DOI: 10.1111/jdv.17972 JEADV

GUIDELINE

2021 European guideline on the management of *Mycoplasma genitalium* infections

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Abstract

Mycoplasma genitalium infection contributes to 10–35% of non-chlamydial non-gonococcal urethritis in men. In women, *M. genitalium* is associated with cervicitis and pelvic inflammatory disease (PID) in 10–25%. Transmission of *M. genitalium* occurs through direct mucosal contact.

Clinical features and diagnostic tests Asymptomatic infections are frequent. In men, urethritis, dysuria and discharge predominate. In women, symptoms include vaginal discharge, dysuria or symptoms of PID – abdominal pain and dyspareunia. Symptoms are the main indication for diagnostic testing. Diagnosis is achievable only through nucleic acid amplification testing and must include investigation for macrolide resistance mutations.

Therapy Therapy for *M .genitalium* is indicated if *M. genitalium* is detected. Doxycycline has a cure rate of 30–40%, but resistance is not increasing. Azithromycin has a cure rate of 85–95% in macrolide-susceptible infections. An extended course of azithromycin appears to have a higher cure rate, and pre-treatment with doxycycline may decrease organism load and the risk of macrolide resistance selection. Moxifloxacin can be used as second-line therapy but resistance is increasing.

Recommended treatment Uncomplicated *M. genitalium* infection without macrolide resistance mutations or resistance testing: Azithromycin 500 mg on day one, then 250 mg on days 2–5 (oral).

Second-line treatment and treatment for uncomplicated macrolide-resistant *M. genitalium* infection: Moxifloxacin 400 mg od for 7 days (oral).

Third-line treatment for persistent *M. genitalium* infection after azithromycin and moxifloxacin: Doxycycline or minocycline 100 mg bid for 14 days (oral) may cure 40–70%. Pristinamycin 1 g qid for 10 days (oral) has a cure rate of around 75%.

Complicated *M. genitalium* infection (PID, epididymitis): Moxifloxacin 400 mg od for 14 days.

Main changes from the 2016 European *M. genitalium* guideline Due to increasing antimicrobial resistance and warnings against moxifloxacin use, indications for testing and treatment have been narrowed to primarily involve symptomatic patients. The importance of macrolide resistance-guided therapy is emphasised.

Received: 9 September 2021; Accepted: 7 January 2022

Conflicts of interest

J.S. Jensen reports grants, personal fees and non-financial support from Hologic, personal fees from Roche, grants and personal fees from SpeeDx, grants and personal fees from Nabriva, grants and personal fees from Cepheid, grants and personal fees from Abbott and grants and personal fees from GSK all outside the submitted work. Other authors have no conflicts of interest related to this guideline.

Funding sources

None.

Introduction

Mycoplasmas are the smallest free-living micro-organisms. In the urogenital tract, the relevant species are *M. genitalium, Ureaplasma urealyticum, U. parvum* and *M. hominis*. *M. hominis* and the ureaplasmas will not be dealt with in the present guideline.[1]

Mycoplasma genitalium was first isolated in 1980.[2] *M. genitalium* infection is unequivocally associated with male non-gonococcal urethritis (NGU)[3] and is even more strongly associated with non-chlamydial non-gonococcal urethritis (NCNGU). The prevalence of *M. genitalium* in men with NCNGU ranges from 10% to 35%,[3] thus contributing significantly to the overall burden of disease. In comparison, *M. genitalium* is detected in only 1% to 3.3% of men and women in the general population.[4–7] In women, several studies have demonstrated the association between *M. genitalium* and urethritis, cervicitis, endometritis and pelvic inflammatory disease (PID).[8–12] In a meta-analysis,[13] significant associations were found between *M. genitalium* and cervicitis (pooled odds ratio (OR) 1.66 [95%CI 1.35–2.04]) and PID (pooled OR 2.14 [95%CI 1.31–3.49]). *M. genitalium* has been associated with preterm birth (pooled OR 1.89 [95%CI 1.25–2.85]) and spontaneous abortion (pooled OR 1.82) [95%CI 1.10–3.03], but the prevalence of *M. genitalium* in pregnant women in Europe is low,[14,15] and therefore, the relative importance of *M. genitalium* is probably small. Studies have also shown an association with increased risk of tubal factor infertility (pooled OR 2.43). In sub-analyses that accounted for co-infections, Lis et al found these associations to be stronger.[13]

