2020 European guideline for the diagnosis and treatment of gonorrhoea in adults

M Unemo1, JDC Ross2, AB Serwin3, M Gomberg4, M Cusini5 and JS Jensen6

Abstract

Gonorrhoea is a major public health concern globally. Increasing incidence and sporadic ceftriaxone-resistant cases, including treatment failures, are growing concerns. The 2020 European gonorrhoea guideline provides up-to-date evidence-based guidance regarding the diagnosis and treatment of gonorrhoea. The updates and recommendations emphasize significantly increasing gonorrhoea incidence; broad indications for increased testing with validated and quality-assured nucleic acid amplification tests and culture; dual antimicrobial therapy including high-dose ceftriaxone and azithromycin (ceftriaxone 1 g plus azithromycin 2 g) OR ceftriaxone 1 g monotherapy (ONLY in well-controlled settings, see guideline for details) for uncomplicated gonorrhoea when the antimicrobial susceptibility is unknown; recommendation of test of cure (TOC) in all gonorrhoea cases to ensure eradication of infection and identify resistance; and enhanced surveillance of treatment failures when recommended treatment regimens have been used. Improvements in access to appropriate testing, test performance, diagnostics, antimicrobial susceptibility surveillance and treatment, and follow-up of gonorrhoea patients are essential in controlling gonorrhoea and to mitigate the emergence and/or spread of ceftriaxone resistance and multidrug-resistant and extensively drug-resistant gonorrhoea. For detailed background, evidence base and discussions, see the background review for the present 2020 European guideline for the diagnosis and treatment of gonorrhoea in adults (Unemo M, et al. Int J STD AIDS. 2020).

Keywords

Neisseria gonorrhoeae, gonorrhoea, sexually transmitted infection, Europe, management, diagnosis, antimicrobial resistance, treatment

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Aetiology, transmission, and epidemiology

• Gonorrhoea (gonococcal infection) is caused by the obligate human pathogenic, Gram-negative bacterium Neisseria gonorrhoeae;2
• Infection predominantly involves the epithelium of the urethra, endocervix, rectum, oropharynx, and

1WHO Collaborating Centre for Gonorrhoea and other STIs, National Reference Laboratory for STIs, Department of Laboratory Medicine, Microbiology, Örebro University Hospital and Faculty of Medicine and Health, Örebro University, Örebro, Sweden
2University Hospital Birmingham NHS Foundation Trust, Birmingham, UK
3Department of Dermatology and Venereology, Medical University of Białystok, Białystok, Poland
4Moscow Scientific and Practical Center of Dermatovenereology and Cosmetology, Moscow, Russia
5Department of Dermatology, Fondazione IRCCS Ca’ Granda Ospedale Policlinico, Milano, Italy
6Infection Preparedness, Research Unit for Reproductive Tract Microbiology, Statens Serum Institut, Copenhagen, Denmark

Corresponding author:
M Unemo, WHO Collaborating Centre for Gonorrhoea and other STIs, National Reference Laboratory for STIs, Department of Laboratory Medicine, Microbiology, Örebro University Hospital, Örebro, Sweden.
Email: magnus.unemo@regionorebro.se
conjunctivae. Infection can ascend to the upper genital tract to cause pelvic inflammatory disease (PID) and epididymo-orchitis;1–3

- Transmission is by direct inoculation of infected secretions from one mucosa to another, i.e., genital-urogenital, urogenital-anorectal, oro-urogenital, or oro-anal contact, or by mother-to-child transmission at birth;1–7

In the European Union (EU)/European Economic Area (EEA), gonorrhoea is the second (after Chlamydia trachomatis infection) most frequently reported bacterial sexually transmitted infection (STI), and the incidence has increased by ~240% since 2008.8 In 2018, 76% of gonorrhoea cases were reported in men,8 reflecting the high prevalence in men who have sex with men (MSM) and the higher proportion of diagnosed symptomatic urogenital infections in men. In 2018, the highest incidence of gonorrhoea in the EU/EEA was among 25–34 year olds, closely followed by 15–24 year olds and, in many countries, there is a disproportionate burden of infection in MSM and/or ethnic minority groups.8–10

Clinical features1–3,11–16

Symptoms and physical signs of gonorrhoea reflect localised inflammation of infected mucosal surfaces in the urogenital tract and several other STIs cause similar symptoms.

