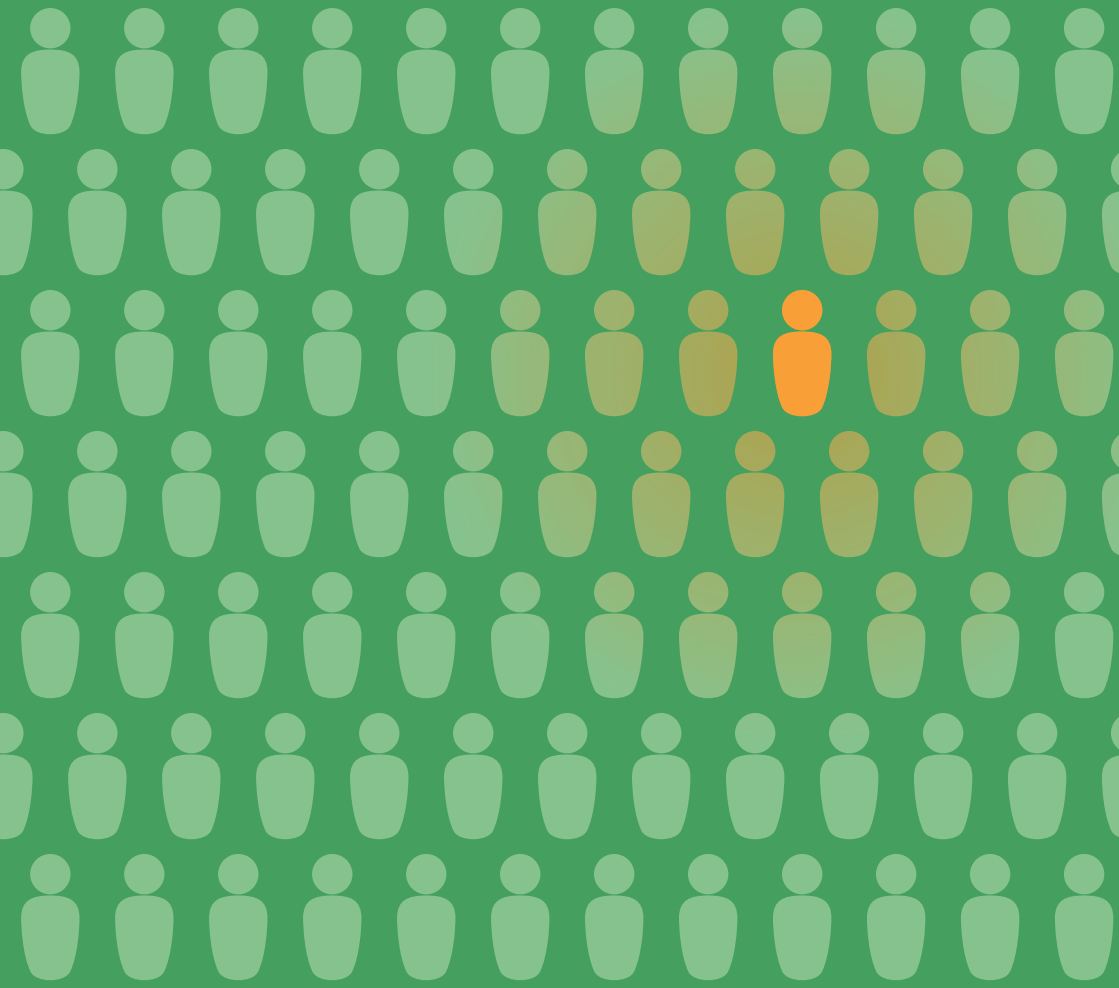
Sexually Transmitted Infections

MANAGEMENT GUIDELINES 2015

Adapted from: Standard Treatment Guidelines and Essential Drugs List PHC



health
Department:
Health
REPUBLIC OF SOUTH AFRICA

Table of Contents

Sexually Transmitted Infections Diagnosis and Management

The syndromic approach to Sexually Transmitted Infection (STI) diagnosis and management is to treat the signs or symptoms (syndrome) of a group of diseases rather than treating a specific disease. This allows for the treatment of one or more conditions that often occur at the same time and has been accepted as the management of choice. This guide includes the current STI syndromic management algorithms.

STI screening should include the following three questions of all persons aged 15-49 years, regardless of clinical presentation:

- *Do you have any genital discharge?*
- *Do you have any genital ulcers?*
- *Has/have your partner(s) been treated for an STI in the last 8 weeks?*

STIs are preventable and many are treatable. Early access to care helps prevent further transmission to partners and from mother-to-child, acquisition of additional STIs, and decreases the risk of STI related complications. Screening for STIs at any and all health care visits, can promote STI prevention and management and provide an opportunity for additional health promotion and education. Where possible, STI screening and prevention should become routine and integrated into all health visits.

In order to perform a proper clinical assessment it is important to take a good sexual history and undertake a thorough ano-genital examination. The history should include questions concerning symptoms, recent sexual history, sexual orientation, type of sexual activity (oral, vaginal, anal sex), the possibility of pregnancy (females), use of contraceptives including condoms, recent antibiotic history, any drug allergies, and recent overseas travel.

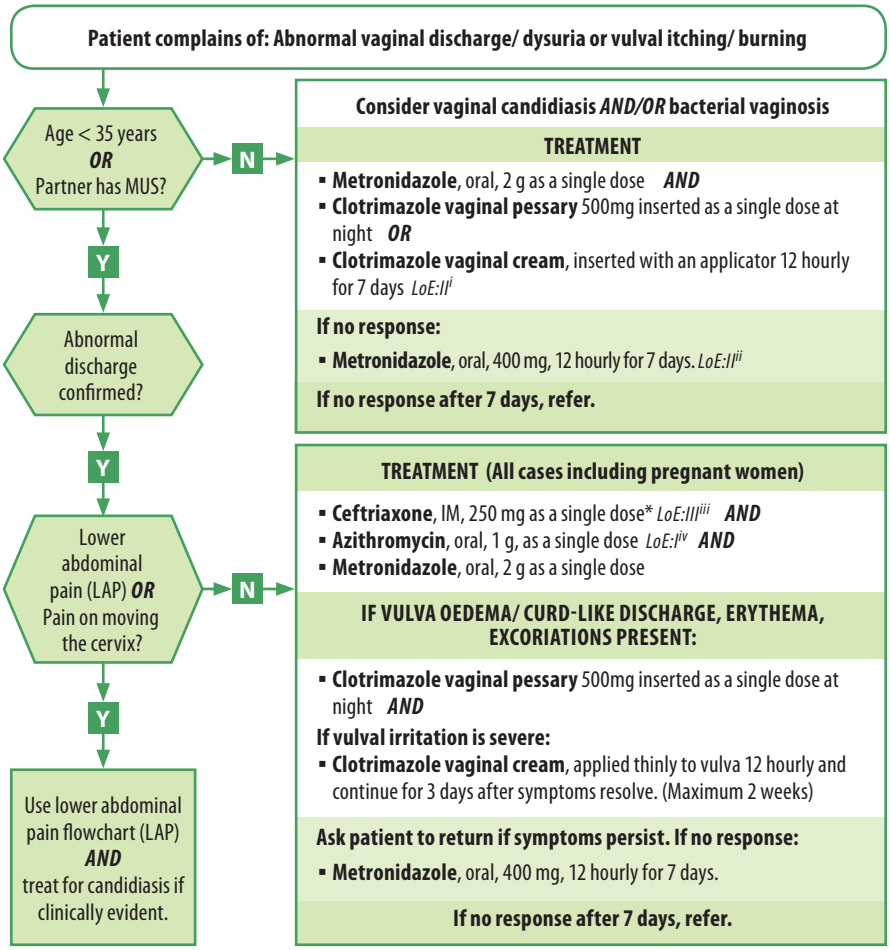
Promote HIV counselling and testing.

