Essential Medicines List
Sexually Transmitted Infections

*Neisseria gonorrhoeae*

WI, Teodora Elvira
12/13/2016
# Table of Contents

Background .......................................................................................................................... 2

Public Health Importance of Appropriate Treatment of Neisseria gonorrhoea .................... 2

Epidemiology ....................................................................................................................... 2

Antimicrobial Resistance in *Neisseria gonorrhoea* ............................................................ 2

Clinical presentation, complications and sequelae .............................................................. 3

Laboratory diagnosis .......................................................................................................... 3

WHO recommendations for the treatment of Neisseria gonorrhoea .................................... 4

Methodology in developing these guidelines .................................................................... 7

Summary Evidence for the six treatment recommendations ............................................. 7

  Genital and anorectal gonococcal infections .................................................................. 8

  Oropharyngeal gonococcal infections ............................................................................ 9

Retreatment of gonococcal infections after treatment failure .......................................... 10

Treatment of ophthalmia neonatorum .............................................................................. 10

  Topical ocular prophylaxis for the prevention of gonococcal and chlamydial ophthalmia neonatorum ......................................................................................................................................................... 10

Research ............................................................................................................................. 11

Conclusions ......................................................................................................................... 12

Lists of references for reviewed evidence ........................................................................ 12

  Recommendation 1 ......................................................................................................... 12

  Recommendation 2 ......................................................................................................... 20

  Recommendation 3 ......................................................................................................... 23

  Recommendation 4 ......................................................................................................... 28

  Recommendations 5 and 6 ........................................................................................... 29
**Background**

WHO have just updated the treatment recommendations for specific Sexually Transmitted Infections (STI) in August 2016. Since the publication of the World Health Organization (WHO) *Guidelines for the management of sexually transmitted infections* in 2003, changes in the epidemiology of STIs and advancements in prevention, diagnosis and treatment necessitate changes in STI management. There is an urgent need to update treatment recommendations for gonococcal infections to respond to changing antimicrobial resistance (AMR) patterns of *N. gonorrhoeae*. High-level resistance to previously recommended quinolones is widespread and decreased susceptibility to the extended-spectrum (third-generation) cephalosporins, another recommended first-line treatment in the 2003 guidelines, is increasing and several countries have reported treatment failures.

The WHO Essential Medicine Lists (EML) provide a list of the most efficacious and safe medicines for the treatment of illnesses that are considered high priority, including antibiotics. The new WHO guidelines for the treatment of Neisseria gonorrhoea are based on the latest evidence-based recommendations and antimicrobial resistance patterns and expert opinions, using the GRADE process. It would be essential that these new recommendations are reflected in the EML to ensure that appropriate treatment for gonorrhoea are accessible.

**Public Health Importance of Appropriate Treatment of Neisseria gonorrhoea**

**Epidemiology**

Gonorrhoea, caused by *Neisseria gonorrhoeae*, is the second most common bacterial sexually transmitted infection (STI) and results in substantial morbidity and economic cost worldwide. The World Health Organization (WHO) estimates that in 2012, 78 million new cases occurred among adolescents and adults aged 15–49 years worldwide with a global incidence rate of 19 per 1000 females and 24 per 1000 males. The estimated 27 million prevalent cases of gonorrhoea in 2012 translates to a global prevalence of gonorrhoea of 0.8% among females and 0.6% among males aged 15–49 years, with the highest prevalence in the WHO Western Pacific and African Regions \(^1\). Co-infection with *Chlamydia trachomatis* is detected in 10–40% of people with gonorrhoea \(^2\–5\).