Symptoms

- In men, acute urethritis is predominant with symptoms of urethral discharge (>80%) and dysuria (>50%), usually starting within 2–8 days of exposure. Asymptomatic urethral infection in men is rare (<10% of infections);
- In women, endocervical and urethral infection include symptoms such as increased or altered vaginal discharge (≤50%), lower abdominal pain (≤25%), dysuria (10–15%), and occasionally intermenstrual bleeding or menorrhagia. Endocervical infection is frequently asymptomatic (≥50%);
- Rectal and oropharyngeal infections in men and women are usually asymptomatic. Rare symptoms include anal discharge and perianal/anal pain or discomfort and sore throat, respectively.

Physical signs

- In men, mucopurulent urethral discharge is most common, which may be accompanied by erythema of the urethral meatus;
- In women, urogenital examination may be normal or a mucopurulent discharge may be evident from the cervix, sometimes accompanied with hyperaemia and contact bleeding of the endocervix.

Complications and sequelae

- PID in women, potentially resulting in ectopic pregnancy and infertility, and epididymo-orchitis in men are complications of infection ascending to the upper genital tract;
- Gonococcal bacteraemia is generally rare,17,18 but can be more common in high-prevalent gonorrhoea areas and may be expected to increase when the gonorrhoea incidence increases.19 This is usually manifested by skin lesions, fever, arthralgia, acute arthritis, and tenosynovitis (disseminated gonococcal infection [DGI]).3,17–21

Indications for testing [2C]

- Symptoms or signs of urethral discharge in men;
- Cervical or vaginal discharge with a risk factor for STI (age <30 years, new sexual contact in the last year, or more than one partner in the last year);8,22–24
- Mucopurulent cervicitis;
- Persons newly diagnosed with other STIs;
- Sexual contact of persons with an STI or PID;
- Acute epididymo-orchitis in a male aged <40 years or with other risk factors for STIs (e.g., new sexual contact in the last year, or more than one partner in the last year);8,22–24
- Acute pelvic pain or signs of PID;
- When performing an STI screen in young adults (<25 years of age) or MSM;
- When performing an STI screen in individuals with new or multiple recent sexual contacts;
- Purulent conjunctivitis in a neonate or adult;
- Mother of a newborn with ophthalmia neonatorum;
- Unplanned termination of pregnancy in areas or populations of high gonorrhoea prevalence;
- Any intrauterine interventions or manipulations in areas or populations of high gonorrhoea prevalence.25,26

Testing and diagnosis

- Diagnosis of uncomplicated gonorrhoea is established by identification of N. gonorrhoeae in urogenital, rectal, oropharyngeal, or ocular secretions;2,27
- N. gonorrhoeae can be detected by nucleic acid amplification tests (NAATs) or culture. The bacterium can also be visualized by microscopy of a stained anogenital tract smear to facilitate rapid diagnosis in symptomatic patients;
- Microscopy (×1000) using Gram or methylene blue staining for identification of characteristic
in intracellular diplococci within polymorphonuclear leukocytes offers adequate sensitivity (90-95%) and specificity (>99%) as a rapid diagnostic test in symptomatic men with urethral discharge [1C].

Microscopy has a low sensitivity in asymptomatic men (50-75%) and from endocervical (16-50%) or rectal (<40%) sites, and microscopy is not recommended as a test of exclusion in these patients [1C]. Microscopy is also not recommended for detection of oropharyngeal gonorrhoea due to low specificity and sensitivity.

**Culture**, including appropriate species confirmation, is a highly specific test, and relatively sensitive for urogenital specimens, provided that specimen collection, transport, storage, and culture procedures are optimised. However, the sensitivity of culture for rectal and oropharyngeal specimens is significantly lower. Diagnostic culture is appropriate for endocervical, urethral, rectal, oropharyngeal and conjunctival specimens but not for urine or vaginal swabs.

