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British Association for Sexual Health and HIV (BASHH) United Kingdom national guideline on the management of *Trichomonas vaginalis* 2021

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Abstract

The main objective of this guideline is to assist practitioners in managing individuals diagnosed with *Trichomonas vaginalis* (TV). It offers recommendations on the diagnostic tests, treatment regimens and health promotion principles needed for the effective management of TV. It covers the management of the initial presentation, as well as how to prevent transmission and future re-infection. It is aimed primarily at people aged 16 years or older presenting to health care professionals, working in departments offering specialist care in sexually transmitted infection (STI) management within the United Kingdom. However, the principles of the recommendations are applicable across all levels of STI care providers (N.B. non-specialist services may need to develop, where appropriate, local care pathways).

Keywords

Protozoal disease, trichomoniasis (trichomonas vaginalis)

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New in the 2021 guidelines

Updated sections:

- when it is appropriate to screen asymptomatic women for *Trichomonas vaginalis*
- diagnosis, incorporating information on nucleic acid amplification tests
- management of infection, including those refractory to first line treatment

Introduction and Methodology

Objectives

The main objective of this guideline is to assist practitioners in managing individuals diagnosed with *Trichomonas vaginalis (TV)*. It offers recommendations on the diagnostic tests, treatment regimens and health promotion principles needed for the effective management of TV. It covers the management of the initial presentation, as well as how to prevent transmission and future re-infection.

It is aimed primarily at people aged 16 years or older (see the BASHH guideline for children and young people for those under 16 https://www.bashhguidelines.org/media/1262/children-and-yp-2021.pdf) presenting to health care professionals, working in departments offering specialist care in sexually transmitted infection (STI) management within the United Kingdom. However, the principles of the recommendations are applicable across all levels of STI care providers (N.B. non-specialist services may need to develop, where appropriate, local care pathways).

Search strategy:

This guideline was produced according to specifications set out in the BASHH Framework for guideline

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development and assessment' (2015, updated 2019) accessed at https://www.bashhguidelines.org/media/1229/2015-guidelines-frameworkamended-dec-2019.pdf. It has been updated by reviewing the previous TV guideline (2014) and medical literature since its publication using abstracts and articles in the English language with relevance for "human" infection. Where there was a paucity of randomised control trials and high quality evidence, expert judgement was considered. Search terms: Trichomonas vaginalis; Trichomonas infections (used for trichomoniasis) and expanded to include Trichomonas vaginitis. Sources: OVID; Medline; PubMed; National Institute for Health and Clinical Excellence; NHS evidence; Cochrane Library and guidelines produced by: the International Union against STIs, BASHH and the US Centres for Disease Control (CDC). For all databases, all abstracts were retrieved and then those with possible relevance were selected.

NHS Evidence has accredited the process used by the British Association for Sexual Health & HIV (BASHH) to produce UK national guidelines. Accreditation is valid until January 2026 and is retrospectively applicable to guidance produced using the processes described in the BASHH Framework for Guideline Development and Assessment dated from September 2010, and all subsequent versions onwards. More information on accreditation can be viewed at www.evidence.nhs.uk

A patient representative from the BASHH Public Panel was involved in all stages of guideline and PIL development.

Equality impact assessment

An assessment of the guideline and its recommendations was undertaken to ensure the principles of equality and diversity were adhered to.

Piloting and feedback

The draft guideline was appraised with the AGREE instrument by members of the BASHH Clinical Effectiveness Group. It was posted on the BASHH website for a public consultation period of two months and then piloted in three English sexual health clinics.

Aetiology

Causative organism

Trichomonas vaginalis is a flagellated protozoon. In women, the organism is found in the vagina, urethra and paraurethral glands. Urethral infection is present in 90% of infected women, although the urethra is the sole site of infection in fewer than 5% of cases. In men, infection is usually of the urethra, although trichomonads have been isolated from the subpreputial sac and lesions of the penis.