Suspected STIs in children should be referred to the hospital for further management.

General Measures

- Counselling and education, including HIV testing
- Condom promotion, provision and demonstration to reduce the risk of STIs
- Compliance/adherence with treatment
- Contact treatment/partner management
- Circumcision promotion with appropriate counselling concerning condoms
- Contraception and conception counselling

Vaginal Discharge Syndrome (VDS)



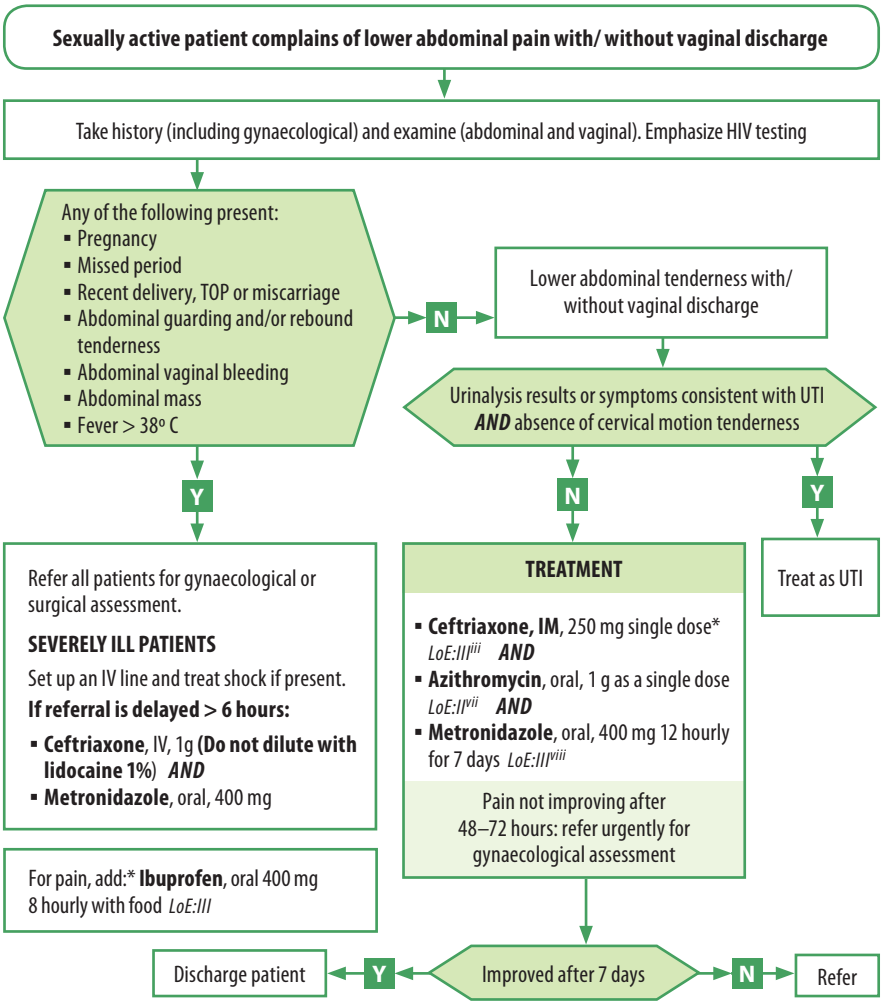
***People who are allergic to penicillin may also react to ceftriaxone.**

If severe penicillin allergy, i.e. angioedema, anaphylactic shock or bronchospasm, omit ceftriaxone and increase azithromycin dose to:

- **Azithromycin**, oral, 2 g, as a single dose. *LoE:I*[v]

For ceftriaxone IM injection: Dissolve ceftriaxone **250 mg** in 0.9 mL lidocaine 1% without epinephrine (adrenaline) *LoE:III*[vi]
Take Pap smear after treatment, if indicated according to screening guidelines.
Note: Suspected STI in children should be referred to hospital for further management.

Lower Abdominal Pain (LAP)



***If severe penicillin allergy, i.e. angioedema, anaphylactic shock or bronchospasm, omit ceftriaxone and increase azithromycin dose to: Azithromycin**, oral, 2 g as a single dose. *LoE:I*[v]

For ceftriaxone IM injection: Dissolve **ceftriaxone** 250 mg in 0.9 mL lidocaine 1% without epinephrine (adrenaline). *LoE:III*[vi]

Male Urethritis Syndrome (MUS)

Patient complains of urethral discharge or dysuria

Take history, including sexual orientation and examine. If no visible discharge; ask patient to milk urethra. Emphasise HIV testing and partner(s) tracing.