**Antimicrobial Resistance in Neisseria gonorrhoea**

The Gonorrhoea Antimicrobial Surveillance Programme (GASP) results show continued widespread resistance to quinolones and azithromycin and emergence of decreased susceptibility to extended spectrum cephalosporins. Gonococcal antimicrobial resistance (AMR) continues to increase worldwide and could lead to a pandemic of extensively drug-resistant (XDR) *Neisseria gonorrhoeae* with serious public health consequences. Decreased susceptibility to the extended spectrum (third-generation) cephalosporins, the last option for monotherapy, is becoming more widespread and ten high income countries have reported treatment failures.
Clinical presentation, complications and sequelae

Uncomplicated gonococcal infection commonly manifests as urethritis in men with symptoms of urethral discharge and dysuria. On examination, the urethral discharge may range from scanty and mucoid to copious and purulent. Gonorrhoea is often asymptomatic in women; less than half of infected women complain of non-specific symptoms such as abnormal vaginal discharge, dysuria, lower abdominal discomfort and dyspareunia. The most common clinical signs are vaginal discharge and cervical friability due to mucopurulent cervicitis. Rectal infections in men and women are largely asymptomatic; occasionally patients complain of rectal and anal pain or discharge. Pharyngeal infections are mainly asymptomatic, but mild sore throat and pharyngitis may occur.

In the majority of women with gonorrhoea, the lack of discernible symptoms results in unrecognized and untreated infections. Untreated infections usually resolve spontaneously but may lead to serious complications such as pelvic inflammatory disease, including endometritis, salpingitis and tubo-ovarian abscess, which can lead to ectopic pregnancy and infertility. Untreated urethral infection in men can lead to epididymitis, urethral stricture and infertility. The risk of complications increases with repeated infection.

Infants of mothers with gonococcal infection can be infected at delivery, resulting in neonatal conjunctivitis manifesting as purulent ocular discharge and swollen eyelids. Untreated conjunctivitis may lead to scarring and blindness.

Laboratory diagnosis

*N. gonorrhoeae* can be diagnosed by culture or nucleic acid amplification tests (NAATs) and, in some instances, Gram stain. NAATs are highly sensitive and specific diagnostic tests that can be conducted on a wide range of samples, including urine, vulvovaginal, cervical and urethral swabs. NAATs have a sensitivity of over 90%, which is higher than for culture (> 85%). The sensitivity varies by NAAT type and is frequently lower for rectal and pharyngeal samples. The lower specificity (98.1–99.7%) of some, particularly early generation, NAATs may result in low positive predictive values, especially in low-prevalence populations, due to cross-reaction with other species of Neisseria. A drawback of currently available commercial NAATs is their inability to provide information on antimicrobial susceptibility. Cultures should be done in parallel with NAATs to allow for susceptibility testing.

Specimens from all cases of suspected gonococcal infection should be collected for microbiological culture and antimicrobial susceptibility testing, to the extent possible considering local availability of resources. Microbiological cultures of *N. gonorrhoeae* are specific and cheap, with a reasonable sensitivity of 85–95% for urethral and endocervical infection. Optimal isolation of *N. gonorrhoeae* requires good specimen collection, timely inoculation into adequate and appropriate culture media, proper transportation and appropriate incubation.

Gram-stained smears can provide a presumptive diagnosis of gonorrhoea, especially among symptomatic men with urethritis. In low-income settings, Gram stains may provide a less expensive alternative to NAATs for symptomatic men. However, only 50–70% of asymptomatic infections in men are positive on Gram stain. Gram stain diagnosis for cervical and rectal infection is less reliable and pharyngeal samples should not be analysed.

Since laboratory diagnostic tests are not available in the majority of countries, diagnosis is often made clinically, based on the presence of symptoms such as vaginal and urethral discharge.
Presumptive treatment is sometimes provided to those at high risk of gonococcal infection, if indicated based on local epidemiological patterns.

**WHO recommendations for the treatment of Neisseria gonorrhoea**

These guidelines provide six treatment recommendations for specific conditions caused by *N. gonorrhoeae*. The recommendations summarized in Table 1 for sexually transmitted gonococcal infections apply to all adults and adolescents (10–19 years of age), including people living with HIV and key populations, including sex workers, men who have sex with men and pregnant women. Specific recommendations are also provided for prophylaxis and treatment of ophthalmia neonatorum caused by *N. gonorrhoeae*.

Table 1: Summary of recommendations for treatment of gonococcal infections.