Please note that TV is not a known issue for people with a neovagina following gender reassignment surgery (N.B. when the guideline refers to a vagina, it is not referring to a neovagina). No adequate quality data on TV infection in transgender men or women were available for inclusion in this guideline and the words 'men', 'women', 'male' and 'female' refer to cisgender individuals unless otherwise stated.

Transmission

In adults, transmission is almost exclusively through sexual intercourse. Due to site specificity, infection can only follow intravaginal or intraurethral inoculation of the organism.

Clinical Features

Females[1–3]

Symptoms

- 10–50% are asymptomatic.
- The commonest symptoms include vaginal discharge, vulval itching, dysuria, or offensive odour, but these are not specific for TV.
- Occasionally the presenting complaint is of lower abdominal discomfort or vulval ulceration.

Signs

- Vaginal discharge is present in up to 70% - varying in consistency from thin and scanty to profuse and thick; the classical frothy yellow discharge occurs in 10–30% of women.
- Vulvitis and vaginitis are associated with trichomoniasis.
- Approximately 2% of patients will have strawberry cervix appearance to the naked eye. Higher rates are seen on colposcopic examination.
- 5–15% will have no abnormalities on examination.

Males[4–6]

Symptoms

- 15–50% diagnosed with TV are asymptomatic and men usually present as the sexual partners of infected women.
- The commonest symptomatic presentation is with urethral discharge and/or dysuria.
- Other symptoms include urethral irritation and urinary frequency.
- Rarely, the patient may complain of a copious purulent urethral discharge, or symptoms of complications such as prostatitis.

Signs

- Urethral discharge (20–60%) - usually small or moderate amounts only.

- No signs, even in the presence of symptoms suggesting urethritis: one recent prospective study of infected TV contacts found 77.3% were asymptomatic.
- Rarely, balanoposthitis.

Complications

There is increasing evidence that TV infection can have a detrimental outcome on pregnancy and is associated with preterm delivery and low birth weight .[7–9]However, further research is needed to confirm these associations and to prove that the association is causal. TV infection at delivery may predispose to maternal postpartum sepsis.[10]

Some studies have shown treatment of TV infection in pregnancy to have a negative impact on the pregnancy[11–13] but others have shown no association between treatment for TV and pre-term delivery or low birth weight.[14] Screening of asymptomatic individuals for TV infection in pregnancy is therefore not currently recommended. (Grade 1B)

Multiple reports support an epidemiological association between HIV and trichomoniasis. There is evidence that trichomonas infection may enhance HIV transmission[15–18] and there may be an increased risk of TV infection in those that are HIV positive.[19]

Diagnosis

Testing for TV should be undertaken in patients complaining of vaginal discharge or vulvitis, or found to have evidence of vulvitis, and/or vaginitis on examination (Grade 1A). Testing is recommended for TV contacts and should be considered in those with persistent penile urethritis (Grade 2B).

Screening of asymptomatic women may be appropriate in settings such as sexual health services in geographical areas of high prevalence and/or in women with associated risk factors (Grade 2B). A study of national STI data, between 2009–2011 in England, found rates of TV were highest in London and the West Midlands. In all patients, TV was significantly associated with older age, non-white ethnicity (particularly black Caribbean and black 'other' ethnic groups), and current gonorrhoea or chlamydia infection in women.[20,21]

Sites sampled

Females [1,2,22,23]

- If the patient is symptomatic and microscopy is available, then a swab taken from the posterior fornix of the vagina at the time of speculum examination is recommended (Grade 1A).
- Self-administered vaginal swabs are likely to give equivalent results to clinician-taken swabs when using nucleic acid amplification tests nucleic acid amplification tests (NAATs) and are the test of choice if microscopy is not being performed (Grade 1A).[24,25]
- Urine testing has been evaluated with some NAATs and has shown acceptable sensitivity in the range 88–90%.

Males[26,27]

- Clinician taken urethral swabs or self-taken penile-meatal swabs will diagnose approximately 80% cases using NAATs and is the recommended sample (Grade 1A).
- Urine is currently approved for only one NAAT.

