Appendix 2: Recommended treatment options

Recommended treatment options for urethral discharge syndrome

• Therapy for uncomplicated *Neisseria gonorrhoeae*
Plus
• Therapy for *Chlamydia trachomatis*

Infections covered	First choice	Effective substitutes
In settings in which local antimicrobial resistance data are not available, the WHO STI guideline suggests dual therapy for gonorrhoea.		
N. gonorrhoeae[a]	**Ceftriaxone 250 mg**, intramuscularly, single dose Plus **Azithromycin 1 gram,** orally, single dose	**Cefixime 400 mg**, orally, single dose Plus **Azithromycin 1 gram**, orally, single dose
C. trachomatis	**Doxycycline 100 mg**, orally, twice daily for seven days (to be given only if gonorrhoea therapy did not include azithromycin)	**Azithromycin 1 gram**, orally, single dose **or** **Erythromycin 500 mg**, orally, 4 times a day for 7 days **or** **Ofloxacin 200–400 mg**, orally, twice a day for 7 days. (to be given only if gonorrhoea therapy did not include azithromycin)
In settings in which local antimicrobial resistance data reliably confirm the susceptibility of *N. gonorrhoeae* to the antimicrobial agent, single therapy may be given.		
N. gonorrhoeae	**Ceftriaxone 250 mg**, intramuscularly, single dose	**Cefixime 400 mg**, orally, single dose **or** **Spectinomycin 2 grams**, intramuscularly, single dose (availability makes this antibiotic impractical)
Additional therapeutic options for recurrent or persistent infections		
T. vaginalis	**Metronidazole 2 grams**, orally, single doses	**Metronidazole 400 or 500 mg**, twice daily for 7 days
M. genitalium	**Azithromycin 500 mg**, orally on day 1, **250 mg** daily on days 2–5	

[a] Because of increasing antimicrobial resistance to azithromycin in *N. gonorrhoeae* and *M. genitalium* and reduced susceptibility of *N. gonorrhoeae* to cephalosporins, WHO is in the process of revising current treatment recommendations and dosages.

Source: World Health Organization. Guidelines for the management of symptomatic sexually transmitted infections. Geneva: WHO; 2021. Licence: CC BY-NC-SA 3.0 IGO.

Recommended treatment options for vaginal discharge syndrome

A. Treatment options for vaginal infections

• Therapy for bacterial vaginosis and trichomoniasis
Plus
• Therapy for yeast infection if curd-like white discharge, vulvovaginal redness and itching are present

Infections covered	First-line options	Effective substitutes	*Note:* In pregnancy, metronidazole should, ideally, be avoided in the first trimester
Bacterial vaginosis	**Metronidazole 400 mg or 500 mg**, orally, twice daily for 7 days	**Clindamycin 300 mg**, orally, twice daily for 7 days **or** Metronidazole 2 grams, orally, single dose	**Metronidazole 200 mg or 250 mg**, orally, 3 times a day for 7 days **or** **Metronidazole gel** 0.75%, one full applicator (5 grams) intravaginally, twice a day for 7 days **or** **Clindamycin 300 mg**, orally, twice daily for 7 days
T. vaginalis	**Metronidazole 2 grams**, orally, in a single dose **or** **Metronidazole 400 mg or 500 mg**, orally, twice daily for 7 days	**Tinidazole 2 grams** orally, single dose **or** **Tinidazole 500 mg** orally, twice daily for 5 days	**Metronidazole 200 mg or 250 mg**, orally, 3 times a day for 7 days **or** **Metronidazole gel** 0.75%, one full applicator (5 grams) intravaginally, twice a day for 7 days
***C. albicans* (yeast infection)**	**Miconazole vaginal pessaries, 200 mg** inserted at night for 3 nights **or** **Clotrimazole vaginal tablet, 100 mg**, inserted at night for 7 nights	**Fluconazole 150 mg (or 200mg)**, orally, single dose **OR** **Nystatin, 200,000-unit vaginal tablet**, inserted at night for 7 nights	**Miconazole 200 mg vaginal pessaries** inserted once daily for 3 days **or** **Clotrimazole vaginal tablet 100 mg** inserted at night for 7 days **or** **Nystatin pessaries 200,000 units**, inserted at night for 7 nights

People taking metronidazole should be cautioned to avoid alcohol. Use of metronidazole in the first trimester of pregnancy is not recommended unless the benefits outweigh the potential hazards.