Persistence of *M. genitalium* after treatment is associated with recurrent or persistent NGU, and up to 40% with this condition are *M. genitalium* positive.[16] In a meta-analysis, persistent *M. genitalium* was associated with a pooled OR of 26 for persistent urethritis.[17] Thus, failure to eradicate *M. genitalium* leads to persistent or recurrent disease in the vast majority of men, and diagnosis and optimal treatment are important. *M. genitalium* has been shown to facilitate HIV transmission, in particular in studies from Sub-Saharan Africa.[18–20] Whether this also applies in regions with good access to effective HIV treatment is not clear.

The present 2021 European *M. genitalium* guideline is modified significantly compared to the previous version from 2016,[21] in particular, in relation to indications for testing, which have been narrowed due to the emerging threat of untreatable *M. genitalium* infections and the potential for serious side effects when using quinolones, the main second-line antimicrobial, highlighted by the European Medicines Agency. With the lack of natural history studies estimating the risk of sequelae of asymptomatic infections, the authors considered the benefits of treating asymptomatic infections to be outweighed by the risk of increased antimicrobial resistance and adverse events from widespread treatment. A summary of the updated recommendatins is presented in Table 1.

Transmission

Transmission is primarily by direct genital–genital mucosal contact. *M. genitalium* has been detected in anorectal samples by culture and NAATs in both men and women,[22–24], and transmission through penile-anal sexual contact has been established.[25]. Oral-genital contact is less likely to contribute to any significant extent, as carriage of *M. genitalium* in the oropharynx is low.[26,27] Mother-to-child transmission at birth has not been widely studied, but *M. genitalium* has been detected in the respiratory tract of newborn children[28] and in the conjunctivae of two children (transmission rate 10.5%).[29] The risk of contracting *M. genitalium* per sexual encounter has not been determined, but because *M. genitalium* is present in lower concentration in genital tract specimens than *Chlamydia trachomatis*,[30,31] it could be considered less contagious than *C. trachomatis*.

There are no estimates of the global burden of infection. In sexually transmitted infection (STI) clinic patients, the prevalence usually ranges from 75% to 90% of that of *C. trachomatis*, but in some settings, it is higher than chlamydia.[32] In the general population, the ratio is generally lower.[4,6,7] Compared to *C. trachomatis*, the prevalence of *M. genitalium*-infected patients appears to peak approximately 5 years later for both men and women and to remain higher in the older age groups.[7,33,34]

Clinical features

Urogenital infections

Symptoms and signs in women

- Among STI clinic attendees and in the general population, 40–75% of *M. genitalium* infections are asymptomatic.[7,11,12]
- Symptoms are related to cervical and urethral infection and include increased or altered vaginal discharge (<50%), dysuria or micturition urgency (30%) and inter-menstrual or post coital bleeding or menorrhagia.[7,11,12,35]
- Mucopurulent cervicitis and urethritis.[36]
- Rectal and pharyngeal infections are usually asymptomatic.
- Lower abdominal pain (<20%) should raise suspicion of PID.