Laboratory investigations

Microscopy. Microscopy remains a simple and rapid test to perfom within any clinic that has access to a microscope and a microscopist (Grade 1A). The specificity with trained personnel is high, although the sensitivity is reported to be as low as 40–60% in vaginal samples [22,23,28–32] in some studies and lower in men,[32,33] and so a negative result should be interpreted with caution.

Detection of motile trichomonads by light-field microscopy can be achieved by collection of vaginal discharge using a swab or loop, which is then mixed with a small drop of saline on a glass slide and a coverslip placed on top. The wet preparation should be read within 10 minutes of collection, as the trichomonads will quickly lose motility and be more difficult to identify.[34] The slide should be scanned, firstly at low magnification (×100), and then at a higher magnification (×400) to confirm the morphology of any trichomonads and to visualise the flagella. Microscopy as a diagnostic aid for TV has the advantage that it can be performed near to the patient and in a clinic setting. The sensitivity is highest in patients presenting with vaginal discharge and a visualisation of motile trichomonads in these patients indicates the presence of infection.

Detection of TV by staining dead organisms with acridine orange can give a higher sensitivity than wet microscopy[35,36] but is not widely used.

Point of care tests. Point of care tests for the detection of TV have been described[32,33,37–41] of which the OSOM® Trichomonas Rapid Test (Sekisui Diagnostics, USA) has demonstrated a high sensitivity (80–94%) and specificity (>95%) (depending on the comparator).[32,33,37–39,42] This test requires no instrumentation, provides a result within 30 minutes and is a suitable alternative to culture or molecular testing. Although these tests are more sensitive than those requiring vaginal wet preparation, false positive might occur, especially in populations with a low prevalence of disease. Consideration should be given to confirming positive results in that situation. Whilst local validation may recommend use

of the OSOM® assay for specimen types other than vaginal swabs this assay should not be used to test urine from male patients, as low sensitivity (38%) and specificity (83%) has been demonstrated when compared with a NAAT.[38]

Molecular detection. Nucleic acid amplification tests offer the highest sensitivity for the detection of TV. They should be the test of choice where resources allow and are the current 'gold standard' (Grade 1A). US Federal Drug Agency (FDA) approved commercial assays are available which can detect TV nucleic material in vaginal or endocervical swabs and in urine samples from women with sensitivities of 88%–100% and specificities of 95–100%, depending on the specimen and reference standard.[40,41,43–45] The site sampled should be that recommended by the manufacturer of the NAAT kit in use by the local laboratory.

Detection of TV in specimens from male patients (urine, penile-meatal and urethral swabs) is currently outside of most commercial NAAT assay scope therefore local validation would be necessary. However, sensitivities of 90–100% and specificities of >99% have been reported depending on the specimen and reference standard.[41,44,46] In addition to offering superior detection of the organism, use of NAAT assays may be more cost-effective than other diagnostic methods.[47]

Culture. Historically considered 'the gold standard', culture has proven less sensitive than molecular testing. It has a higher sensitivity (88%) compared to microscopy[28,30,31,33] and can detect TV in men.[32,33] A commercially available culture system (InPouch TV; BioMed Diagnostics, USA), offers many advantages over previous culture media such as Diamond's medium.[48–51] Once inoculated the pouches can be transferred to the laboratory for incubation and the entire pouch read microscopically each day for 5 days, negating the need to prepare wet preparations every day that only sample a portion of the culture medium.

Management

General Advice

Sexual partner(s) should be treated simultaneously (Grade 1B). Patients should be advised to avoid sexual intercourse for at least 1 week and until they and their partner(s) have completed treatment and follow-up**.**

Patients should be given a detailed explanation of their condition with particular emphasis on the long-term implications for the health of themselves and their partner(s). This should be reinforced by giving them clear and accurate written information. (See www.bashh.org/guidelines for a TV patient information leaflet).

Further Investigations

Screening for coexistent sexually transmitted infections should be undertaken in anyone diagnosed with TV (Grade 1A).