B. Treatment options for cervical infection

• Therapy for uncomplicated *N. gonorrhoeae*
Plus
• Therapy for *C. trachomatis*

Infections covered	First choice (choose one from each cell below)	Effective substitutes	Options for pregnant women or during breastfeeding
In settings in which local antimicrobial resistance data are not available, the WHO STI guidelines suggest dual therapy for gonorrhoea.			
N. gonorrhoeae[a]	**Ceftriaxone 250 mg, intramuscularly, single dose plus Azithromycin 1 gram, orally, single dose**	**Cefixime 400 mg, orally, single dose plus Azithromycin 1 gram, orally, single dose**	**Ceftriaxone 250 mg, intramuscularly, single dose plus Azithromycin 1 gram, orally, single dose or Cefixime 400 mg, orally, single dose plus Azithromycin 1 gram, orally, single dose**
C. trachomatis	**Doxycycline 100 mg, orally, twice daily for 7 days (to be given only if gonorrhoea therapy did not include azithromycin)**	**Azithromycin 1 gram, orally, single dose or Erythromycin 500 mg, orally, 4 times a day for 7 days or Ofloxacin 200–400 mg, orally, twice daily for 7 days (to be given only if gonorrhoea therapy did not include azithromycin)**	**Erythromycin 500 mg, orally, 4 times a day for 7 days or Azithromycin 1 gram, orally, single dose (to be given only if gonorrhoea therapy did not include azithromycin)**
M. genitalium	**Azithromycin 500 gram,** orally day 1, 250 mg daily, days 2–5 (absence of macrolide resistance)		**Azithromycin 500 gram,** orally, day 1, 250 mg daily, days 2–5 (absence of macrolide resistance)

[a] Because of increasing antimicrobial resistance to azithromycin in *N. gonorrhoeae* and *M. genitalium* and reduced susceptibility of *N. gonorrhoeae* to cephalosporins, WHO is in the process of revising current treatment recommendations and dosages.

Source: World Health Organization. Guidelines for the management of symptomatic sexually transmitted infections. Geneva: WHO; 2021. Licence: CC BY-NC-SA 3.0 IGO.

Treatment options for pelvic inflammatory disease

• Therapy for uncomplicated *N. gonorrhoeae*
Plus
• Therapy for *C. trachomatis*
Plus
• Therapy for anaerobic infections

Infections covered	First choice	Effective substitutes
In settings in which local antimicrobial resistance data are not available, the WHO STI guidelines suggest dual therapy for gonorrhoea.		
N. gonorrhoeae[a]	**Ceftriaxone 250 mg**, intramuscularly, single dose plus **Azithromycin 1 gram**, orally, single dose	**Cefixime 400 mg**, orally, single dose plus **Azithromycin 1 gram**, orally, single dose
C. trachomatis	**Doxycycline 100 mg**, orally, twice daily for 14 days	**Erythromycin 500 mg**, four times daily for 14 days (to be given only if gonorrhoea therapy did not include azithromycin)
In settings in which local antimicrobial resistance data reliably confirm the susceptibility of *N. gonorrhoeae* to the antimicrobial agent, single therapy may be given as below.		
N. gonorrhoeae[a]	**Ceftriaxone 250 mg**, intramuscularly, single dose	**Cefixime 400 mg**, orally, single dose
The treatment for anaerobes must be included in either treatment option above.		
Anaerobes	**Metronidazole 400 mg or 500 mg**, orally, twice daily for 14 days	

[a] Because of increasing antimicrobial resistance to azithromycin in *N. gonorrhoeae* and reduced susceptibility to cephalosporins, WHO is in the process of revising current treatment recommendations and dosages.

Source: World Health Organization. Guidelines for the management of symptomatic sexually transmitted infections. Geneva: WHO; 2021. Licence: CC BY-NC-SA 3.0 IGO.