Complications in women:[13]

- PID (endometritis, salpingitis)
- Tubal factor infertility (probably, further studies needed)
- Adverse pregnancy outcome (possibly, further studies needed)
- Sexually acquired reactive arthritis (SARA) may occur.[37]

Symptoms and signs in men:[3]

- 70% of *M. genitalium* infections are symptomatic in STI clinic settings.[38]

Table 1 Summary of recommendations

Recommendation	Grading
Indications for testing	
Test men for *M. genitalium* with	1B
Symptoms or signs of urethritis	
Acute epididymo-orchitis if aged <50 years	
Proctitis after exclusion of *N. gonorrhoeae* and *C. trachomatis* as causative pathogens	
Test women for *M. genitalium* with	1B
Mucopurulent cervicitis	
Intermenstrual or post-coital bleeding	
Dysuria with no known other aetiology	
Acute pelvic pain and/or PID	
Proctitis after exclusion of *N. gonorrhoeae* and *C. trachomatis* as causative pathogens	
Test for *M. genitalium* in on-going sexual contacts of persons treated for *M. genitalium* infection	1B
Consider to test for *M. genitalium* before termination of pregnancy	2B
All *M. genitalium* positive tests must be followed up with an assay capable of detecting macrolide resistance mutations	1B
Detection of QRAMs in *parC* is not indicated on a routine basis, but is useful in treatment failure after moxifloxacin treatment	1D
Clinical specimens	
First void urine (FVU) from men and vaginal swabs from women provide good diagnostic specimens, which may be self-obtained	1B
Rectal samples are only indicated in symptomatic proctitis after exclusion of *N. gonorrhoeae* and *C. trachomatis* as causative pathogens	1D
Testing oropharyngeal samples is not recommended	1D
Careful consideration should be given to transport medium and nucleic acid extraction procedure	1C
Management of patients	
Patients with *M. genitalium* infection should abstain from unprotected sexual contact until they and their partners have completed treatment, their symptoms have resolved and their test of cure (TOC) is negative	1D
Patients with *M. genitalium* infection (and their sexual contacts) should be given verbal and written information about the infection, including details about transmission, prevention and complications.	1D
Patients with *M. genitalium* infection should be screened for other STIs, including *C. trachomatis*, *N. gonorrhoeae*, syphilis and HIV, plus *T. vaginalis* where appropriate	1D
M. genitalium infections during pregnancy may be treated with azithromycin or pristinamycin. Treatment may be postponed until after delivery, but the neonate should be observed for signs of infection, primarily conjunctivitis and respiratory tract infection	1D
Indications for therapy	
Detection of *M. genitalium*-specific nucleic acid in a clinical specimen	1B
Current partners of *M. genitalium-positive* patients should be treated with the same antimicrobial as the index patient	1B
Therapy	
Uncomplicated *M. genitalium* infection in the absence of macrolide resistance mutations or resistance testing	
Azithromycin 500 mg on day one, then 250 mg od days 2-5 (oral)	1B
Josamycin 500 mg 3 times daily for 10 days (oral)	2C
Uncomplicated *M. genitalium* infection in the presence of macrolide resistance mutations	
Moxifloxacin 400 mg od for 7 days (oral)	1B
Second-line treatment for uncomplicated persistent *M. genitalium* infection after azithromycin treatment	
Moxifloxacin 400 mg od for 7 days (oral)	1B
Third-line treatment for persistent *M. genitalium* infection after azithromycin and moxifloxacin treatment	
Pristinamycin 1 g four times daily for 10 days (oral), 75% cure	1B
Minocycline 100 mg two times daily for 14 days (oral), 70% cure	2B
Doxycycline 100 mg two times daily for 14 days (oral), 40% cure	2B
Complicated *M. genitalium* infection (PID, epididymitis)	
Moxifloxacin 400 mg od for 14 days (oral)	1C
Partner notification	
Current partner(s) should always be tested and treated with the same antimicrobial as the index patient	2B
Follow-up and test of cure	
A TOC should be considered in all patients	2C
TOC samples should be collected no earlier than three weeks after completion of treatment	1B

- In the general population, less than 5% of those infected report symptoms.[6,7]
- Urethritis (acute, persistent and recurrent)
- Dysuria
- Urethral discharge
- Proctitis
- Balanoposthitis has been associated with *M. genitalium* infection in one study.[39]

Complications in men

- SARA may occur.[37]
- Epididymitis may occur.[40,41]

Ocular infections

Ocular infections can result in conjunctivitis in adults[42] but has not been systematically studied. Neonatal conjunctivitis has not been systematically studied.