Treatment

Systemic antibiotic therapy with nitroimidazoles is required to effect a permanent cure due to the high frequency of infection of the urethra and paraurethral glands in addition to the vagina.[52] A meta-analysis of single-dose oral metronidazole compared with multidose oral metronidazole for the treatment of TV in women found an increased risk of treatment failure with single dose treatment (RR 1.87 (95% Confidence Intervals 1.23–2.82; $p = < .01$).[53] A subsequent RCT of metronidazole 500 mg twice daily for 7 days versus metronidazole 2 g single dose for the treatment of TV in women reported a positive test-of-cure in 11% of the 7-days dose group versus 19% in the single-dose group (relative risk 0·55, 95% CI 0·34–0·70; $p = < ·0001$).[54]

Intravaginal metronidazole gel treatment does not reach therapeutic levels in the urethra, periurethral and perivaginal glands. A small study comparing 0.75% metronidazole vaginal gel twice daily for 7 days with 7 days oral metronidazole reported 44% parasitological cure rate with metronidazole vaginal gel compared with 100% with oral metronidazole.[55] This cure rate is unacceptably low so intravaginal metronidazole alone should not be used except in circumstances where oral nitroimidazoles are contraindicated. There is a spontaneous cure rate in the order of 20–25%.

Recommended regimen (Grade 1A)

- Metronidazole 400–500 mg twice daily for 7 days

While it is recognised that 400 mg is the standard dose of metronidazole used in the UK, most of the recent evidence is based on 500 mg and this dose is also listed in the British National Formulary. It is therefore recommended to use 500 mg twice daily for 7 days where 500 mg tablets are available. 400 mg twice daily for 7 days is an acceptable alternative. The combination of alcohol and metronidazole has been said to cause disulfiram type reactions in about 10% of individuals (metronidazole SmPC) and should be avoided for 48 hours post-last dose.

Alternative regimens

Metronidazole 2 g orally in a single dose (Grade 2A)

Pregnancy and breast feeding

400 mg oral metronidazole twice daily for 7 days in preference to the use of short high-dose regimens which are not recommended during pregnancy (Grade 1A).

Meta-analyses have concluded that there is no evidence of teratogenicity from the use of metronidazole during the first trimester of pregnancy.[56–59] Although there is currently no signal that metronidazole is a human teratogen, general prescribing advice for pregnant women is to use the lowest effective dose of a medicine to reduce the risk of possible teratogenic effects above a threshold dose specific to the exposure, although this is likely to be influenced by inter-individual variation in drug metabolism. No studies were located which compare/comment on feto-maternal outcomes for women treated with a single high dose of metronidazole versus a course of lower doses, and no threshold dose for metronidazole teratogenicity has been demonstrated. In the absence of data on the use of single high stat doses in pregnancy and the theoretical risk of a threshold dose above which teratogenicity may occur in humans, single dose regimens are not recommended.

Metronidazole can be used in all stages of pregnancy and during breast feeding. Metronidazole is likely to cure trichomoniasis, but it is not known whether treatment will have any effect on pregnancy outcomes.[56] Symptomatic patients should be treated at diagnosis, although some clinicians have preferred to defer treatment until the second trimester. The British National Formulary advises against high dose regimens in pregnancy. Metronidazole enters breast milk and may affect its taste. The manufacturers recommend avoiding high doses if breastfeeding.

Tinidazole is FDA pregnancy category C (animal studies have demonstrated an adverse event, and no adequate, well-controlled studies in pregnant women have been conducted), and its safety in pregnant women has not been well-evaluated. The manufacturer states that the use of tinidazole in the first trimester is contraindicated.