Discharge

Y

TREATMENT

- **Ceftriaxone**, IM, 250 mg single dose* *LoE:III*[ii] ***AND***
- **Azithromycin**, oral, 1 g as a single dose *LoE:I*[iv]

If sexual partner has VDS, add:

- **Metronidazole**, oral, 2 g as a single dose

Urethral discharge persists after 7 days

Suspected ceftriaxone 250 mg treatment failure:

- **Ceftriaxone**, IM, 1 g single dose ** *LoE:III*[ix] ***AND***
- **Azithromycin**, oral, 2 g as a single dose ***AND***
- **Metronidazole**, oral, 2 g as a single dose, if not already given

Refer all **ceftriaxone treatment failures** within 7 days for **gentamicin**, IM, 240 mg as a single dose. *LoE:III*[ix, x]

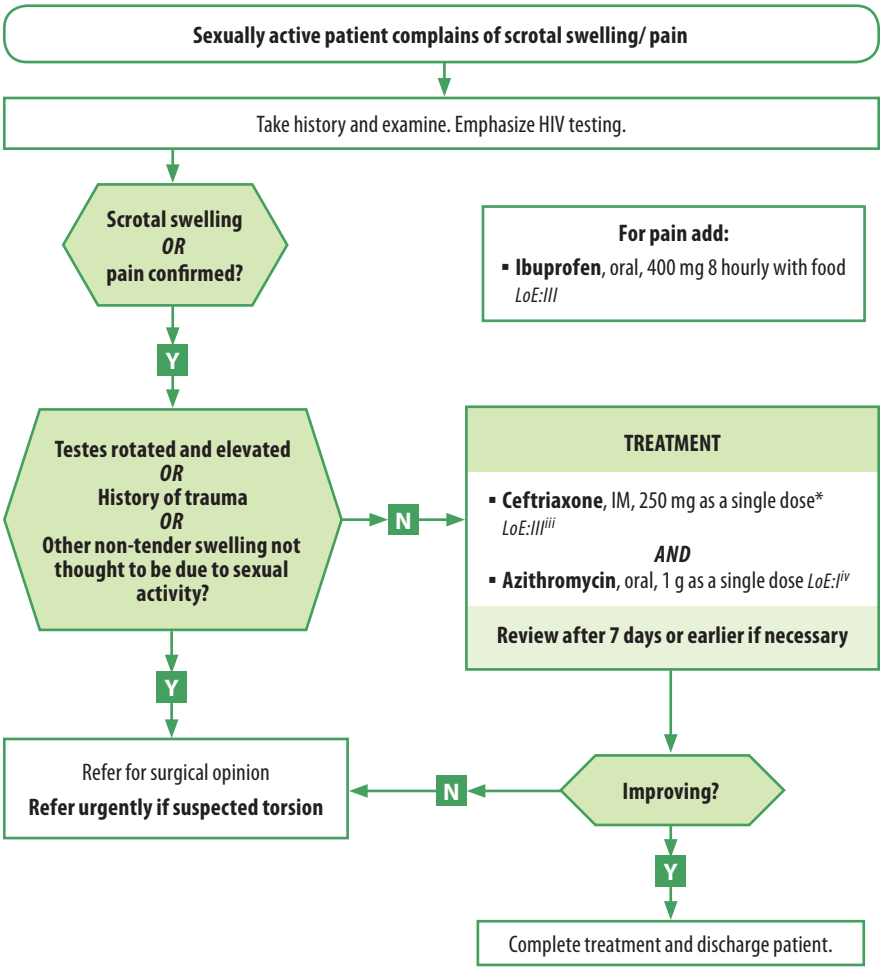
EMPHASISE PARTNER(S) TRACING

If severe penicillin allergy, i.e. angioedema, anaphylactic shock or bronchospasm:
*omit **ceftriaxone**, IM, 250 mg and increase azithromycin dose to azithromycin, oral, 2 g as a single dose *LoE:I*[v]
omit **ceftriaxone, IM, 1 g and refer to a centre for gentamicin, IM, 240 mg as a single dose plus azithromycin, oral, 2 g as a single dose. *LoE:III*[ix, x]

For ceftriaxone IM injection:

- Dissolve **ceftriaxone 250 mg** in 0.9 mL lidocaine 1% without epinephrine (adrenaline).
- Dissolve **ceftriaxone 1 g** in 3.6 mL lidocaine 1% without epinephrine (adrenaline). *LoE:III*[vi]

Scrotal Swelling (SSW)

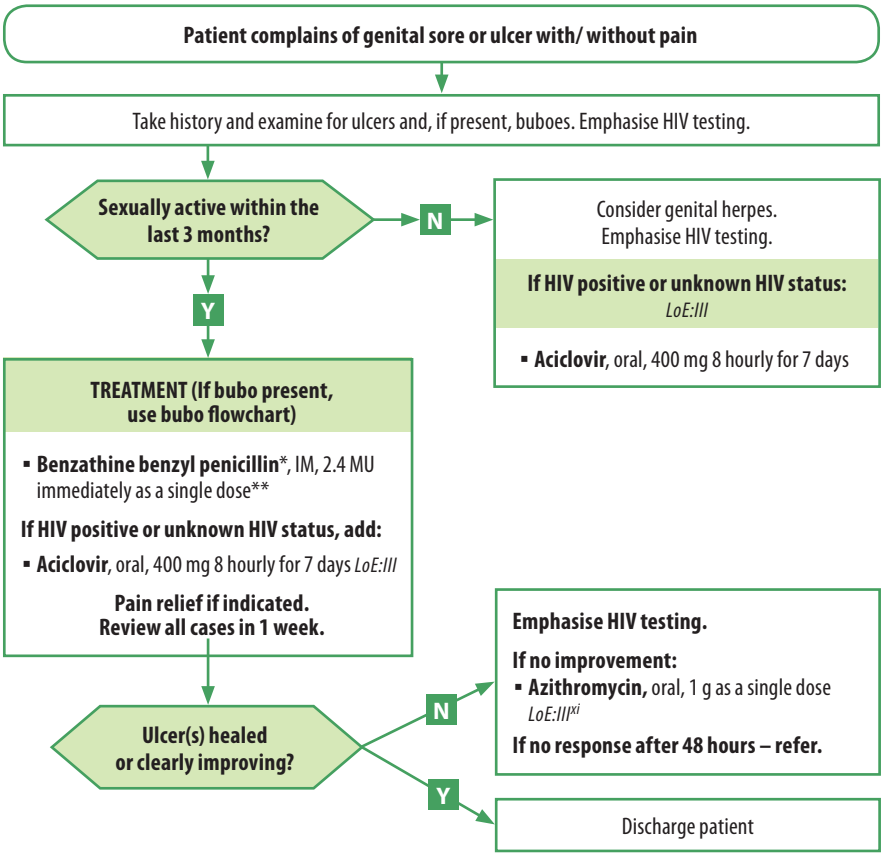


***If severe penicillin allergy, i.e. angioedema, anaphylactic shock or bronchospasm, omit ceftriaxone and increase azithromycin dose to:**

- **Azithromycin**, oral, 2 g as a single dose *LoE:I, III*[v]

For ceftriaxone IM injection: dissolve ceftriaxone **250 mg** in 0.9 mL lidocaine 1% without epinephrine (adrenaline). *LoE:III*[vi]