Indications for laboratory testing

Symptoms and signs (Grade 1B)

- Symptoms or signs of urethritis in men
- Mucopurulent cervicitis
- Intermenstrual or post-coital bleeding
- Dysuria with no known other aetiology in women
- Acute pelvic pain and/or PID
- Acute epididymo-orchitis in a male aged <50 years
- Proctitis after exclusion of *N. gonorrhoeae* and *C. trachomatis* as causative pathogens

Risk factors

- On-going sexual contacts of persons being treated for *M. genitalium* infection (Grade 1B)
- Before termination of pregnancy, testing could be considered (Grade 2B)

Laboratory diagnostics

Recommended diagnostic assays

Nucleic acid amplification tests (NAATs) identifying *M. genitalium*-specific nucleic acid (DNA or RNA) in clinical specimens are the only useful methods for diagnosis. Some commercially available NAATs have been evaluated up to the US Food and Drug Administration (FDA) approval standard.[43] However, currently, none include detection of macrolide resistance mutations and some of the tests on the market which have been Conformité Européenne (CE) marked to document conformity according the European Union (EU) legislation suffer from limited validation. Consequently, it is extremely important that diagnostic laboratories use carefully validated and quality assured commercial or in-house assays, including participation in external quality assessment (EQA) schemes such as the Quality Control for Molecular Diagnostics (QCMD; www.qcmd.org) EQA scheme and act upon the results.

With the widespread macrolide resistance in Europe, all *M. genitalium*-positive tests must be followed up with an assay capable of detecting macrolide resistance mutations (Grade 1B). A variety of laboratory developed tests are available for this purpose,[34,44–49,] and CE-marked, commercially available methods have also become available.[50–52] The main determinants for the selection of a macrolide resistance assay are (1) its practical implementation in the laboratory, (2) its sensitivity (proportion of *M. genitalium* screening positive tests that can be resistance typed) and (3) its specificity. As for the *M. genitalium* diagnostic NAATs, the sensitivity of the macrolide resistance assays varies significantly.

Determination of quinolone resistance-associated mutations (QRAMs) located in the *parC* gene can be carried out using molecular methods although the correlation between mutations in *parC* and treatment failure is less clear.[53,54] Mutations in *gyrA* alone are not predictive of treatment failure, but may potentiate the effect of QRAMs in *parC*.[53] At present, detection of QRAMs is not indicated on a routine basis in Europe because of the suboptimal correlation between QRAMs and treatment outcome and the low prevalence of QRAMs (<5–10%).[32,55,56] However, *parC*-based resistance testing is useful in treatment failure after moxifloxacin treatment in order to reserve third-line antimicrobials for patients with documented moxifloxacin resistance (Grade 1D). Detection of QRAMs is mainly available in specialised laboratories, and these laboratories should provide guidance in the interpretation of the detected *parC* mutations. Some mutations do not lead to increased rates of treatment failure.

Clinical specimens

It is difficult to make accurate recommendations regarding the optimal sample type because of variations in nucleic acid extraction methods and assay performance. No data are available regarding time after exposure to testing, but in analogy with *C. trachomatis*, a two-week period is considered the minimal incubation time.

First void urine (FVU) from men provides a good diagnostic specimen, which may be self-obtained (Grade 1B).[33,57,58] No data regarding the importance of holding urine for a certain time are available, so procedures already in place for *C. trachomatis* and *N. gonorrhoeae* sampling can be followed. Vaginal swab (physician or self-collected) provides the best performance if only one sample is taken in women (Grade 1B).[57–61]

Rectal samples may be useful in MSM where as many as 70% of the infections will be missed if this site is not sampled.[62,63] However, due to the high risk of combined macrolide and quinolone resistance in MSM, testing from this location is only indicated in men with symptomatic proctitis where other aetiologies have been excluded (Grade 1D). Rectal infection in women at risk is not uncommon.[23,24] The association between a

rectal infection and symptoms is uncertain, but it is possible to transmit the infection from the rectal site. Also in women, rectal samples are only indicated in symptomatic proctitis after exclusion of *N. gonorrhoeae* and *C. trachomatis* as causative pathogens (Grade 1D).