People living with HIV (Grade 1A)

The recommended treatment regimen should also be used in those living with HIV. A randomized clinical trial demonstrated that 500 mg of metronidazole twice daily for 7 days was superior to a 2 g single oral dose of metronidazole for trichomoniasis among women diagnosed with HIV.[60]

Allergy

There is no effective alternative to 5-nitroimidazole compounds. Hypersensitivity reactions have been reported in patients using metronidazole and tinidazole and it is unknown whether there is cross reactivity between the two agents. It is important to take an accurate history to establish that a true allergy exists. Adverse reactions which may occur include anaphylaxis, skin rashes, pustular eruptions, pruritis, flushing, urticaria, and fever.[61] In cases of true allergy, desensitization to metronidazole has been described in case reports and could be considered (see Appendix 1).[62,63] Helms et al.[64] reported data collected from clinicians who consulted the US CDC on 59 patients with suspected hypersensitivity to metronidazole. All 15 patients who underwent metronidazole desensitization and were treated with metronidazole had their infections eradicated. Alternative treatment regimens were used for 17 study subjects with a cure rate of only 29.4%.

Treatment failure

Persistent or recurrent TV is due to inadequate therapy, re-infection, or resistance. Therefore check:

- Compliance and exclude vomiting of metronidazole
- Sexual history for possibility of re-infection and ask if partner(s) have been treated

Development of resistance against metronidazole and other nitroimidazoles can be due to aerobic and anaerobic resistance. In the USA, it is estimated that 5% of clinical isolates of TV exhibit some degree of metronidazole resistance, predominantly low level.[66] Clinical and microbiological cure rates were higher in women with previous treatment failure who were treated in accordance with a treatment protocol utilising the results of a resistance test.[67] Clinical isolates resistant to metronidazole can be resistant to tinidazole but usually with significantly lower minimal lethal concentrations to tinidazole.[68,69] In vitro resistance may not predict clinical response to treatment[68] which may be relative rather than absolute and may be overcome by high dose metronidazole or tinidazole therapy. Tinidazole has a longer serum half-life,[70] good tissue penetration, a better side-effect profile and lower levels of resistance than metronidazole.[66,69]

Treatment protocol for non-response to standard TV therapy (having excluded re-infection and non-adherence)

1. Repeat course of 7-days standard therapy

- Metronidazole 400–500 mg twice daily for 7 days (Grade 1B) - in those who failed to respond to a first course of treatment, 40% responded to a repeat course of standard treatment.[71]

For patients failing this second regimen:

2. Higher dose course of nitroimidazole (Grade 2B)

- Metronidazole 2 g daily for 5–7 days[67] or
- Metronidazole 800 mg three times daily for 7 days[71] - in those who failed to respond to a second course of treatment, 70% responded to a higher dose course of metronidazole.[72]

Please also refer to appendix 2

Availability

For those failing this regimen, it is now difficult to make recommendations. Resistance testing is not available in the UK and the manufacture of tinidazole has been discontinued since March 2021. If tinidazole is able to be sourced, high dose tinidazole regimens are recommended. If tinidazole is not available expert opinion recommends using very high dose courses of metronidazole in combination with vaginal treatment. With the exception of metronidazole all the medicines suggested for use in treatment failure are unlicensed products that can be difficult to source and expensive. The pharmacy purchasing department may be able to source some of these products from specialist manufacturers or importers but consider lead times.

3. Very high dose course of nitroimidazole and very high dose course of nitroimidazole with intravaginal nitroimidazole or paromomycin cream (Grade 2D)

- Metronidazole 2 g twice daily for 14 days with metronidazole vaginal gel 5 g twice daily for 14 days.

There are reports of peripheral neuropathy with metronidazole which suggest that a cumulative dose of >42 g is a risk factor.[72] Caution should also be used with very high doses in women who weigh less than 53 kg as the UK toxbase suggests anyone who has ingested more than 150 mg/kg/24 h should be referred for medical assessment.