Ideally, all gonococcus-positive individuals diagnosed by NAAT should have cultures performed before initiation of gonorrhoea treatment to permit antimicrobial resistance (AMR) testing and surveillance to be performed. Selective culture media containing antimicrobials such as vancomycin, colistin, nystatin, and trimethoprim are recommended [1C]. Culture (ideally supplemented with a NAAT for optimal sensitivity), including AMR testing, should also be performed in patients with proven infection (i.e., positive test of cure [TOC]) or in the presence of symptoms following treatment with a recommended regimen;

**NAATs** are the recommended diagnostic tests for symptomatic and asymptomatic individuals, however, culture of individuals with urogenital symptoms and in gonococcal NAAT-positive individuals prior to treatment to obtain isolates for AMR testing is also encouraged. NAATs are more sensitive than culture (particularly for oropharyngeal and rectal specimens); less demanding in specimen quality, transportation and storage; offer testing on a wider range of specimen types; and show high sensitivity (>95%) in both symptomatic and asymptomatic gonorrhoea.

In men, urine (up to 20 mL sampled >1 h after previous micturition) is preferable, providing a high sensitivity and non-invasive sampling.

In women, vulvo-vaginal swabs (health care worker-or self-collected) are recommended due to their superiority and being less invasive since they do not require a speculum examination [1A].

**NAATs** are significantly more sensitive than culture for detection of rectal and oropharyngeal gonorrhoea, and appropriately-validated and quality-assured NAATs are recommended for testing and/or screening for infections at these sites. However, most commercially available gonococcal NAATs are not licensed for testing oropharyngeal and rectal specimens, and differ in their sensitivity and especially specificity, particularly when examining oropharyngeal specimens due to the frequent presence of non-gonococcal *Neisseria* species.

**NAAT confirmatory testing**: The positive predictive value (PPV) of NAAT testing to detect *N. gonorrhoeae* should exceed 90%. The PPV is highly influenced by the gonorrhoea prevalence in the tested population and the specificity of the NAAT. If the diagnostic NAAT used does not display a PPV exceeding 90%, positive specimens should be confirmed, i.e., by repeat testing with a NAAT targeting another genetic sequence, particularly if oropharyngeal specimens are tested [1C].

**Point-of-care tests (POCTs)**: rapid, validated and quality-assured POCTs for diagnosis of gonorrhoea with sufficient sensitivity compared to NAATs are still lacking; however, several NAAT-based POCTs with high sensitivity and specificity are in late development (https://www.who.int/reproductivehealth/topics/rtis/Diagnostic-Landscape-for-STIs-2019.pdf).

**Testing of pooled specimens** should be routine in MSM, considered in women who are sexual contacts of gonorrhoea patients [1C], and be guided based on sexual history, risk and symptoms or signs in all other patients.

**Testing of pooled specimens** (oropharyngeal, rectal, and urine/urogenital) is not recommended, due to potentially decreased sensitivity, increased complexity, including risk of cross-contamination of sample, and lack of approval by US Food and Drug Administration (FDA) or other regulatory agencies.

**Management of patients**

*Information, explanation and advice for the patient*

- Patients with gonorrhoea should be advised to abstain from sexual contact (or if this is not possible to consistently use barrier contraception) for 14 days (seven days if ceftriaxone monotherapy) after they and their sexual partners have completed ceftriaxone plus azithromycin dual treatment and their symptoms have resolved [2D]. This is to limit possible re-exposure in the presence of residual azithromycin;
• Patients (and their sexual partners) should be given information (verbal and written) about their infection, including details about transmission, prevention, complications, and treatment [ID];
• A patient information leaflet is available in different languages from IUSTI (https://iusti.org/patient-information/).
• Patients with verified gonorrhoea (and their sexual contacts) are recommended to be offered testing for other STIs, e.g. including C. trachomatis, Mycoplasma genitalium (only in symptomatic patients and always including macrolide resistance testing), syphilis, HBV, HCV, and HIV [IC].