Recommended treatment options for genital ulcer disease

• Multiple-dose therapy for herpes simplex virus infection
plus
• Single-dose long-acting penicillin therapy or multi-dose therapy of alternatives

Infections covered	First-line options	Effective substitutes	For pregnant and breastfeeding women and people younger than 16 years
Genital herpes	**Primary infection** **Acyclovir 400 mg**, orally, 3 times a day for 10 days **or** **Acyclovir 200 mg**, orally, 5 times a day for 10 days	**Primary infection** **Valaciclovir 500 mg**, twice a day for 10 days **or** **Famciclovir 250 mg**, orally, 3 times a day for 10 days	**Primary infection** Use acyclovir only when the benefit outweighs the risk. The dosage is the same as for primary infection in non-pregnancy.
	Recurrent infection – episodic therapy **Acyclovir 400 mg**, orally, 3 times a day for 5 days **or** **Acyclovir 800 mg**, orally, twice daily for 5 days **or** **Acyclovir 800 mg**, 3 times a day for 2 days	**Recurrent infection – episodic therapy** **Valaciclovir 500 mg**, twice daily for 5 days **or** **Famciclovir 250 mg**, orally, twice daily for 5 days	**Recurrent infection – episodic therapy** **Acyclovir 400 mg**, orally, 3 times a day for 5 days **or** **Acyclovir 800 mg**, orally, twice daily for 5 days **or** **Acyclovir 800 mg**, 3 times a day, for 2 days
	Suppressive therapy for recurrent herpes[a] **Acyclovir 400 mg**, orally, twice daily **or** **Valaciclovir 500 mg**, once daily	**Suppressive therapy for recurrences**[a] **Famciclovir 250 mg**, orally, twice daily	**Suppressive therapy for recurrent herpes**[a] **Acyclovir 400 mg**, orally, twice daily **or** **Valaciclovir 500 mg**, once daily
Syphilis (early) (treatment for primary, secondary and early latent [less than two years since infection] syphilis)	**Benzathine penicillin 2.4 million units**, intramuscularly in a single dose	**Doxycycline 100 mg**, orally, twice a day for 14 days **or** **Erythromycin 500 mg**, 4 times a day for 14 days	**Benzathine penicillin 2.4 million units**, intramuscularly in a single dose **or** **Erythromycin 500 mg**, orally, 4 times a day for 14 days[b]

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Syphilis (late) (treatment for late latent and tertiary syphilis)	**Benzathine penicillin 2.4 million units** by intramuscular injection, once weekly for 3 consecutive weeks	**Procaine penicillin 1.2 million units** by intramuscular injection, once daily for 20 consecutive days **or** **Doxycycline 100 mg**, orally, twice daily for 30 days	**Erythromycin 500mg** orally, 4 times a day for 30 days[b]

[a] Suppressive therapy for recurrent herpes is recommended for individuals with 4–6 or more recurrent episodes per year, severe symptoms or episodes that cause distress. Increased dosages or duration of treatment are required for people living with HIV (*27*).

[b] Although erythromycin is used to treat pregnant women, it does not cross the placental barrier completely and the fetus is not treated. The newborn infant therefore needs treatment soon after delivery.

Treatment options for people with anorectal discharge

Recommended treatment regimens for anorectal infections		
Infections covered	**Recommended choice**	**Effective substitutes**
N. gonorrhoeae[a]	**Ceftriaxone 250 mg**, intramuscularly, single dose **plus** **Azithromycin 1 gram**, orally, single dose	**Cefixime 400 mg**, orally, single dose **plus** **Azithromycin 1 gram**, orally, single dose
C. trachomatis	**Doxycycline 100 mg** orally, twice daily, for 7 days **or** **Doxycycline for 21 days** (to cover rectal lymphogranuloma venereum) if suspected or confirmed on NAAT (to be given only if dual therapy did not include azithromycin)	**Erythromycin 500 mg**, orally, 4 times a day for 14 days (to be given only if dual therapy did not include azithromycin)
Syphilis (if ulcer present)	**Benzathine penicillin 2.4 million units** intramuscularly, single dose People with a positive syphilis test and no ulcer: administer the same dose at weekly intervals for a total of three doses	**Doxycycline 100 mg** orally, twice daily for 14 days **Erythromycin 500 mg** 4 times a day, orally, for 14 days Extend treatment to 30 days if syphilis serology is positive