Oropharyngeal carriage of *M. genitalium* is rare[32] and not associated with symptoms. Testing from this site is not recommended (Grade 1D).

In most settings, it will be appropriate to use the same sampling procedure as for *C. trachomatis* and *N. gonorrhoeae* testing. For assays that have regulatory approval, the sampling procedure and transport medium recommended by the manufacturer should be used. For all in-house assays and assays where a validated collection and nucleic acid purification kit is not included, careful consideration should be given to the transport medium and nucleic acid extraction procedure (Grade 1C). This is the responsibility of the diagnostic laboratory.

Management of patients

Information, explanation and advice for the patient

- Patients with *M. genitalium* infection should be advised to abstain from unprotected sexual contact until they and their partners have completed treatment, their symptoms have resolved and their test of cure (TOC) is negative (Grade 1D). This is due to the risk of further transmission of infection but also the risk of antimicrobial resistance selection during treatment and subsequent failure of eradication.
- Patients with *M. genitalium* infection (and their sexual contacts) should be given information about the infection, including details about transmission, prevention and complications. It is recommended that both verbal and written information be provided. Patient information leaflets are available at the International Union against Sexually Transmitted Infections (IUSTI) website (https://iusti.org/treatment-guidelines/) (Grade 1D).
- Patients with *M. genitalium* infection should be screened for other STIs, including *C. trachomatis*, *N. gonorrhoeae*, syphilis and HIV, plus *T. vaginalis* where appropriate (Grade 1D).

Pregnancy

- *M. genitalium* infections during pregnancy may be associated with a modest increase in the risk of spontaneous abortion and preterm birth.[13] However, most studies have not controlled for other conditions associated with these outcomes. In macrolide susceptible *M. genitalium* infections, a five-day-course of azithromycin is generally acceptable. The choice of drugs for macrolide-resistant infections is difficult, and the risk associated with treatment using available antibiotics may outweigh the risk of adverse pregnancy outcome. Thus, treatment, especially in women with infection with a macrolide-resistant *M. genitalium* strain, may be postponed until after delivery. Pristinamycin is considered safe in pregnancy and may be considered in symptomatic women after specialist consultation. Although little is known about transmission during birth, the neonate should be observed for signs of infection, primarily conjunctivitis and respiratory tract infection (Grade 1D).

Indications for therapy

- Detection of *M. genitalium*-specific nucleic acid in a clinical specimen (Grade 1B)
- Current partners of *M. genitalium*-positive patients should be tested and treated with the same antimicrobial as the index patient (Grade 1B)

Therapy

Treatment of individuals with *M. genitalium* urogenital infection prevents sexual transmission and is likely to reduce the risk of complications, including PID[5] and tubal-factor infertility.[13] The recommended treatment strategy has been summarised in Figure 1.

Only a few antimicrobial classes have activity against mycoplasmas including tetracyclines, macrolides, fluoroquinolones and streptogramins.

Doxycycline has limited efficacy[64–67] with microbiological cure rates between 30% and 40%. However, it may also decrease the load of *M. genitalium* in patients despite failing to eradicate it.[68] Azithromycin given as a 1 g single oral dose has a cure rate of approximately 85% in macrolide susceptible infections but will select for macrolide resistance in more than 10% of the treated patients.[64,65,69] The rapidly increasing prevalence of macrolide resistance[70] is drastically decreasing the overall cure rate. Most likely, this is caused by widespread use of azithromycin as a 1 g single dose for other STIs and when *M. genitalium* is treated without a TOC leading to the subsequent spread of macrolide-resistant strains.