**Therapy**

For detailed background, evidence base and discussions regarding gonorrhoea therapy and antimicrobial resistance in *N. gonorrhoeae*, see the background review for the present guideline (Unemo M, et al. Int J STD AIDS. 2020).1,36,37,90–206

Briefly, ceftriaxone plus azithromycin dual therapy aims to provide cure for all gonorrhoea cases and, accordingly, to delay the emergence and/or spread of multi-drug resistance and particularly ceftriaxone resistance. It has very high cure rates; effectively targets both intracellular and extracellular bacteria;117 has likely been involved in decreasing the level of resistance to extended-spectrum cephalosporins (ESCs; mainly ceftriaxone and cefixime) internationally,118–122 and inhibiting spread of ESC-resistant and azithromycin-resistant gonococcal strains (because concurrent resistance to ceftriaxone and azithromycin has been exceedingly rare globally [https://www.ecdc.europa.eu/en/publications-data]).118,120–122,138 This dual therapy also effectively eradicates concomitant *C. trachomatis* infections,1,36,123 and a proportion of *M. genitalium* infections, and adherence appears high.124 Ceftriaxone 1 g effectively cures ceftriaxone-susceptible anogenital and oropharyngeal gonorrhoea.99,100 However, failures to treat ceftriaxone-resistant infections, particularly oropharyngeal gonorrhoea, have occurred also with ceftriaxone 1 g,138 and additional treatment failures can be expected when using ceftriaxone monotherapy for currently circulating gonococcal strains.138–146 ESCs combined with another anti-gonococcal antimicrobial, including azithromycin, can more effectively cure gonorrhoea, including oropharyngeal infection.1,93,106,107,119,138,152–154 Azithromycin 2 g, but not azithromycin 1 g, effectively cures azithromycin-resistant gonococcal infections, including in the oropharynx.1,36,94,126,127,153,154 Nevertheless, azithromycin 2 g single oral dose may also result in more gastrointestinal side effects, particularly if taken on an empty stomach,95,96,154 although the reported incidence of gastrointestinal side effects varies widely between studies.153,162,163 Dividing the dose of azithromycin to give it over a longer period of time reduces the high and sustained tissue concentration, but also reduces the risk of gastrointestinal side effects.117,155–161

Recent published randomised controlled clinical trials (RCTs) on the treatment of gonorrhoea are few and do not address the rapidly evolving situation of gonococcal AMR. Treatment regimens recommended in this guideline are based on early clinical efficacy trials, pharmacokinetic/pharmacodynamic (PK/PD) considerations,152 in vitro AMR surveillance data,118,120–122,138 case reports of verified treatment failures,110,111,138 and expert opinion. Significant variations between different European countries in STI health care, patient and partner management, including follow up, and gonococcal AMR and AMR surveillance exist. Accordingly, national adoption of the European gonorrhoea guideline based on comprehensive, recent, quality-assured AMR data and an effective patient management strategy, e.g. including mandatory TOC, locally can be reasonable.1,165,206

**Indications for therapy [IC]**

- Identification of characteristic intracellular diplococci within polymorphonuclear leukocytes in a sample from a urogenital site, by Gram-stained or methylene blue-stained microscopy;
- Positive culture or confirmed NAAT from any site for *N. gonorrhoeae* (or unconfirmed NAAT from urogenital specimens in settings where PPV >90%);
- On epidemiological grounds, if a recent sexual contact has confirmed gonorrhoea,207 mother of a neonate with verified gonorrhoea, and can be considered following sexual assault. When giving treatment based on epidemiological grounds, specimen(s) for laboratory testing should be collected;
- On demonstration of a purulent urethral discharge in men or mucopurulent cervicitis in women when rapid diagnostic tests such as microscopy are not available and after specimen collection for laboratory testing. In this circumstance, empirical treatment covering also *C. trachomatis* infection should be considered.

**Recommended treatment for uncomplicated *N. gonorrhoeae* infections of the urethra, cervix and rectum in adults and adolescents when the antimicrobial susceptibility of the infection is unknown**

- Ceftriaxone 1 g intramuscularly (IM) as a single dose together with azithromycin 2 g as a single oral dose [IC]
• If gastrointestinal side effects are anticipated: ceftriaxone 1 g IM single dose plus azithromycin 1 g oral dose followed by azithromycin 1 g oral dose 6–12 h later may be used to limit gastrointestinal side effects.\(^{1,17,161}\)

**NOTE:** Azithromycin tablets should not be taken on an empty stomach due to possible gastrointestinal side effects. If required, a snack or crackers can be given to patients before taking the azithromycin tablets.\(^{1,53,154,208}\) For patients perceived to be at risk of vomiting, an anti-emetic can be provided.\(^{91}\)

**OR**

• Ceftriaxone 1 g IM as a single dose [2C]

**NOTE:** Only recommended in settings where:

(i) comprehensive, recent and quality-assured local *in vitro* ceftriaxone susceptibility testing has shown lack of ceftriaxone resistance;
(ii) TOC is mandatory;
(iii) the patient is considered very likely to return for TOC;
(iv) doxycycline 100 mg oral dose twice daily for 7 days is administered at the same time to cover any concomitant *C. trachomatis* infection, if *C. trachomatis* infection has not been excluded by NAAT.