Genital Ulcer Syndrome (GUS)



Penicillin allergic men and non-pregnant women: Perform a baseline RPR and replace benzathine penicillin with:

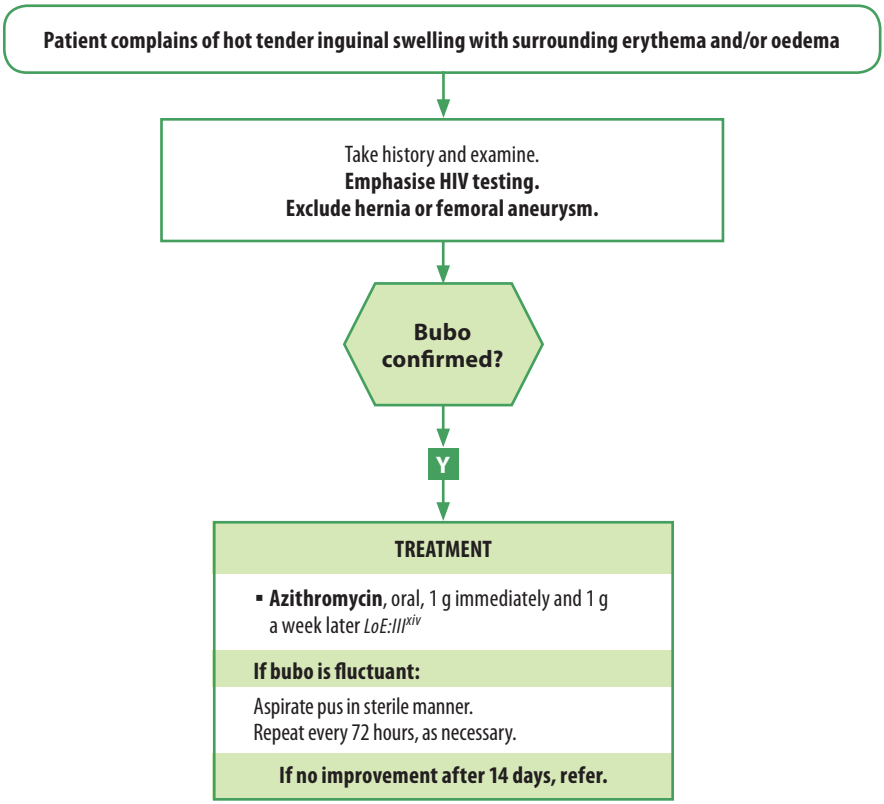
▪ **Doxycycline**, oral, 100 mg 12 hourly for 14 days.

Patient to return for a follow-up RPR 6 months later. *LoE:III*

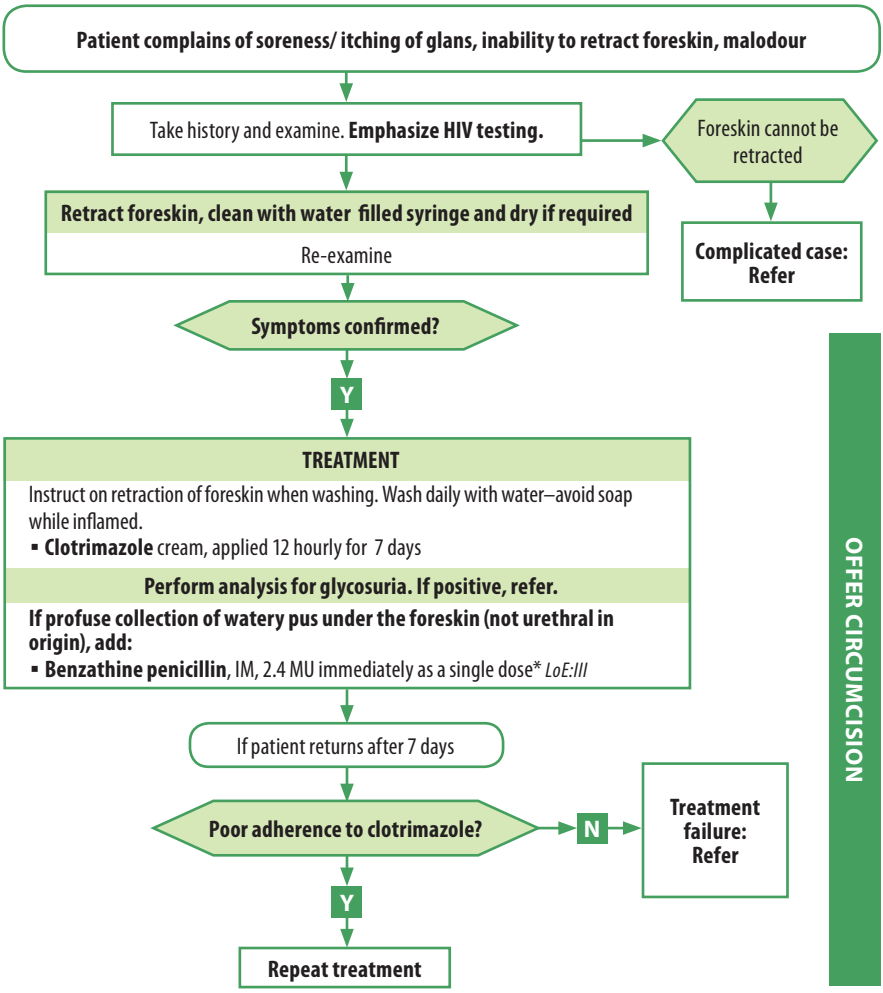
***Penicillin allergic pregnant women/ breast feeding women, refer for confirmation of new syphilis infection and possible penicillin desensitisation.** *LoE:III*[xii]

****For benzathine benzylpenicillin**, IM, 2.4 MU: Dissolve benzathine benzylpenicillin **2.4 MU** in 6 mL lidocaine 1% without epinephrine (adrenaline). *LoE:III*[xiii]

Bubo


Patient complains of hot tender inguinal swelling with surrounding erythema and/or oedema
Take history and examine.
Emphasise HIV testing.
Exclude hernia or femoral aneurysm.
Bubo confirmed?
Y
TREATMENT
▪ Azithromycin, oral, 1 g immediately and 1 g a week later LoE:III[xiv]
If bubo is fluctuant:
Aspirate pus in sterile manner.
Repeat every 72 hours, as necessary.
If no improvement after 14 days, refer.

Balanitis/Balanoposthitis (BAL)



***Penicillin allergic men:**

▪ Replace benzathine penicillin with: **Doxycycline**, oral, 100 mg 12 hourly for 14 days.