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Strength of recommendation and quality of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Genital and anorectal gonococcal infections</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Recommendation 1</strong></td>
<td><strong>Good practice statement</strong></td>
</tr>
<tr>
<td>The WHO STI guideline recommends that local resistance data should determine the choice of therapy (both for dual therapy and single therapy).</td>
<td><strong>Conditional recommendation, low quality evidence</strong></td>
</tr>
</tbody>
</table>

In settings where local resistance data are not available, the WHO STI guideline suggests dual therapy over single therapy for people with genital or anorectal gonorrhoea.

The WHO STI guideline suggests the following options:

**Dual therapy** (one of the following)

- ceftriaxone 250 mg intramuscular (IM) as a single dose PLUS azithromycin 1 g orally as a single dose
- cefixime 400 mg orally as a single dose PLUS azithromycin 1 g orally as a single dose

**Single therapy** (one of the following, based on recent local resistance data confirming susceptibility to the antimicrobial)

- ceftriaxone 250 mg IM as a single dose
- cefixime 400 mg orally as a single dose
- spectinomycin 2 g IM as a single dose.

**Remarks:** Because of the emerging resistance data for gonococcal infections and
Reduced effectiveness of some medicines, good practice dictates that the choice of treatment depends on reliable local data on antimicrobial susceptibility. Alternative single-medicine therapies, such as gentamicin or kanamycin, have not been suggested due to lack of surveillance data. Guidance for surveillance of antimicrobial resistance in *N. gonorrhoeae* is available from WHO. This recommendation applies to pregnant women, who should be closely monitored for complications.

### Oropharyngeal gonococcal infections

#### Recommendation 2

In adults and adolescents with gonococcal oropharyngeal infections, the WHO STI guideline suggests dual therapy over single therapy.

The WHO STI guideline suggests the following options:

- **Dual therapy** (one of the following)
  - ceftriaxone 250 mg intramuscular (IM) as a single dose PLUS azithromycin 1 g orally as a single dose
  - cefixime 400 mg orally as a single dose PLUS azithromycin 1 g orally as a single dose

- **Single therapy** (based on recent local resistance data confirming susceptibility to the antimicrobial)
  - ceftriaxone 250 mg IM as single dose.

**Remarks:** Treatment failures have been observed after single therapy for gonococcal oropharyngeal infections and therefore dual therapy is suggested over single therapy. This recommendation applies to pregnant women, who should be closely monitored for complications.

#### Retreatment of gonococcal infections after treatment failure

**Recommendation 3**

In people with gonococcal infections who have failed treatment, the WHO STI guideline suggests the following options.

- If reinfection is suspected, re-treat with a WHO-recommended regimen, reinforce sexual abstinence or condom use, and provide partner treatment.

---

• If treatment failure occurred after treatment with a regimen not recommended by WHO, re-treat with a WHO-recommended regimen.

• If treatment failure occurred and resistance data are available, re-treat according to susceptibility.

• If treatment failure occurred after treatment with a WHO-recommended single therapy, re-treat with WHO-recommended dual therapy.

• If treatment failure occurred after a WHO-recommended dual therapy, re-treat with one of the following dual therapies:
  - ceftriaxone 500 mg IM as a single dose PLUS azithromycin 2 g orally as a single dose
  - cefixime 800 mg orally as a single dose PLUS azithromycin 2 g orally as a single dose
  - gentamicin 240 mg IM as a single dose PLUS azithromycin 2 g orally as a single dose
  - spectinomycin 2 g IM as a single dose (if not an oropharyngeal infection) PLUS azithromycin 2 g orally as a single dose.

Remarks: Before retreatment, reinfection should be distinguished from treatment failure, resistance data should be obtained when possible, and the WHO-recommended regimens should be used.

### Gonococcal ophthalmia neonatorum

#### Recommendation 4

In neonates with gonococcal conjunctivitis, the WHO STI guideline suggests one of the following treatment options:

- ceftriaxone 50 mg/kg (maximum 150 mg) IM as a single dose
- kanamycin 25 mg/kg (maximum 75 mg) IM as a single dose
- spectinomycin 25 mg/kg (maximum 75 mg) IM as a single dose.