- A case series using tinidazole 1g three times daily plus intravaginal tinidazole 500 mg twice daily for 14 days in women (56 g total dose) with moderately or highly metronidazole resistant TV reported cure in 9/11 (82%).[67].
- A case series of women with TV unresponsive to higher dose course of metronidazole, used tinidazole 500 mg four times daily plus intravaginal tinidazole 500 mg twice daily for 14 days (42 g total dose) or tinidazole 1g three times daily plus intravaginal tinidazole 500 mg three times daily for 14 days (63 g total dose). TV cure was reported in 22/24 (92%).[73].
- A case series of women who had failed to respond to at least two courses of standard therapy used tinidazole 2 g twice daily for 14 days (56 g total dose) and reported TV cure in 9/11 (90%).[74].
- There have been four published cases of women who had failed multiple treatments for TV who were cured with a combination of very high dose tinidazole plus intravaginal paromomycin cream daily for 14 days.[73,75,76] Two of the four had received the individual components separately but with treatment failure of each. However, the infections cleared when given in combination suggesting possible additive or synergistic effect between the two drugs.

If very high dose tinidazole plus intravaginal cream has been unsuccessful or are unavailable, it is difficult to recommend further treatments at present. These cases can be a therapeutic challenge as treatment options are limited with little evidence to support them. Options include:

- The largest published case series of alternative treatments have been with intravaginal paromomycin alone with 56–58% cure rates reported.[73,77].
- Boric acid pessaries have been suggested as an alternative but a literature review found only four cases of successful treatment using 600 mg alternate nights to 600 mg two times daily for between 1–5 months.[78].
- There is one case report of clearance of TV with dequalinium chloride 10 mg vaginal tablets for 18 weeks. Dequalinium chloride is a licensed product for the treatment of bacterial vaginosis in Europe.

Secnidazole is a new second-generation 5-nitroimidazole product with a broad spectrum of activity against anaerobic bacteria and a longer half-life than metronidazole, making it suitable for single-dose therapy, and therefore potentially offers an advantage over multiple-dose metronidazole regimes. This has shown promise for treatment of TV in phase 3 trials as a single 2g dose, in 64 adult females with trichomoniasis of whom 59 (92.2%) having a negative TV culture 6–12 days after treatment, and has US FDA approval for TV treatment at this dose[79,80]

Follow up

Tests of cure are only recommended if the patient remains symptomatic following treatment, or if symptoms recur (Grade 2C). The optimum timing of NAAT for TV test of cure is four weeks after the start of treatment.[81]

Management of sexual partners

Services should have appropriately trained staff in partner notification (PN) skills to improve outcomes. All patients identified with TV should have PN discussed at the time of diagnosis by a trained healthcare professional. The method of PN for each partner/contact identified should be documented, as should PN outcomes.

Current partners and any partner(s) within the 4 weeks prior to presentation should be offered, and encouraged to take up, full STI screening, including HIV testing and treated for TV irrespective of the results of investigations.[82–84] (See www.bashh.org/guidelines for partner notification statement).

In a contact of TV found to have urethritis on screening, it is reasonable to treat initially for TV and repeat the urethral smear before treating additionally for non-gonococcal urethritis.[85]

There are no data available to guide treatment of the male partners of women with nitroimidazole treatment failure. Expert opinion suggests male partners should be evaluated and treated with metronidazole 400–500 mg twice daily for 7 days (Grade 2C). There has been one report of a male partner requiring very high dose tinidazole therapy before re-infection was prevented.[74]

Organisational and financial considerations

The first line treatments are cheap and easy to administer. For allergy and resistant case management the relative costs, time to obtain drug and access to safe desensitisation facilities will incur additional costs and resources, or appropriate referral.

Auditable Outcome Measures

- All patients diagnosed with TV infection should receive first line treatment with metronidazole 400 mg twice daily for at least 7 days, or have a documented reason for exception (i.e. allergy). Performance standard: 97%
- Individuals should be offered information (written or digital) about their diagnosis and treatment. Performance standard: 97%
- Individuals diagnosed with TV infection should be tested for all sexually transmitted infections including HIV (unless previously diagnosed with HIV). Performance standard 97%

Recommendations for further research

- Utility of secnidazole in cases of TV where metronidazole has failed
- Most effective dose of secnidazole – single dose versus multidose

Qualifying statement

The recommendations in this guideline may not be appropriate for use in all clinical situations. Decisions to follow these recommendations must be based on the professional judgement of the clinician and consideration of individual patient circumstances and available resources. All possible care has been undertaken to ensure the publication of the correct dosage of medication and route of administration. However, it remains the responsibility of the prescribing physician to ensure the accuracy and appropriateness of the medication they prescribe.