For benzathine benzylpenicillin, IM, 2.4 MU: Dissolve benzathine benzylpenicillin **2.4 MU** in 6 mL lidocaine 1% without epinephrine (adrenaline). *LoE:III*[xiii]

Syphilis Serology and Treatment

Syphilis Serology

The Rapid Plasmin Reagin (RPR) measures disease activity, but is not specific for syphilis. False RPR positive reactions may occur, notably in patients with connective tissue disorders (false positive reactions are usually low titre < 1:8). For this reason, positive RPR results should be confirmed as due to syphilis by further testing of the serum with a specific treponemal test, e.g.:

- *Treponema pallidum* haemagglutination (TPHA) assay.
- *Treponema pallidum* particle agglutination (TPPA) assay.
- Fluorescent Treponemal Antibody (FTA) assay.
- *Treponema pallidum* ELISA.
- Rapid treponemal antibody test.

Screening can also be done the other way around starting with a specific treponemal test followed by a RPR in patients who have a positive specific treponemal test. This is sometimes referred to as the "reverse algorithm".

Once positive, specific treponemal tests generally remain positive for life.

The RPR can be used:

- To determine if the patient's syphilis disease is active or not,
- To measure a successful response to therapy (at least a fourfold reduction in titre, e.g. 1:256 improving to 1:64), or
- To determine a new re-infection.

Some patients, even with successful treatment for syphilis, may retain life-long positive RPR results at low titres (≤1:8), which do not change by more than one dilution difference (up or down) over time (so-called serofast patients).

Note:

- Up to 30% of primary syphilis cases, i.e. those with genital ulcers may have a negative RPR.
- The RPR is always positive in the secondary syphilis stage and remains high during the first two (infectious) years of syphilis.

Medicine Treatment

Early Syphilis Treatment

Check if treated at initial visit.

- Benzathine benzylpenicillin, IM, 2.4 MU immediately as a single dose.
  - Dissolve benzathine benzylpenicillin, IM, 2.4 MU in 6 mL lidocaine 1% without epinephrine (adrenaline).

In penicillin-allergic patients:

- Doxycycline, oral, 100 mg twice daily for 14 days.

If penicillin-allergic and pregnant: Refer for penicillin desensitisation.

Late Syphilis Treatment

Check if treatment was commenced at initial visit.

- Benzathine benzylpenicillin, IM, 2.4 MU once weekly for 3 weeks.
  - Dissolve benzathine benzylpenicillin, IM, 2.4 MU in 6 mL lidocaine 1% without epinephrine (adrenaline).

If penicillin-allergic and pregnant: Refer for penicillin desensitisation.

Syphilis in Pregnancy

Mother-to-child transmission of syphilis occurs in up to 40% of cases in untreated mothers. Untreated maternal syphilis may lead to miscarriage, stillbirth, non-immune hydrops fetalis, or congenital syphilis in the newborn. Syphilis may be asymptomatic in pregnant women with diagnosis made by positive serology, preferably with on-site rapid testing.

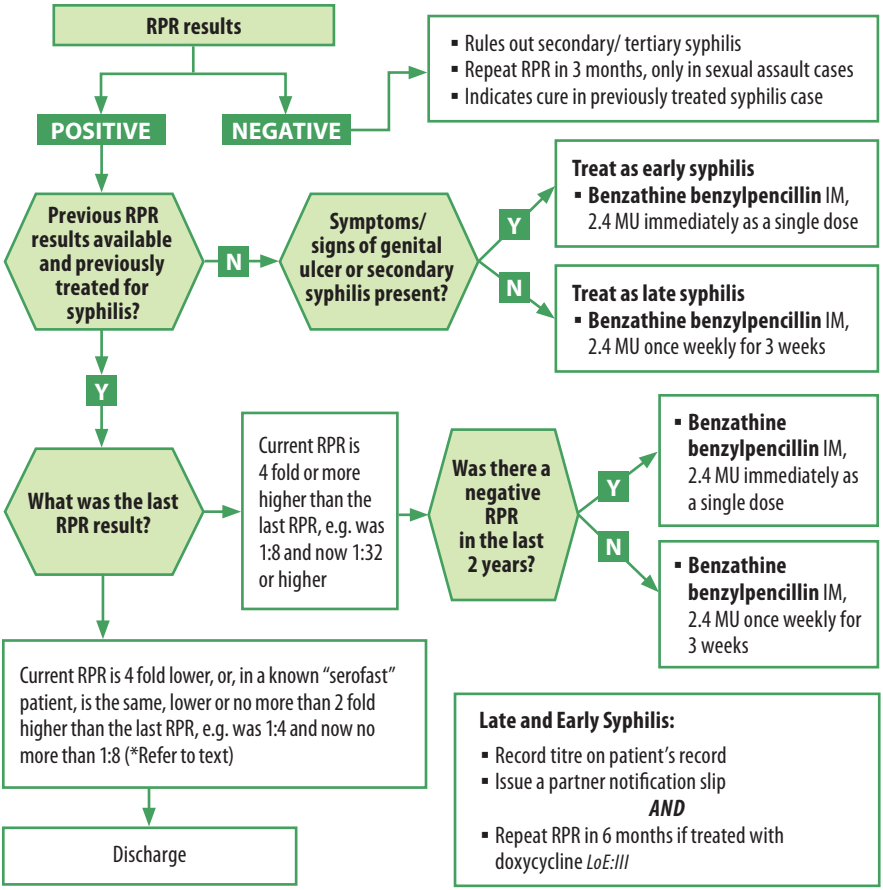
Referral

- Neurosyphilis.
- Clinical congenital syphilis.

Syphilis

Perform RPR if indicated:

- sexual assault case
- suspected secondary syphilis
- suspected tertiary syphilis
- 6 month follow-up of early syphilis cases treated with doxycycline



For benzathine benzylpenicillin, IM, 2.4 MU: Dissolve benzathine benzylpenicillin **2.4 MU** in 6 mL lidocaine 1% without epinephrine (adrenaline). *LoE:III*[xii]

Syphilis in Pregnancy

All pregnant women at first antenatal visit and repeat testing at 32 weeks for women testing negative in the first trimester

Take history and examine, explain need for syphilis screening, do pre-test counselling for HIV

Take blood for RPR test (always), for HIV test (if consent), and for other ANC routines

Any STI syndrome or illness?

Y

Use appropriate flowchart, manage appropriately

Syphilis test positive?