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Genital herpes	Recurrent infection: **Acyclovir 400 mg**, orally, 3 times a day for 5 days **or** **Acyclovir 800 mg**, orally, 3 times a day for 2 days **or** **Acyclovir 800 mg**, orally, 2 times a day for 5 days	**Recurrent infection:** **Valaciclovir 500 mg**, twice daily for 3 days
	Primary genital herpes: **Acyclovir 400 mg**, orally, 3 times a day for 10 days **or** **Acyclovir 200 mg**, 5 times a day for 10 days	**Primary genital herpes:** **Valaciclovir 500 mg**, orally, twice daily for 10 days
	Suppressive therapy for recurrent herpes **Acyclovir 400 mg**, orally, twice daily **or** **Valaciclovir 500 mg**, once daily For duration, see the genital ulcer disease section	**Suppressive therapy for recurrences** **Famciclovir 250 mg**, orally, twice daily **(Famciclovir 500 mg**, twice daily for people living with HIV or immunocompromised**)**

a Because of increasing antimicrobial resistance to azithromycin in *N. gonorrhoeae* and reduced susceptibility to cephalosporins, WHO is in the process of revising current treatment recommendations and dosages.

Source: World Health Organization. Guidelines for the management of symptomatic sexually transmitted infections. Geneva: WHO; 2021. Licence: CC BY-NC-SA 3.0 IGO.

Treatment for genital warts caused by human papillomavirus (HPV) types 6 and 11

No one treatment is completely satisfactory. Local treatment can remove the warts, but they may recur. This should be explained to the client before commencing therapy. Note that management of vaginal and/or cervical warts, urethral meatal warts, and anal warts should be undertaken in a higher-level or specialist facility.

Chemical methods

a. Podophyllin 25 per cent in compound tincture of benzoin, to be applied *by the healthcare provider* carefully to the warts, avoiding normal tissue. The client should be instructed to wash the podophyllin off after 4–6 hours. Treatment is repeated once a week. If warts persist after 6–8 applications, refer the client to a higher facility.

b. Podophyllotoxin 0.5 per cent solution/gel could be applied *by the client* using a cotton swab to visible genital warts twice a day for 3 days, followed by 4 days of no therapy. This cycle may be repeated, as necessary, for up to 4–5 cycles. The total volume of podophyllin/podophyllotoxin should be limited to 0.5 ml per day and the total wart area treated should not be more than 10 cm^2.

c. Trichloroacetic acid (TCA) 80–90 per cent can be applied *by the healthcare provider* carefully to the warts, avoiding normal tissue, followed by powdering of the treated area with talc or sodium bicarbonate to remove excess acid. Repeat application at weekly intervals. TCA causes immediate chemical cauterization. It is not absorbed systemically and therefore can be safely used in pregnancy.

- If the warts persist after 2 months of treatment with podophyllin, podophyllotoxin, or TCA, refer the client to a higher-level facility for further management.

d. Imiquimod 5 per cent cream can be applied *by the client* with a finger/cotton swab at bedtime, left on overnight, 3 times a week on every other day for as long as 16 weeks. The treated area should be washed with soap and water 6–10 hours after application.

Important: The use of podophyllin/podophyllotoxin is contraindicated during pregnancy and lactation. The safety of imiquimod during pregnancy has not been established.

Physical methods (may not be feasible at the primary healthcare level)

a. Cryotherapy can be given with liquid nitrogen, solid carbon dioxide, or a cryoprobe. Repeat applications every 1–2 weeks. Cryotherapy is non-toxic, does not require anaesthesia and, if carried out properly, does not result in scarring.

b. Electrosurgery

c. Surgical removal

Source: World Health Organization. Regional Office for South-East Asia. Management of sexually transmitted infections: regional guidelines. WHO; 2011. Available at: https://apps.who.int/iris/handle/10665/205471. Accessed 31 March 2020.

Treatment for hepatitis B virus (HBV)

Acute hepatitis B:

- There is no specific treatment, but care can help to maintain comfort and adequate nutritional balance, including replacement of fluids lost from vomiting and diarrhoea.
- Avoid unnecessary medications. Acetaminophen/paracetamol and medication against vomiting should not be given [1].