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Declarations of of conflicting interests

All members of the guideline writing committee completed the BASHH conflict of interest declaration at the time the guideline's final draft was submitted to the CEG. No authors have any conflicts of interest to declare and the content of the guideline is not attributed to any organisation they are associated with.

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Statement of editorial independence

This guideline was commissioned, edited and endorsed by the BASHH CEG without external funding being sought or obtained.

Membership of the clinical effectiveness group

Current membership of the BASHH Clinical effectiveness group is available at https://www.bashh.org/bashh-groups/clinical-effectiveness-group/

Review arrangements

An author group will be invited by the BASHH CEG to review and revise the guideline in 2026 using the BASHH framework for guideline development. However, addenda may be issued sooner than 2026, particularly if relevant new data are available relating to testing or treatment options.

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Appendix 1

Metronidazole de-sensitisation

Patients must be monitored carefully throughout the desensitisation regimen, and local policies and procedures for desensitisation should be followed, which may include the use of day care facilities as well as admission, ideally under an allergy specialist where available. It is important

Metronidazole desensitisation – oral desensitisation protocol (66 - adapted)

Step	Time (hr)	Dose (mg)	Metronidazole concentration*	Volume (mL)
1	0	0.0025	0.025 mg/mL	0.1
2	1	0.025	0.025 mg/mL	1
3	2	0.25	0.25 mg/mL	1
4	3	2.5	2.5 mg/mL	1
5	4	25	2.5 mg/mL	10
6	5	200	200 mg	1 × 200 mg tablet
7	6	400	400 mg	1 × 400 mg tablet
8	7	800	800 mg	2 × 400 mg tablet
9	8	1000	1 g	2 × 400 mg and 1 × 200 mg tablet

to prescribe chlorphenamine, hydrocortisone and adrenaline for use if needed. Some sources recommend commencing an antihistamine regimen 1 day prior to regimen and up to completion of desensitisation programme e.g. cetirizine or chlorphenamine, but this decision remains controversial. Based on desensitisation protocols for other antibacterial agents,[65] the desensitization regimen should be terminated if a severe reaction (anaphylaxis) occurs at any step. If the reaction is minor and subsides with antihistamine use then advance to the next step; if the reaction worsens, the desensitization regimen should be terminated. If the patient does not experience any adverse reactions during the desensitisation process, the patient should be monitored for 4 hours; if the patient does experience a reaction, the patient should be monitored for a minimum of 24 h.

Extemporaneous preparation of metronidazole liquid dilutions for use in the desensitisation regimen

In order to achieve the correct concentrations of metronidazole suspension for the desensitisation regimen above the method below may be used. This should be extemporaneously prepared in a pharmacy using local procedures. After dilution of metronidazole suspension with syrup BP the product should be discarded after 1 day.[1]

Metronidazole 2.5 mg/mL (concentration 1)

1. Take 1 mL of the 200 mg/5 mL metronidazole liquid (40 mg/mL).
2. Make this up to 16 mL with syrup BP to give a 2.5 mg/mL concentration.

Metronidazole 0.25 mg/mL (concentration 2)

1. Take 1 mL of concentration 1 (2.5 mg/mL) liquid and make up to 10 mL with syrup BP to give 0.25 mg/mL.

Metronidazole 0.025 mg/mL (concentration 3)

1. Take concentration 2 (0.25 mg/mL) and make up to 10 mL with syrup BP to make 0.025 mg/mL.

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Appendix 2

Treatment protocol for non-response to standard TV therapy

N.B. This protocol assumes that re-infection and non-adherence to prior therapy have been excluded