Y

Treat pregnant woman with:

- **Benzathine benzylpenicillin** 2.4 MU imi once weekly for 3 weeks. Reconstitute with 6mL of lidocaine 1% without epinephrine (adrenaline)

OR In case of penicillin allergy:

- Refer for penicillin desensitisation

HIV test positive?

Y

Post test counselling, same day TB screen, HIV education, CD4 count, creatinine, clinical staging, support, and same day ART start

N

Repeat HIV testing every 3 months throughout pregnancy, at labour/ delivery, at 6 week EPI visit, every 3 months throughout breastfeeding

Symptomatic newborns of mothers with positive syphilis test during pregnancy:

- Refer all symptomatic babies

Notify: Notification of medical conditions, form GQ17/5

Treat asymptomatic newborns of mothers with positive syphilis test if mother was not treated, ***OR*** if mother received < 3 doses of benzathine benzylpenicillin, ***OR*** if mother delivers within 4 weeks of commencing treatment, with**:**

- **Benzathine benzylpenicillin** (depot formulation), IM, 50,000 units/kg as a single dose into lateral thigh*

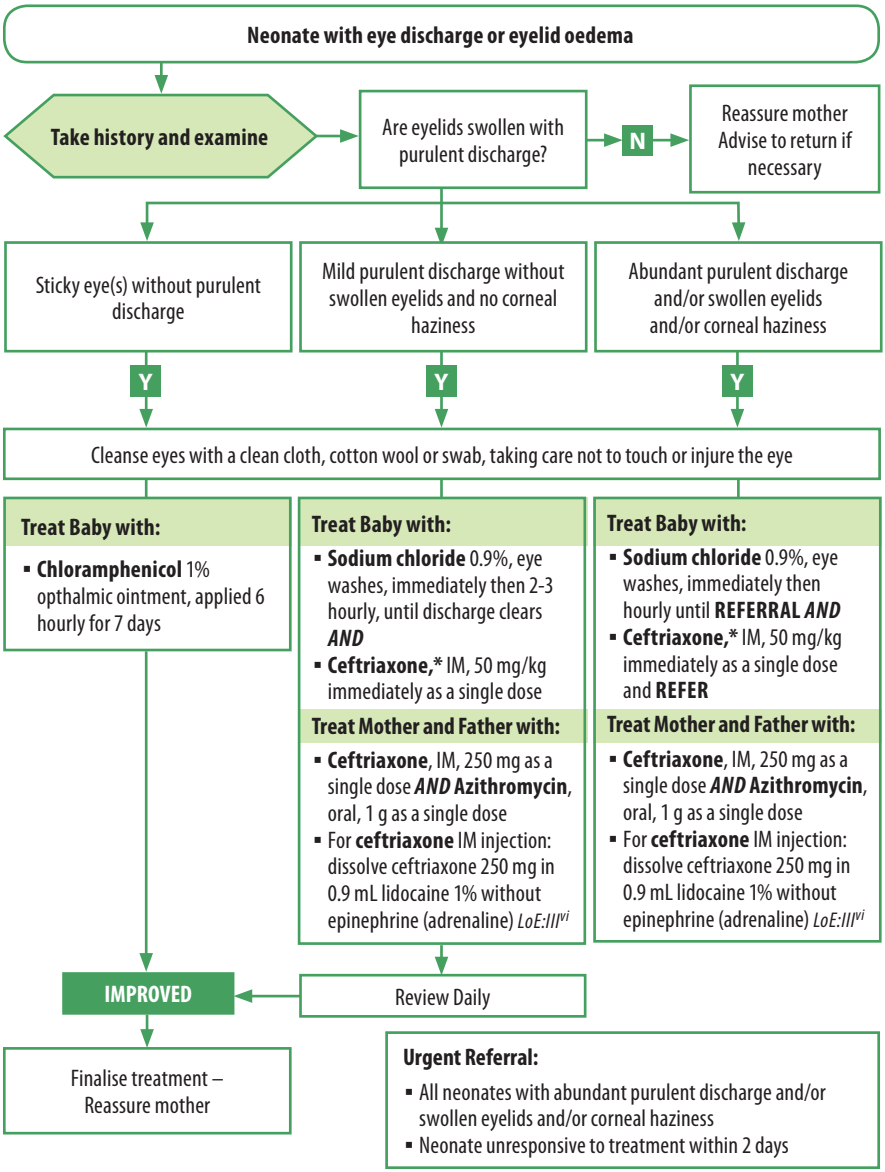
**Benzathine benzylpenicillin (depot formulation) must never be given IV*

Follow up at 3 months after the last injection to confirm a fourfold (i.e. 2 dilution) reduction in RPR titres, provided the initial titre was > 1.8. If the initial titre was < 1.8, further reduction may not occur.

All pregnant women: Educate, ensure compliance and counsel; promote couple-counselling if applicable

- Explain the risk of vertical transmission
- Promote consistent condom use particularly during pregnancy, demonstrate condom use, provide condoms
- Stress the importance of partner treatment, issue one notification slip for each sexual partner
- Promote HIV counselling and testing of partner

Neonatal Conjunctivitis



Parents of baby with confirmed neonatal conjunctivitis:
- Educate, ensure compliance, and counsel; promote couple-counselling if applicable.
- Promote abstinence from penetrative sex during the course of treatment.
- Promote and demonstrate condom use, retain condoms.
- Stress the importance of partner treatment and issue one notification slip for each sexual partner. Follow up partner treatment during review visit.
- Promote HIV counselling and testing. For negative results repeat test after 3 months.

*Infant Dosing of Ceftriaxone

Weight kg	**Dose** mg	**Use one of the following injections mixed with water for injection (WFI):**		**Age** months/years
		250 mg/2 mL (250 mg diluted in 2 mL WFI)	500 mg/2 mL (500 mg diluted in 2 mL WFI)	
>2–2.5 kg	100 mg	0.8 mL	0.4 mL	>34-36 weeks
>2.5-3.5 kg	150 mg	1.2 mL	0.6 mL	>36 weeks–1 month
>3.5-5.5 kg	200 mg	1.6 mL	0.8 mL	>1-3 months

LoE: III[V]

CAUTION: Use of ceftriaxone in severely ill neonates and children

Ceftriaxone should be used in neonates that are seriously ill only, and must be given even if they are jaundiced. In infants < 28 days of age, ceftriaxone should not be administered if a calcium containing intravenous infusion e.g. Ringer-Lactate, is given or is expected to be given. After 28 days of age, ceftriaxone and calcium containing fluids may be given but only sequentially with the giving set flushed well between the two products if given IV.

Annotate the dosage and route of administration in the referral letter.

