually preferred. Nausea and vomiting are potential side effects, and drooling occur when the capsule content is mixed with too little food. Since it can cause bronchial spasm, it should be used with caution in animals with asthma. While NAC is readily available, care should be taken when selecting a product, as some formulations are prohibitively large capsules that will not be tolerated by cats. We have currently been using Prowise NAC by Prowise Healthcare.

NAC helps to restore blood glutathione concentrations, restoring antioxidant capacity. It has been also been shown to reduce bacterial counts and reduce the severity of lesions. Restoration of antioxidant capacity helps reduce the toxic side effects of anti-TB drugs such as rifampicin and isoniazid, which is mediated by oxidant-driven damage to the liver. Short-term studies have also shown that it has some direct anti-mycobacterial activity and can reduce growth of bacteria both *in vitro* and *in vivo*.

ISONIAZID is also hepatotoxic and can cause neurological signs, including peripheral neuropathy and seizures. **Pyridoxine hydrochloride** is advised in humans showing neurological signs of isoniazid neurotoxicity; where seizures occur, they will only respond to pyridoxine supplementation. It has also been shown to reduce side effects in people when given prophylactically. While not trialled in cats, it is very safe and supplementation at 5mg/cat po q24h for cats weighing < 5kg, or 10mg/cat po q24h for those ≥5kg can be considered. A pack of 28 costs **£40**; please contact the pharmacy @ DickVetPharmacy@ed.ac.uk for more information.

SECOND LINE TREATMENTS FOR FELINE TB

Where resistance occurs, initially replace one of the drugs with **ETHAMBUTOL**. Ideally, this would be either pradofloxacin or azithromycin, but if **RIFAMPICIN TOXICITY** is a problem, then replace this drug. In very severe cases, potentially consider a **RIFAMPICIN-ISONIAZID-ETHAMBUTOL** combination, although toxicity can be severe (Gunn-Moore *et al.*, 2010). If necessary, ethambutol can be substituted with dihydrostreptomycin or pyrazinamide. However, *M. bovis* is naturally resistant to pyrazinamide. Rifampicin and ethambutol or isoniazid are less toxic than dihydrostreptomycin and are consequently more appropriate choices – that said, few cats have been treated with these combinations and side effects appear common.

Tx to TB & NAC?	N-Acetylcysteine (NAC)	≥100 PO	12	Nausea, vomiting, allergic skin reactions
2 nd line tx for TB	Isoniazid ^{bc}	10-20 PO	24	Hepatotoxicity, peripheral neuritis, seizures, acute renal failure; Vit B6 (anti-neuropathy), SAME/milk thistle can help. Possible, stay off fish.
Prophylaxis for TB		10 PO	24	As above.
2 nd line tx for TB	Ethambutol ^{bc}	10-25 PO	24	Optic neuritis (stop Tx if any signs of potential visual difficulties), weakness, polyneuropathy; Vits B and K, and SAME/milk thistle can help.
2 nd line tx for TB	Pyrazinamide ^{bce}	15-40 PO	24	Hepatotoxicity, GI signs; SAME/milk thistle can help.
2 nd line tx for TB	Dihydro - streptomycin ^{bc}	15 IM	24	Ototoxicity
?	Selamectin, moxidectin, ivermectin	?	?	?

^bThese drugs are not licensed for use in pets.

^cThese drugs may cause potentially serious side effects e.g. hepatotoxicity or nephrotoxicity. It is advisable to monitor these cats closely, and check routine haematology and serum biochemistry before starting treatment and two weeks after starting treatment, and then if there is any change in the cat's demeanour.

^eNot effective against *M. bovis* infection.

ISONIAZID is used in the prevention and treatment of tuberculosis. Care with liver and renal cases.

So, for a 4kg cat:

Capsule 50mg: @ 10-20mg/kg q24h = 50mg/cat so 1 capsule a day @ £0.25/capsule, so for 4 weeks = £7.50, and for 6 months = **£45.00**

Liquid 25mg/ml: @10-20mg/kg = 50mg/cat = 2.0ml/cat/day: 2ml ampules @ £25.00, so for 4 weeks = £750, and for 6 months = **£4500.00**

To reduce possible neurological side effects consider adding in **pyridoxine** (B₆) – however, no feline-specific dose is known, and despite this being a water-soluble B-vitamin excessive doses in dogs (e.g., 444 mg/kg) have been shown to cause nerve damage, rather than prevent it. A sensible dose appears to be 20-30mg/Cat PO q24h (this is based on 50mg per dog PO q8hr for dogs during chemotherapy doxorubicin, or 25mg per dog PO q24hr while on penicillamine chelation therapy).

PYRAZINAMIDE is largely bacteriostatic, but can be bactericidal on actively replicating tuberculosis bacteria. Has no effect on *M. bovis*. Care with liver and renal cases.

So, for a 4kg cat:

Tablets 500mg: @ 15-40mg/kg q24h = 80-125mg/cat so 1/6-1/4 tablet a day @ £1/tablet, so for 4 weeks = £8, and for 6 months = **£48.00**

ETHAMBUTOL is bacteriostatic. Care with liver and renal cases.

So, for a 4kg cat:

Tablets 100mg: @ 10-25mg/kg q24h = 40-100mg/cat so 0.5-1 tablet a day @ £0.22/tablet, so for 4 weeks = £6.70, and for 6 months = **£40.00**

Please be aware that these prices are an approximate on the date of writing this document and can change significantly. Check the prices with your supplier before making estimates to your clients.

*For compounding, please contact **NOVA Laboratories** @ sales@novalabs.co.uk or **BOVA UK** @ orders@bova.co.uk. For help with sourcing rifampicin, azithromycin and pradofloxacin contact our pharmacy team @ DickVetPharmacy@ed.ac.uk*

Doses updated April 2024; costs last updated January 2022