Remarks: Due to the large net benefit with treatment, good practice dictates that neonates should be treated for gonococcal conjunctivitis. The choice of treatment may depend on the cost and quality of the medicine in different settings and on equity considerations. Side-effects should be monitored in neonates.

#### Recommendation 5

For all neonates, the WHO STI guideline recommends topical ocular prophylaxis for the prevention of gonococcal and chlamydial ophthalmia neonatorum.

Conditional recommendation, very low quality evidence

Strong recommendation, low quality evidence
Recommendation 6

For ocular prophylaxis, the WHO STI guideline suggests one of the following options for topical application to both eyes immediately after birth:

- tetracycline hydrochloride 1% eye ointment
- erythromycin 0.5% eye ointment
- povidone iodine 2.5% solution (water-based)
- silver nitrate 1% solution
- chloramphenicol 1% eye ointment.

Remarks: Recommendations 5 and 6 apply to the prevention of both chlamydial and gonococcal ophthalmia neonatorum. Cost and local resistance to erythromycin, tetracycline and chloramphenicol in gonococcal infection may determine the choice of medication. Caution should be taken to avoid touching eye tissue when applying the topical treatment and to provide a water-based solution of povidone iodine. **DO NOT USE ALCOHOL-BASED POVIDONE IODINE SOLUTION.**

Methodology in developing these guidelines

These guidelines were developed following the methods outlined in the 2014 WHO handbook for guideline development. The Guideline Development Group (GDG) included international STI experts, clinicians, researchers and programme managers. The GDG prioritized questions and outcomes related to treatment of gonococcal infections to include in this update, and a methodologist and a team of systematic reviewers from McMaster University, the WHO Collaborating Centre for Evidence-Informed Policy, independently conducted systematic reviews of the effectiveness of different treatments for gonorrhoea. The evidence was assessed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach and presented to the GDG. Conflicts of interest were managed according to WHO guidelines and declared before the recommendations were discussed and finalized. Research implications were also developed by the GDG.

Details of the methods for developing these guidelines are described on page 33 to 40 of the WHO Guidelines for the Treatment of *Neisseria gonorrhoeae*.\(^2\)

Summary Evidence for the six treatment recommendations

The list of references of reviewed evidence are detailed below, and details of the evidence reviewed, including evidence profiles and evidence-to-decision frameworks used to make these recommendations are in Annex D.\(^3\)

---


\(^3\)
Genital and anorectal gonococcal infections

The quality of the evidence for the effects of treatments for gonococcal infections is low. Evidence is available from 108 studies, including 14 randomized and 94 non-randomized studies, which were conducted in a broad range of high-, middle- and low-income countries. Although high cure rates were shown (> 95%), the evidence is outdated and regionally specific, and therefore is considered to be indirect due to emerging resistance data. Available data on AMR in N. gonorrhoeae revealed high rates of resistance to quinolones, emerging azithromycin resistance and decreased susceptibility to ceftriaxone and cefixime.

Low quality evidence suggests similar cure rates with azithromycin using single doses of 1 g or 2 g, but there are data on emerging resistance for azithromycin from many countries. Cure rates for kanamycin and gentamycin vary and are based on older studies. Currently, there is little surveillance data for these two medicines. There are similar cure rates with cefixime using single doses of 400 mg or 800 mg. The evidence for dual versus single therapy is low quality, as there are few studies evaluating different combinations with azithromycin.

Side-effects of the medicines were often not measured, but when measured were trivial. In particular, the evidence for differences in side-effects between 1 g or 2 g single doses of azithromycin is uncertain, but the Guideline Development Group (GDG) agreed that side-effects, such as nausea, could be greater with higher doses.

Overall, the GDG therefore agreed that the success of the available treatments is based on in vitro susceptibility of gonococcal infections, and should therefore be based on recent local surveillance data.