Azithromycin given as an extended regimen with 500 mg day one followed by 250 mg days 2–5 (1.5 g total dose) is recommended as the primary choice for treatment of *M. genitalium* infections. This regimen will also eradicate a concurrent urogenital *C. trachomatis* infection.[71] Using extended azithromycin or other macrolide antibiotics after failure with the 1 g single-dose regimen or in the presence of pre-existing macrolide resistance mutations is usually ineffective.

Macrolide resistance rates vary significantly geographically and between patient groups, but in areas where azithromycin 1 g single dose is used for treatment of NGU, it is usually found in at least 30-45% of samples.[34,72–74,]

Josamycin is widely used in Russia with 500 mg three times a day for 10 days, but will not eradicate macrolide-resistant strains and macrolide resistance can be selected during treatment.[75]

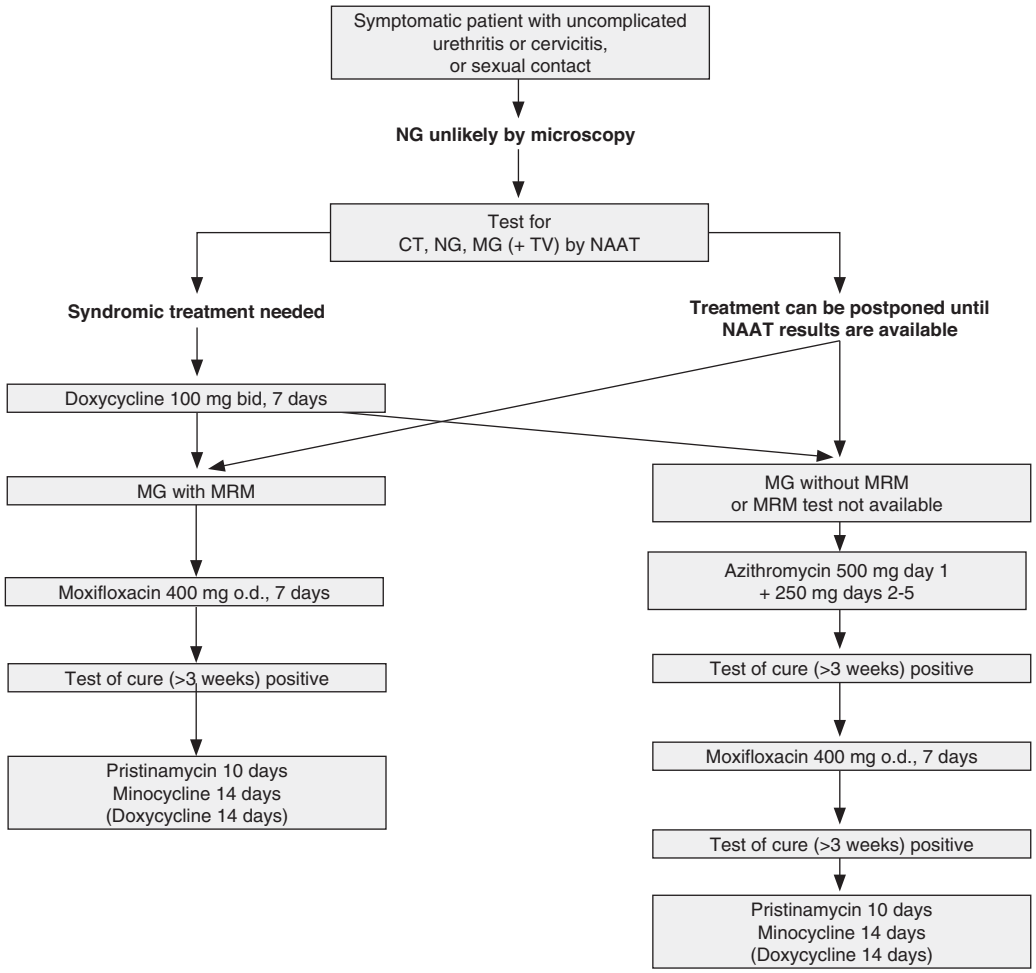

Figure 1 Summary of *Mycoplasma genitalium* diagnosis and treatment. NG, *Neisseria gonorrhoeae*; CT, *Chlamydia trachomatis*; MG, *Mycoplasma genitalium*; TV, *Trichomonas vaginalis*; NAAT, nucleic acid amplification test; MRM, macrolide resistance mutation.