In other settings, ceftriaxone 1 g IM monotherapy is only an alternative option if azithromycin is not available or patient is unable to take oral medication.

**Treatment when patient has history of severe hypersensitivity (e.g. anaphylaxis) to any β-lactam antimicrobial (penicillins, cephalosporins, monobactams or carbapenems)**\(^{1,36,37}\)

Third-generation cephalosporins, such as ceftriaxone, show negligible cross-allergy with penicillins and allergy to these cephalosporins is rare.\(^{166–170}\)

**Recommended treatment.**

• Spectinomycin 2 g IM as a single dose [1B] together with azithromycin 2 g as a single oral dose [1B]

• If gastrointestinal side effects are anticipated: spectinomycin 2 g IM single dose plus azithromycin 1 g oral dose followed by azithromycin 1 g oral dose 6–12 h later may be used.\(^{1,17,161}\)

**NOTE:** See use of azithromycin 2 g for treatments of uncomplicated *N. gonorrhoeae* infections of the urethra, cervix and rectum.

**Alternative treatment.** For susceptible gonococcal infections, early clinical trials demonstrated that ciprofloxacin (500 mg) had high efficacy.\(^{97,98,171}\) Accordingly, this is an alternative treatment when the infection has been confirmed to be susceptible to ciprofloxacin; using phenotypic AMR testing or validated and quality-assured molecular *gyrA*-based fluoroquinolone resistance testing (only for anogenital samples due to potential cross-reactions with commensal *Neisseria* species in pharyngeal samples).\(^{63,172–175,209–211,1}\)

• Ciprofloxacin 500 mg as a single oral dose [1B]

• Gentamicin 240 mg IM as a single dose together with azithromycin 2 g as a single oral dose [1B]

• If gastrointestinal side effects are anticipated: gentamicin 240 mg IM single dose plus azithromycin 1 g oral dose followed by azithromycin 1 g oral dose 6–12 h later may be used.\(^{1,17,161}\)

**NOTE:** The European Medicines Agency (EMA) has alerted a risk of serious side effects associated with the use of quinolone/fluoroquinolone antibiotics.\(^{1,76}\) Ciprofloxacin should be avoided in people who have previously had serious side effects with any quinolone, and it should be used with caution in those aged >60 years, taking a corticosteroid, having kidney disease, and who have had an organ transplantation. However, the single ciprofloxacin 500 mg oral dose likely limits the risk of side effects. See note regarding use of azithromycin 2 g for treatments of uncomplicated *N. gonorrhoeae* infections of the urethra, cervix and rectum.

**Treatment when administration of an intramuscular injection is contraindicated or refused**

Multiple reports of cefixime treatment failures, PK/PD investigations, and *in vitro* resistance levels have raised serious concerns over the adequacy of 400 mg of cefixime for treatment, particularly for monotherapy and treatment of oropharyngeal gonorrhoea (https://www.ecdc.europa.eu/en/publications-data).\(^{110,111,138,152,178–180}\)

**Recommended treatment.**

• Cefixime 400 mg as a single oral dose together with azithromycin 2 g as a single oral dose [1B]

• If gastrointestinal side effects are anticipated: cefixime 400 mg single oral dose plus azithromycin 1 g oral dose followed by azithromycin 1 g oral dose 6-12 h later may be used.\(^{1,17,161}\)
NOTE: See use of azithromycin 2 g for treatments of uncomplicated \textit{N. gonorrhoeae} infections of the urethra, cervix and rectum.

**Alternative treatment.** When the infection has been confirmed before treatment to be susceptible to ciprofloxacin; using phenotypic AMR testing or validated and quality-assured molecular \textit{gyrA}-based fluoroquinolone resistance testing (only for anogenital samples).

- Ciprofloxacin 500 mg as a single oral dose [1B].