Due to global resistance patterns, quinolones are no longer an option for treatment of gonococcal infections. The GDG agreed that dual therapy should be suggested due to the emergence of resistance and the paucity of surveillance data in most settings to guide decisions about susceptibility to single therapy. Additional studies comparing different combinations of dual therapy (such as gentamicin, ceftriaxone, cefixime or gemifloxacin plus azithromycin) will inform recommendations in future.

No studies were found that assessed patient values and preferences, acceptability, equity or feasibility specific to gonococcal infections. There is some evidence from the literature about acceptability of injections versus oral medications in people with syphilis. Approximately 10–20% of people refused injections. The GDG also noted that some health-care providers are, in practice, averse to providing injections, and that additional labour time and costs are associated with IM administration. The GDG agreed that there is probably no variability in the values people place on the outcomes. However, IM injection may be less desirable among patients than oral administration, and dual therapy is acceptable to patients based on current use. Although azithromycin is perceived by some GDG members to require greater resources, the costs of the suggested treatments were similar. Since azithromycin is currently recommended for treatment of other STIs (e.g. chlamydia), it may provide additional benefit by treating possible co-infections.

For pregnant women: The quality of evidence for the effects of treatments for genital and anorectal gonococcal infections in pregnant women is low. Evidence was reviewed from three studies, including two randomized studies and one non-randomized study. When data for pregnant women were not available, evidence in non-pregnant adults was used to inform the recommendations.

In summary, there is low quality evidence for benefits and harms of dual therapy compared to single therapy, but due to emerging resistance to single therapies and lack of local surveillance data in most regions, dual therapy is favoured over single therapy. Dual therapy is currently being used in some settings and it appears to be acceptable, and the costs compared to effectiveness are not greater than single therapy.

Oropharyngeal gonococcal infections
The quality of the evidence for the effects of different treatments for oropharyngeal gonococcal infections is low and very low, and therefore, overall, the evidence for this recommendation is very low. Evidence from 28 studies was identified: eight randomized and 20 non-randomized studies (including two non-randomized studies with two or more groups, and 18 non-randomized studies with one group). These studies were conducted in a broad range of high-, middle- and low-income countries. This evidence is outdated and regionally specific, and therefore is considered to be indirect due to emerging resistance data. The GDG agreed that the success of the available treatments is based on in vitro susceptibility of gonococcal infections, and should therefore be based on recent local surveillance data. Similar treatments were provided to people with oropharyngeal infections and anorectal infections (typically people had co-infection at other sites). The data showed a higher risk of treatment failure with oropharyngeal infections, and the GDG agreed that the consequences of treatment failure are severe. Based on these considerations, the GDG agreed that treatment should be as aggressive for oropharyngeal infections as for anorectal infections. Low quality evidence showed that spectinomycin may result in lower cure rates (75%, ranging from 49% to 100%). Data for the effects of gentamycin or kanamycin are not available.

No studies were found to assess patient values and preferences, acceptability, equity or feasibility. The GDG agreed that there is probably no variability in values. However, IM injection may be less desirable than oral administration, and dual therapy is acceptable. Although azithromycin may be perceived by health-care providers, programme managers, policy-makers and funders to require greater resources, in fact the costs were similar across different treatments.

In summary, there is very low quality evidence for benefits and harms of dual therapy compared to single therapy, but due to emerging resistance to single therapies and lack of local surveillance data in most regions, dual therapy is favoured over single therapy. Dual therapy is currently being used in some settings and it appears to be acceptable, and the costs compared to effectiveness are not greater than single therapy. The recommendations for genital, anorectal and oropharyngeal infections are similar; however, single therapy with spectinomycin was less effective in oropharyngeal infections.
Retreatment of gonococcal infections after treatment failure

The quality of the evidence is very low. The evidence is from 34 randomized and non-randomized studies that evaluated a treatment or many treatments and then reported on retreatment of individual cases of treatment failure. No studies specifically recruited people who had treatment failure. Most studies reported on cases of treatment failure or reinfection (a distinction was often not made). These studies also reported the medicine used for initial treatment, the medicine used for retreatment, and sometimes reported whether or not the case was cured. Cure rates for different medicines were not consistent across the studies.