Treatment of More than One STI Syndrome

STI Syndromes	Treatment (new episode)
MUS + SSW	Treat according to SSW flow chart.
MUS + BAL	Treat according to MUS flow chart ***AND*** ▪ **Clotrimazole** cream, 12 hourly for 7 days
MUS + GUS	▪ **Ceftriaxone**, IM, 250 mg immediately as a single dose** ***AND*** ▪ **Azithromycin**, oral, 1 g as a single dose ***AND*** ▪ **Aciclovir**, oral, 400 mg 8 hourly for 7 days*
VDS + LAP	Treat according to LAP flow chart ***AND*** Treat for candidiasis, if required (see VDS flow chart)
VDS + GUS	▪ **Ceftriaxone**, IM, 250 mg immediately as a single dose** ***AND*** ▪ **Metronidazole**, oral, 2 g immediately as a single dose ***AND*** ▪ **Azithromycin**, oral, 1 g as a single dose ***AND*** ▪ **Aciclovir**, oral, 400 mg 8 hourly for 7 days* ***AND*** Treat for candidiasis, if required (see VDS flow chart)
LAP+ GUS	▪ **Ceftriaxone**, IM, 250 mg immediately as a single dose** ***AND*** ▪ **Metronidazole**, oral, 400 mg 12 hourly for 7 days ***AND*** ▪ **Aciclovir**, oral, 400 mg 8 hourly for 7 days*.
SSW+ GUS	▪ **Ceftriaxone**, IM, 250 mg immediately as a single dose** ***AND*** ▪ **Aciclovir**, oral, 400 mg 8 hourly for 7 days*

***Treat with aciclovir only if HIV status is positive or unknown.**

****Penicillin allergic men and non-pregnant women avoid ceftriaxone and refer to relevant algorithms.**

Penicillin allergic pregnant or breastfeeding women, refer for penicillin desensitisation.

Genital Molluscum Contagiosum (MC)

Description

This is a viral infection which can be transmitted sexually and non-sexually. It is usually self-limiting but can be progressive in an advanced stage of immunodeficiency.

- Clinical signs include papules at the genitals or other parts of the body.
- The papules usually have a central dent (umbilicated papules).

Medicine Treatment

- Tincture of iodine BP.
  - Apply with an applicator to the core of the lesions.

Genital Warts (GW): Condylomata Accuminata

Description

The clinical signs include:

- Warts on the ano-genital areas, vagina, cervix, meatus or urethra.
- Warts can be soft or hard.

In most cases, warts resolve without treatment after 2 years in non-immunosuppressed patients.

General Measures

- If warts do not look typical or are fleshy or wet, perform an RPR/VDRL test to exclude secondary syphilis, which may present with similar lesions.
- Emphasise HIV testing.

Referral

All patients with:

- Warts > 10 mm
- Inaccessible warts, e.g. intra-vaginal or cervical warts
- Numerous warts

Pubic Lice (PL)

Description

Infestation of lice mostly confined to pubic and peri-anal areas, and occasionally involves eyelashes.

The bites cause intense itching, which often results in scratching with bacterial super-infection.

General Measures

Thoroughly wash clothing and bed linen that may have been contaminated by the patient in the 2 days prior to the start of treatment in hot water and then iron.

Medicine Treatment

- Benzyl benzoate 25%
  - Apply to affected area.
  - Leave on for 24 hours, then wash thoroughly.
  - Repeat in 7 days.

Pediculosis of the Eyelashes or Eyebrows

- Petroleum jelly.
  - Apply to the eyelid margins (cover the eyelashes) daily for 10 days to smother lice and nits.
  - Do not apply to eyes.

Referral

All children with lice on pubic, perianal area and eyelashes to exclude sexual abuse.

Treatment Protocol for Asymptomatic Partner(s)

Female Patient	Male Partner	Male Patient	Female Partner
VDS	MUS plus metronidazole 2 g stat	**MUS**	VDS
LAP	MUS plus metronidazole 2 g stat	**SSW**	VDS
GUS	GUS	**GUS**	GUS
GW	GW if signs	**GW**	GW if signs
PL	PL	**PL**	PL
MC	MC if signs	**MC**	MC if signs
RPR+	Benzathine Benzylpenicillin 2.4mu im stat in addition RPR test	**RPR+**	Benzathine Penicillin 2.4mu im stat in addition RPR test
		BAL	Cotrimazole vaginal pessary 500mgs inserted stat 2
In addition: treat any symptomatic STI		In addition: treat any symptomatic STI	

Footnotes

i: Criteria for STI therapy in VDS: Unpublished surveillance data for VDS at Alexander Health Centre, Gauteng (2007-2012) shared by NICD: Centre for STI and HIV.

ii: Metronidazole: Swedberg J, Steiner JF, Deiss F, Steiner S, Driggers DA. Comparison of single-dose vs. one-week course of metronidazole for symptomatic bacterial vaginosis. JAMA. 1985 Aug 23-30;254(8):1046-9.

Metronidazole: Kissinger P, Secor WE, Leichliter JS, Clark RA, Schmidt N, Curtin E, Martin DH. Early repeated infections with Trichomonas vaginalis among HIV-positive and HIV-negative women. Clin Infect Dis. 2008 Apr 1;46(7):994-9.

Metronidazole: Kissinger P, Mena L, Levison J, Clark RA, Gatski M, Henderson H, Schmidt N, Rosenthal SL, Myers L, Martin DH. A randomized treatment trial: single versus 7-day dose of metronidazole for the treatment of Trichomonas vaginalis among HIV-infected women. J Acquir Immune DeficSyndr. 2010 Dec 15;55(5):565-71.

iii: Ceftriaxone: Newman LM, Moran JS, Workowski KA. Update on the management of gonorrhea in adults in the United States. Clin Infect Dis. 2007 Apr 1;44Suppl 3:S84-101.Review.

Ceftriaxone: Ito M, Yasuda M, Yokoi S, Ito S, Takahashi Y, Ishihara S, Maeda S, Deguchi T. Remarkable increase in central Japan in 2001-2002 of Neisseria gonorrhoeae isolates with decreased susceptibility to penicillin, tetracycline, oral cephalosporins, and fluoroquinolones. Antimicrob Agents Chemother. 2004 Aug;48(8):3185-7

Ceftriaxone: Tanaka M, Nakayama H, Tunoe H, Egashira T, Kanayama A, Saika T, Kobayashi I, Naito S. A remarkable reduction in the susceptibility of Neisseria gonorrhoeae isolates to cephems and the selection of antibiotic regimens for the single-dose treatment of gonococcal infection in Japan. J Infect Chemother. 2002 Mar; 8(1):81-6.