Chronic hepatitis B (persistence of hepatitis B surface antigen [HBsAg] for 6 months or more):

- Only a proportion (10–40 per cent depending on setting and eligibility criteria) of people with chronic hepatitis B infection will require treatment. Treatment for chronic hepatitis B must be continued for life in most people who start it (cure/clearance of HBsAg is rare). The treatment suppresses the virus and can slow the progression of cirrhosis, reduce incidence of liver cancer, and improve long-term survival. For information on who to treat and who not to treat among people with chronic hepatitis B, monitoring treatment, and when to stop treatment, refer to the full WHO guidelines [2].
- In high-income countries, surgery and chemotherapy can prolong life for up to a few years. Liver transplantation is sometimes used in people with cirrhosis in high-income countries, with varying success.

First-line antiviral therapies for chronic hepatitis B

- In all adults, adolescents, and children aged 12 years or older in whom antiviral therapy is indicated, the nucleos(t)ide analogues (NAs) that have a high barrier to drug resistance (tenofovir or entecavir) are recommended. Entecavir is recommended in children aged 2–11 years.
- NAs with a low barrier to resistance (lamivudine, adefovir, or telbivudine) can lead to drug resistance and are not recommended.

For HBV/HIV-coinfected people (adults/adolescents/children), please check the recommended antiretroviral therapy regimen.

Second-line antiviral therapies for the management of treatment failure

- In people with confirmed or suspected antiviral resistance (i.e. history of prior exposure or primary non-response) to lamivudine, entecavir, adefovir, or telbivudine, a switch to tenofovir is recommended.

Prevention of perinatal HBV transmission using antiviral therapy

- In HBV-monoinfected pregnant individuals, the indications for treatment are the same as for other adults, and tenofovir is recommended. No recommendation was made on the routine use of antiviral therapy to prevent perinatal HBV transmission.

For HIV-infected pregnant and breastfeeding individuals, check the recommended antiretroviral therapy regimen.

References

[1] World Health Organization. Hepatitis B. Key facts. June 2022. Available at: https://www.who.int/news-room/fact-sheets/detail/hepatitis-b. Accessed 20 June 2022.

[2] World Health Organization. Guidelines for the prevention, care and treatment of persons with chronic hepatitis B infection. Geneva: WHO; 2015. Available at: https://www.who.int/publications/i/item/9789241549059. Accessed 31 March 2020.

Treatment for hepatitis C virus (HCV)

WHO recommends offering treatment to all individuals diagnosed with HCV infection who are 12 years of age or older, irrespective of disease stage, as described below.

In adults (aged 18 years and older) with chronic HCV infection, the following pangenotypic direct-acting antiviral regimens can be used:

- For adults without cirrhosis:
  - sofosbuvir/velpatasvir 12 weeks
  - sofosbuvir/daclatasvir 12 weeks
  - glecaprevir/pibrentasvir 8 weeks
- For adults with compensated cirrhosis:
  - sofosbuvir/velpatasvir 12 weeks
  - glecaprevir/pibrentasvir 12 weeks
  - sofosbuvir/daclatasvir 24 weeks
  - sofosbuvir/daclatasvir 12 weeks

In adolescents aged 12–17 years or weighing at least 35 kg with chronic HCV infection:

- sofosbuvir/ledipasvir for 12 weeks in genotypes 1, 4, 5, and 6
- sofosbuvir/ribavirin for 12 weeks in genotype 2
- sofosbuvir/ribavirin for 24 weeks in genotype 3

In children younger than 12 years with chronic HCV infection, WHO recommends:

- deferring treatment until 12 years of age (conditional recommendation, very low quality of evidence)
- treatment with interferon-based regimens should no longer be used

For further information on clinical considerations, including coinfections, refer to the source guidelines.

Source: World Health Organization. Guidelines for the care and treatment of persons diagnosed with chronic hepatitis C virus infection. Geneva: WHO; 2018. CC BY-NC-SA 3.0 IGO. Available at: https://www.who.int/publications/i/item/9789241550345. Accessed 31 March 2020.