In summary, there is very low quality evidence for the effects of specific medicines for people who fail treatment. Therefore, the recommendation was based on first determining whether or not the initial treatment was according to a WHO-recommended regimen; if it was not, then retreatment is suggested according to a WHO-recommended regimen; but if the initial treatment was according to a WHO-recommended regimen, then the suggestion for retreatment is for increasing dosages.

Treatment of ophthalmia neonatorum

The evidence is from two randomized and 13 non-randomized studies. There was very low quality evidence for cure rates, which were typically 100% for all treatments, with the exception of penicillin (81–84%). The quality of evidence was very low for adverse effects across treatments, generally indicating little to no difference among treatments. No evidence is available for patient values and preferences. The costs for treatments were relatively low and similar, and most treatments are currently being used.

Topical ocular prophylaxis for the prevention of gonococcal and chlamydial ophthalmia neonatorum.

Overall, the quality of the evidence is low to very low from 16 studies: 15 randomized studies and one non-randomized study with two comparison groups. There are few data for the effects of chloramphenicol. Large benefits were reported for prophylaxis compared with no prophylaxis, in particular in babies born to women with known infection (approximately 70% reduction in conjunctivitis with prophylaxis using different medications). The benefits of treatment with different medications are similar; however, the low to very low quality evidence indicates that the benefits of tetracycline hydrochloride, erythromycin or povidone iodine may be slightly greater than for silver nitrate.

Few data are available for the incidence of non-infectious conjunctivitis after prophylaxis or no prophylaxis. Low quality evidence shows a slight reduction or little difference and indicates that
between 4 and 50 per 1000 infants have non-infectious conjunctivitis after application of different prophylactic medications. There is little evidence for patient values and preferences, but the GDG agreed that there would likely be little difference in the high value placed on avoiding long-term consequences of both gonococcal and chlamydial conjunctivitis. The GDG also agreed that there would be little effect on acceptability, equity and feasibility, as prophylaxis is currently used in many countries. The GDG reported that alcohol-based povidone iodine has erroneously been used as prophylaxis resulting in serious harm to babies. Silver nitrate is the most expensive prophylaxis option.

In summary, there are large benefits for prophylaxis to prevent ophthalmia neonatorum, and these benefits outweigh the risk of non-infectious conjunctivitis due to prophylaxis with any of the topical medications. Some topical medications may provide greater protection (tetracycline hydrochloride, erythromycin or povidone iodine), but all are feasible to provide.

**Research**

While surveillance data should be collected – including breakpoints for resistance, frequency of collection, number of isolates, and interpretation of local data – research into current and new medicine options is needed for genital, anorectal and oropharyngeal infections. This research is essential in light of the increasing antimicrobial resistance (AMR) to currently recommended treatments. Appropriately designed randomized controlled trials should be conducted on new medicine options, dual therapy and other alternatives, such as gentamicin and kanamycin.

Specifically, studies should compare different combinations of dual therapy (such as gentamicin, ceftriaxone, cefixime or gemifloxacin plus azithromycin). Trials should include both men and women, and key populations, such as MSM and sex workers. In addition to commonly reported outcomes (e.g. cure and side-effects), other important outcomes should be evaluated, including transmission of gonorrhoea to partners, HIV transmission and acquisition, quality of life, and gonorrhoea antimicrobial in vitro resistance.

Treatment failure has been particular poorly researched. Although it is difficult to recruit a whole study population who had treatment failure, studies that conduct follow-up with patients who had treatment failure should improve their reporting. Studies should distinguish between cases of treatment failure and reinfection, and should report the first treatment, the follow-up treatment and the outcome. Related to cause of treatment failure, studies should explore and report the susceptibility of the organism in those who have experienced treatment failure.

Regarding the prevalence and treatment of ophthalmia neonatorum, there is little research into the risk of resistance to medications that are currently available. The state of resistance to the medications should be explored and it should be established whether these organisms would be killed by ocular prophylaxis despite resistant strains being established in the organisms. The prevalence of gonococcal ophthalmia should be determined given the high prevalence of maternal gonorrhoea in some settings.
There is very little research into the values that people place on outcomes such as cure, burden of disease or risk of transmission. There is also little research specifically for people with gonococcal infections and their preferences for treatments, in particular their preference for injection versus oral administration of medicine, which may also be reflected in compliance in the context of randomized controlled trials.