**NOTE:** Co-infection with \textit{C. trachomatis} is common in young (<30 years) heterosexual patients and MSM with gonorrhoea.\textsuperscript{1,8,9,36,37} If treatment for gonorrhoea does not include azithromycin, doxycycline 100 mg oral dose twice daily for 7 days should be considered for possible \textit{C. trachomatis} co-infection unless co-infection has been excluded with NAAT testing.\textsuperscript{1,36,37}

**Treatment for gonococcal infection of the pharynx or when such infection has not been excluded**

Many antimicrobials, including ceftriaxone, have a lower efficacy in curing oropharyngeal gonorrhoea compared to urogenital and anorectal infection.\textsuperscript{1,36,37,97,98,105,110,111,126,138,149,164,165,177–186}

**Recommended treatment.**

- Ceftriaxone 1 g IM as a single dose \textit{together with} azithromycin 2 g as a single oral dose [1D]
- If gastrointestinal side effects are anticipated: ceftriaxone 1 g IM single dose \textit{plus} azithromycin 1 g oral dose followed by azithromycin 1 g oral dose 6-12 h later may be used\textsuperscript{117,161}

**NOTE:** See use of azithromycin 2 g for treatments of uncomplicated \textit{N. gonorrhoeae} infections of the urethra, cervix and rectum.

**Alternative regimens.**

- Ceftriaxone 1 g IM as a single dose [2D]

**NOTE:** This regimen is only an option if azithromycin is not available or patient is unable to take oral medication.

- Ciprofloxacin 500 mg as a single oral dose [1B]

**NOTE:** This regimen is only an alternative for treatment when the infection has been confirmed before treatment to be susceptible; using phenotypic AMR testing or validated and quality-assured molecular \textit{gyrA}-based fluoroquinolone resistance testing (only for anogenital samples).

**Recommended treatment for genital, anorectal and oropharyngeal gonococcal infection when ceftriaxone resistance identified\textsuperscript{1,92,153,154}**

The management of patients with ceftriaxone-resistant gonorrhoea or verified treatment failures following other recommended antimicrobial regimens requires advice from specialist STI clinicians and microbiologists, and should include sexual contact notification and follow-up with TOC. Where relevant, these cases should be notified to local, regional and/or national authorities as mandated by statute. Three-site testing for \textit{N. gonorrhoeae}, including culture and AMR testing, is recommended for all patients with ceftriaxone-resistant gonorrhoea. AMR testing, when available, should inform further treatment.

- Ceftriaxone 1 g IM as a single dose \textit{together with} azithromycin 2 g as a single oral dose [1D], i.e. when ceftriaxone monotherapy, a lower ceftriaxone dose, or another treatment regimen was given initially.
- Spectinomycin 2 g IM as a single dose [1B] \textit{together with} azithromycin 2 g as a single oral dose [1C]
- Gentamicin 240 mg IM as a single dose \textit{together with} azithromycin 2 g as a single oral dose [1B]

The high efficacy (100\% [95\%CI 95–100\%]) of the gentamicin 240 mg plus azithromycin 2 g regimen for treatment of anogenital and oropharyngeal gonorrhoea was confirmed in two recent RCTs.\textsuperscript{153,154} Notable, gentamicin 240 mg IM combined with only 1 g of azithromycin orally is suboptimal to eradicate rectal (90\%) and oropharyngeal gonorrhoea (82\%).\textsuperscript{126}

**NOTE:** See use of azithromycin 2 g for treatments of uncomplicated \textit{N. gonorrhoeae} infections of the urethra, cervix and rectum.

- Ertapenem 1 g IM once daily for three days [2D]

This treatment has only been used in a very small number of patients with oropharyngeal gonorrhoea resistant to a regimen of ceftriaxone with or without azithromycin.\textsuperscript{138,146,149}

**Treatment for gonococcal infections in pregnancy or when breastfeeding\textsuperscript{199–201}**

**Recommended treatment.**

- Ceftriaxone 1 g IM as a single dose \textit{together with} azithromycin 2 g as a single oral dose [1D]
• If gastrointestinal side effects are anticipated: ceftriaxone 1 g IM single dose plus azithromycin 1 g oral dose followed by azithromycin 1 g oral dose 6-12 h later may be used.\(^{117,161}\)

**Alternative regimen.**

• Spectinomycin 2 g IM as a single dose together with azithromycin 2 g as a single oral dose \([1D]\)

• If gastrointestinal side effects are anticipated: spectinomycin 2 g IM single dose plus azithromycin 1 g oral dose followed by azithromycin 1 g oral dose 6-12 h later may be used.\(^{117,161}\)

**NOTE:** See use of azithromycin 2 g for treatments of uncomplicated *N. gonorrhoeae* infections of the urethra, cervix and rectum.