Moxifloxacin is the most commonly used second-line antimicrobial. It is bactericidal and has a cure rate approaching 100% in infections with susceptible strains.[76–79] However, resistance has developed with treatment failures in up to 30%, primarily in patients from the Asia-Pacific region. A significant proportion of the *M. genitalium* strains have concurrent macrolide resistance mutations leaving very few available treatment options.[80–84]

Pristinamycin has been the primary third-line antimicrobial in patients failing azithromycin and moxifloxacin.[83] In Europe, pristinamycin is registered in France, but can be acquired with a special permit in most European countries. It is generally used in the maximal recommended dose of 1 g four times a day for 10 days (oral), but combination therapy with doxycycline or doses as low as 2 g per day does not significantly change the cure rate from around 75%.[85,86] The use of extended doxycycline regimen (100 mg twice daily for 14 days) as third-line treatment has not been systematically evaluated, but considering the slow growth rate of *M. genitalium* and the bacteriostatic nature of the tetracyclines, an extended duration of treatment may theoretically improve cure rate.

Due to the observation that cure rates with azithromycin were lower for high-load infections[83,87], the concept of resistance-guided sequential therapy (RGST) has developed.[68] In RGST, patients are treated with doxycycline 100 mg twice daily for 7 days, which lowers the *M. genitalium* bacterial load while waiting for results of microbiological testing and macrolide resistance testing in those found to be *M. genitalium* positive. Subsequently, the patient is treated with a 2.5 g dose of azithromycin (1 g day 1 followed by 500 mg days 2–4) or moxifloxacin for 7–10 days.[68,88] RGST is now the recommended treatment in

the Australian *M. genitalium* guidelines[89] and in a modified form also in the UK *M. genitalium* guideline.[90] Although RGST has shown higher cure rates and lower selection of resistance in observational studies,[68,88] no controlled trials have confirmed this and giving two antimicrobials for up to 17 days depending on the dosing regimen may lead to selection of resistance in other STIs as well as non-STI pathogens. There is no clinical evidence that the higher dose (2–2.5 g) of azithromycin is better than the 1.5 g extended dosage scheme previously recommended or that moxifloxacin for 10 days is better than 7 days in uncomplicated infection although one observational study has suggested a higher cure-rate after 10 days of treatment in cervicitis.[80] However, if treatment of symptomatic patients is indicated before the results of microbiological tests are available, RGST is recommended, with initial doxycycline followed by the dosages for azithromycin and moxifloxacin suggested below. In compliant patients, it is acceptable not to give further treatment if symptoms have resolved during the doxycycline treatment. TOC should then be offered no earlier than 3 weeks after completion of treatment and condoms used until a negative TOC is obtained. If symptoms recur or if the TOC is *M. genitalium* positive, the patient should be treated according to initial resistance testing as described below without repeat treatment with doxycycline. Clinical trials, preferably randomised and controlled, evaluating this approach would be valuable.