Conclusions
The updated recommendations for the treatment of gonorrhoea, were developed based on the WHO guidelines using the GRADE process. These are evidenced based recommendations taking into consideration antimicrobial susceptibility patterns, quality of evidence, balance between benefits and harms, patient values and preferences, acceptability, feasibility, cost and cost effectiveness. These guidelines provide six treatment recommendations for specific conditions caused by N. gonorrhoeae. Specific recommendations are also provided for prophylaxis and treatment of ophthalmia neonatorum caused by N. gonorrhoeae. Notable changes from the 2003 WHO STI guidelines include the following: quinolones are no longer recommended for the treatment of gonorrhoea due to the reported high level of resistance; there are now recommendations for oropharyngeal infections, and retreatment of gonococcal infections after treatment failure; dual therapy is a preferred option for treatment of gonococcal infections over single therapy; single therapy is based on local resistance data and changes have been made to some dosages; and new topical medications have been suggested for prophylaxis of ophthalmia neonatorum.

Lists of references for reviewed evidence

Recommendation 1
Treatments for gonorrhoea (genital or cervix) among adults and adolescents, HIV positive patients, men who have sex with men (MSM) or pregnant women

Systematic reviews

Included studies: randomized and non-randomized studies
1. Aplasca De Los Reyes MR, Pato-Mesola V, Klausner JD, Manalastas R, Wi T, Tuazon CU,


73. Panikabutra K, Lee CT, Ho B, Bamberg P. Single dose oral norfloxacin or intramuscular


**Systematic review for pregnant women**


**Included studies: randomized and non-randomized studies for pregnant women**


For references on antimicrobial resistance in Neisseria gonorrhoeae, please see p. X.

**Recommendation 2**

**Treatments for gonococcal oropharyngeal infections in adults and adolescents**

*Systematic review*


*Included studies: randomized and non-randomized studies*


Patient values and preferences, acceptability and cost: specific to gonorrhoea infections


Patient values and preferences, acceptability and cost: other sexually transmitted infections


Patient values and preferences, acceptability and cost: other conditions

Systematic reviews


Included studies


For references on antimicrobial resistance in Neisseria gonorrhoeae, please see p. X.
Recommendation 3
Treatments for people with treatment failure of *N. gonorrhoeae* (genital or oropharyngeal)

**Included studies: randomized and non-randomized studies**

17. Mroczkowski TF, Hook EW 3rd, Jones RB, McCormack WM, Martin DH. Grepafloxacin


Patient values and preferences, acceptability and cost: specific to gonorrhoea infections


Patient values and preferences, acceptability and cost: other sexually transmitted infections


Patient values and preferences, acceptability and cost: other conditions

Systematic reviews


Included studies


Antimicrobial resistance in Neisseria gonorrhoeae

References for recommendations 1–3

Extended-spectrum cephalosporin resistance:

Cefixime verified treatment failures:


Ceftriaxone verified treatment failures:


*Ceftriaxone and cefixime resistance:*

*N. gonorrhoeae* strains with high ceftriaxone MIC values have been reported in Japan (H041 strain), France and Spain (F89 strain), and Australia (A8806 strain):


*Azithromycin resistance*

*Based on the literature reviews, countries have reported high level of azithromycin resistance.*


**Recommendation 4**

**Treatment of gonococcal ophthalmia neonatorum**

*Included studies: randomized and non-randomized studies*


Patient values and preferences, acceptability and cost: Other sexually transmitted infections


Recommendations 5 and 6
Prevention of gonococcal and chlamydial ophthalmia neonatorum

Systematic reviews
Quality; 2010.

Included studies: randomized and non-randomized studies
References for data on resistance to prophylaxis:


References related to patient values and preferences, acceptability and cost


Additional references