• Ceftriaxone 1 g IM as a single dose \([2D]\)

**NOTE:** Pregnancy does not significantly affect the efficacy of treatment. Pregnant and breastfeeding women should not be treated with fluoroquinolones or tetracyclines. The safety of azithromycin 2 g in pregnancy cannot be completely guaranteed but clinical experience indicates that it can be used safely. However, it should only be used under medical supervision if the expected benefit to the mother is thought to be greater than the possible risk to the foetus.\(^{202}\)

**Treatment for upper genital tract gonococcal infection**

**Epididymo-orchitis**

• See the ‘European guideline on the management of epididymo-orchitis’ (https://iusti.org/treatment-guidelines/).

**Pelvic inflammatory disease**

• See the ‘European guideline for the management of pelvic inflammatory disease’ (https://iusti.org/treatment-guidelines/ . . . . .).

**Recommended treatment for disseminated gonococcal infection** \([2D]\)

There have been no clinical trials on the treatment of DGI since the progressive development of gonococcal AMR. Recommended treatment is based on current AMR data, observational data from case series, and the principals of treating septicaemia. Hospitalization is recommended for initial therapy,\(^{1,17,20,36,37,203,204}\) and gonococcal culture and AMR testing should be performed.

**Initial therapy:**

• Ceftriaxone 1 g IM or intravenously (IV) every 24 hours OR

• Cefotaxime 1 g IV every 8 hours OR

• Spectinomycin 2 g IM every 12 hours.

Therapy should continue for 7 days, but may be switched 24–48 hours after substantial clinical improvement to one of the following oral regimens guided by AMR testing:

• Cefixime 400 mg oral dose twice daily OR

• Ciprofloxacin 500 mg oral dose twice daily.

**NOTE:** Ciprofloxacin should only be used when the infection has been confirmed before treatment to be susceptible; using phenotypic AMR testing or validated and quality-assured molecular gyrA-based fluoroquinolone resistance testing (only for anogenital samples).\(^ {63,172–175,209–211}\)

**Recommended treatment for gonococcal conjunctivitis** \([1,36,37,205]\)

There is a lack of recent clinical data for treatment of gonococcal conjunctivitis. The eye should be irrigated frequently with sterile saline solution.

• Ceftriaxone 1 g IM as a single dose together with azithromycin 2 g as a single oral dose \([2D]\)

• If gastrointestinal side effects are anticipated: ceftriaxone 1 g IM single dose plus azithromycin 1 g oral dose followed by azithromycin 1 g oral dose 6-12 h later may be used.\(^ {117,161}\)

**NOTE:** See use of azithromycin 2 g for treatments of uncomplicated *N. gonorrhoeae* infections of the urethra, cervix and rectum.

**Recommended treatment for ophthalmia neonatorum** (*gonococcal neonatal conjunctivitis*) \([1,36,37]\)

The eye should be irrigated frequently with sterile saline solution.

• Ceftriaxone 25-50 mg/kg IV or IM as a single dose, not to exceed 125 mg

**Recommended treatment for people living with HIV** \([1,36,37]\)

People living with HIV with gonorrhoea should be treated in an identical way to HIV-negative individuals.
Recommended treatment for uncomplicated Neisseria meningitidis infection of the urethra

Individuals with uncomplicated urethritis caused by *N. meningitidis* should be treated in an identical way to patients with gonococcal urethritis.