Recommended treatment for uncomplicated *M. genitalium* infection in the absence of macrolide resistance mutations or resistance testing

- Azithromycin 500 mg on day one, then 250 mg od days 2–5 (oral) (Grade 1B)
- Josamycin 500 mg 3 times daily for 10 days (oral) (Grade 2C)

Recommended treatment for uncomplicated *M. genitalium* infection in the presence of macrolide resistance mutations

- Moxifloxacin 400 mg od for 7 days (oral) (Grade 1B)

Recommended second-line treatment for uncomplicated persistent *M. genitalium* infection after azithromycin treatment

- Moxifloxacin 400 mg od for 7 days (oral) (Grade 1B)

Recommended third-line treatment for persistent *M. genitalium* infection after azithromycin and moxifloxacin treatment

No optimal therapies can be suggested at present. Pristinamycin is the best evaluated third-line treatment but has only approximately 75% cure rate.[85,86]

- Pristinamycin 1 g four times daily for 10 days (oral) (Grade 1B)
- Minocycline 100 mg two times daily for 14 days (oral) is more active than doxycycline and was shown to have a microbiological cure rate of 71% among 35 evaluable patients,[86] and this is supported by in vitro data (Jensen JS, unpublished). However, no systematic comparisons have been performed (Grade 2B).
- Doxycycline 100 mg two times daily for 14 days (oral) may eradicate *M. genitalium* from approximately 30–40% of the patients, but the patient must be informed about the poor eradication rate and agree to comply with advice regarding sexual abstinence or condom use (Grade 2B).

Lefamulin has recently been registered in Europe for community-acquired bacterial pneumonia. It is highly active in vitro against *M. genitalium* with combined macrolide and fluoroquinolone resistance;[91] however, only anecdotal experience with treatment of *M. genitalium* is available. (Grade 2D).

Recommended treatment for complicated *M. genitalium* infection (PID, epididymitis)

- Moxifloxacin 400 mg od for 14 days (oral) (Grade 1C).[92]

Partner notification

- Current partner(s) (i.e. one or more partners with whom the index patient has recently had unprotected sex and with whom the patient will continue to have sex) should always be tested and treated with the same antimicrobial as the index patient (Grade 2B).

Follow-up and test of cure (TOC)

- A TOC should be considered in all patients due to the high prevalence of resistance present either pre-treatment or developing during treatment and due to the subsequent risk for spread of resistance in the community (Grade 2C). TOC samples should be collected no earlier than three weeks after completion of treatment (Grade 1B). In patients responding to treatment, *M. genitalium* will be undetectable within one week in most patients, but tests may become temporarily false negative in patients failing treatment due to a transient reduction in bacterial load.[93]

Acknowledgements

Andrew Winter, Jonathan Ross, Jackie Sherrard, Agnieszka B Serwin, Keith Radcliffe, Michel Janier and Ricardo Werner on behalf of the EDF and IUMS are thanked for comments to the guideline.

Composition of the European STI Guideline Editorial Board

Current composition can be found at: https://iusti.org/wp-content/uploads/2019/12/Editorial_Board.pdf.

List of contributing organizations

Current list can be found at: https://iusti.org/treatment-guidelines/.

Proposed date of revision: 2025.

Qualifying statement

Decisions to follow these recommendations must be based on professional clinical judgement, consideration of individual patient circumstances and available resources. All possible care has been undertaken to ensure publication of the correct dosage of medication and route of administration. However, it remains the responsibility of the prescribing clinician to ensure the accuracy and appropriateness of the medication they prescribe.

Data availability statement

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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Appendix

Search strategy

A Medline search was conducted in December 2020 using PubMed. The search heading was kept broad (*Mycoplasma genitalium*) to include epidemiology, diagnosis, antimicrobial resistance, drug therapy, clinical trials and prevention and control. Only publications and abstracts in the English language were considered. The Cochrane library was searched for all entries related to mycoplasma. Sexually transmitted diseases guidelines produced by the US Centers for Disease Control and Prevention (www.cdc.gov/std/), the British Association for Sexual Health and HIV (http://www.bashh.org), and the Australasian Sexual Health Alliance (ASHA) (https://www.sexualhealthalliance.org.au) were also reviewed.

Levels of evidence

Levels of evidence and grading of recommendations that were used in the present guideline as well as the review and hearing proves can be found in the protocol for production and revision of European STI guidelines at: https://iusti.org/wp-content/uploads/2020/04/ProtocolForProduction2020.pdf