**Sexual contact notification and management of sex contact(s)**

- Sexual contact notification should be performed and documented by appropriately trained professionals at the time of diagnosis to prevent reinfection and reduce onwards transmission [1B];
- Sexual contacts should be contacted and offered (and encouraged to have) testing for gonorrhoea (and other STIs) together with antimicrobial treatment if appropriate (i.e. if positive *N. gonorrhoeae* test or clinician considers contacts will not return for treatment after testing results are available) and receive counseling for gonorrhoea and other STIs [1D];
- All sexual contact(s) within the preceding 3 months of onset of symptoms or diagnosis should be tested and treated if positive [2D].
- Sexual contact notification should be performed and documented by appropriately trained professionals at the time of diagnosis to prevent reinfection and reduce onwards transmission [1B];
- Sexual contacts should be contacted and offered (and encouraged to have) testing for gonorrhoea (and other STIs) together with antimicrobial treatment if appropriate (i.e. if positive *N. gonorrhoeae* test or clinician considers contacts will not return for treatment after testing results are available) and receive counseling for gonorrhoea and other STIs [1D];
- All sexual contact(s) within the preceding 3 months of onset of symptoms or diagnosis should be tested and treated if positive [2D].
- The ‘European guidelines for the management of partners of persons with sexually transmitted infections’ (https://iusti.org/treatment-guidelines/).

**Follow-up and test of cure**

- Assessment after treatment is recommended to confirm eradication of infection, compliance with therapy, enquire about adverse effects, resolution of symptoms and signs, take a sexual history to explore the possibility of re-infection, and pursue partner notification and health promotion [1D];
- A TOC is recommended in all cases to identify persisting infection (possible treatment failure) and emerging AMR. When symptoms and/or signs persist after treatment, culture is recommended to identify persisting infection and for AMR testing, and should be performed 3-7 days after completion of therapy, possibly supplemented a week later with a NAAT for increased sensitivity if culture is negative. TOC in asymptomatic patients can be performed with a NAAT 2 weeks after completion of treatment and ideally, all TOC-positive patients should be cultured and AMR testing performed before further treatment is given. A positive TOC can be due to treatment failure, but also reinfection or, when NAATs are used, residual nucleic acid from non-viable gonococci, and needs to be followed up and interpreted in the clinical context.

**Identification, confirmation and reporting of treatment failures**

The surveillance of possible and confirmed failures with recommended treatment regimens should be enhanced, as detailed in the ECDC Response Plan. As much clinical and laboratory data as feasible should be collected and reported on treatment failures, including a detailed clinical history (including all antimicrobial treatments given), the exclusion of reinfection, whole genome sequencing of pre-treatment and post-treatment gonococcal isolates or other highly discriminative molecular epidemiological typing of NAAT specimens (identifying indistinguishable isolates/genetic variants) and phenotypic and/or molecular assessment of resistance (AMR determinants) to the prescribed treatment using the gonococcal isolates or NAAT specimens.

**Notification**

Gonorrhoea cases should be notified to local, regional and national authorities as mandated by statute. The ECDC is responsible for the EU/EEA-wide gonorrhoea surveillance.

**Composition of the European STI guidelines editorial board**


**Search strategy**

The present guideline was produced according to the protocol for production and revision of European STI guidelines, which has been written and approved by the IUSTI European STI Guidelines Editorial Board (https://iusti.org/wp-content/uploads/2020/04/ProtocolForProduction2020.pdf). A Medline search was conducted up to June 2020 using PubMed for articles published since the development of the 2012 European gonorrhoea guideline. Search headings were kept broad (i) gonorrhoea, iii) gonorrhea or ii) Neisseria gonorrhoeae to include epidemiology, diagnosis, antimicrobial susceptibility/resistance, therapy, clinical trials, prevention, and control. Only publications and abstracts in the English language were considered. The Cochrane Library was searched for all entries related to gonorrhoea/gonorrhea or *Neisseria gonorrhoeae*. Relevant STI guidelines produced by the WHO (www.who.int), US Centers for Disease Control and Prevention (www.cdc.gov/std/) and the British
Association for Sexual Health and HIV (www.bashh.org) were also reviewed.

**Levels of evidence and grading of recommendations**

Levels of evidence and grading of recommendations that were used in the present guideline can be found in the protocol for production and revision of European STI guidelines at: https://iusti.org/wpcontent/uploads/2019/12/Euro_Guidelines_Protocol_2010.pdf

**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.

**Proposed date of revision**

2023.

**Authors’ note**

A list of contributing organisations can be found at: https://iusti.org/treatment-guidelines/

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**ORCID iDs**

M Unemo https://orcid.org/0000-0003-1710-2081

JS Jensen https://orcid.org/0000-0002-7464-7435

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