Ceftriaxone: Deguchi T, Yasuda M, Yokoi S, Ishida K, Ito M, Ishihara S, Minamidate K, Harada Y, Tei K, Kojima K, Tamaki M, Maeda S. Treatment of uncomplicated gonococcal urethritis by double-dosing of 200 mg cefixime at a 6-h interval. J Infect Chemother. 2003 Mar;9(1):35-9.

Ceftriaxone: Lewis DA. Gonorrhoea resistance among men-who-have-sex-with-men: what's oral sex got to do with it? S Afr J Epid Infect. 2013;28: 77.

Ceftriaxone: Lewis DA, Sriruttan C, Müller EE, Golparian D, Gumede L, Fick D, de Wet J,Maseko V, Coetzee J, Unemo M. Phenotypic and genetic characterization of the first two cases of extended-spectrum-cephalosporin-resistant Neisseria gonorrhoeae infection in South Africa and association with cefixime treatment failure. J Antimicrob Chemother. 2013 Jun;68(6):1267-70.

Ceftriaxone: Lewis DA. The role of core groups in the emergence and dissemination ofantimicrobial-resistant N gonorrhoeae. Sex Transm Infect. 2013 Dec;89Suppl4:iv47-51. Review.

Ceftriaxone: Health Protection Agency. Gonoccocal Resistance to Antimicrobials Surveillance Programme (GRASP) Action Plan for England and Wales: Informing the Public Health Response. (Ed.^(Eds) (HPA, London, 2013)

Ceftriaxone: Bignell C, Fitzgerald M; Guideline Development Group; British Association for Sexual Health and HIV UK. UK national guideline for the management of gonorrhoea in adults, 2011. Int J STD AIDS. 2011 Oct;22(10):541-7.

Ceftriaxone: Centers for Disease Control and Prevention. Cephalosporin-resistant Neisseria gonorrhoeae public health response plan. (Ed.^(Eds) (CDC, Atlanta, 2012)

Ceftriaxone: Centers for Disease Control and Prevention. Update to CDC's Sexually transmitted diseases treatment guidelines, 2010: oral cephalosporins no longer a recommended treatment for gonococcal infections. MMWR Morb Mortal Wkly Rep. 2012;6: 590-594.

iv: Azithromycin: Lau CY, Qureshi AK. Azithromycin versus doxycycline for genital chlamydial infections: a meta-analysis of randomized clinical trials. Sex Transm Dis. 2002 Sep;29(9):497-502.

Azithromycin: Bignell C, Garley J. Azithromycin in the treatment of infection with Neisseria gonorrhoeae. Sex Transm Infect. 2010 Nov;86(6):422-6

Azithromycin: Stamm WE, Hicks CB, Martin DH, Leone P, Hook EW 3rd, Cooper RH, Cohen MS, Batteiger BE, Workowski K, McCormack WM. Azithromycin for empirical treatment of the non gonococcal urethritis syndrome in men. A randomized double-blind study.JAMA. 1995 Aug 16;274(7):545-9.

Azithromycin: Lister PJ, Balechandran T, Ridgway GL, Robinson AJ. Comparison of azithromycin and doxycycline in the treatment of non-gonococcal urethritis in men. J Antimicrob Chemother. 1993 Jun;31Suppl E:185-92.

Azithromycin: Schwebke JR, Rompalo A, Taylor S, Seña AC, Martin DH, Lopez LM, Lensing S, Lee JY. Re-evaluating the treatment of non gonococcal urethritis: emphasizing emerging pathogens--a randomized clinical trial. Clin Infect Dis. 2011 Jan 15;52(2):163-70.

Azithromycin: Manhart LE, Gillespie CW, Lowens MS, Khosropour CM,Colombara DV, Golden MR, Hakhu NR, Thomas KK, Hughes JP, Jensen NL, Totten PA. Standard treatment regimens for non gonococcal urethritis have similar but declining cure rates: a randomized controlled trial. Clin Infect Dis. 2013 Apr;56(7):934-42.

Azithromycin: Handsfield HH, Dalu ZA, Martin DH, Douglas JM Jr, McCarty JM, Schlossberg D. Multicenter trial of single-dose azithromycin vs. ceftriaxone in the treatment of uncomplicated gonorrhea. Azithromycin Gonorrhea Study Group. Sex Transm Dis. 1994 Mar-Apr;21(2):107-11.

Azithromycin: Riedner G, Rusizoka M, Todd J, Maboko L, Hoelscher M, Mmbando D, Samky E, Lyamuya E, Mabey D, Grosskurth H, Hayes R. Single-dose azithromycin versus penicillin G benzathine for the treatment of early syphilis. N Engl J Med. 2005 Sep 22;353(12):1236-44.

Azithromycin: Hook EW 3rd, Martin DH, Stephens J, Smith BS, Smith K. A randomized, comparative pilot study of azithromycin versus benzathine penicillin G for treatment of early syphilis. Sex Transm Dis. 2002 Aug;29(8):486-90

Azithromycin: McLean CA, Wang SA, Hoff GL, Dennis LY, Trees DL, Knapp JS, Markowitz LE, Levine WC. The emergence of Neisseria gonorrhoeae with decreased susceptibility to Azithromycin in Kansas City, Missouri, 1999 to 2000. Sex Transm Dis. 2004 Feb;31(2):73-8

Azithromycin: Galarza PG, Abad R, Canigia LF, Buscemi L, Pagano I, Oviedo C, Vázquez JA. New mutation in 23S rRNA gene associated with high level of azithromycin resistance in Neisseria gonorrhoeae. Antimicrob Agents Chemother. 2010 Apr;54(4):1652-3. doi: 10.1128/AAC.01506-09.

Azithromycin: Bignell C, Fitzgerald M; Guideline Development Group; British Association for Sexual Health and HIV UK. UK national guideline for the management of gonorrhoea in adults, 2011. Int J STD AIDS. 2011 Oct;22(10):541-7.

Azithromycin: Workowski KA, Berman S; Centers for Disease Control and Prevention (CDC). Sexually transmitted diseases treatment guidelines, 2010. MMWR Recomm Rep. 2010 Dec 17;59(RR-12):1-110. Erratum in: MMWR Recomm Rep. 2011 Jan 14;60(1):18. Dosage error in article text.

Azithromycin: Chisholm SA, Mouton JW, Lewis DA, Nichols T, Ison CA, Livermore DM. Cephalosporin MIC creep among gonococci: time for a pharmacodynamic rethink? J Antimicrob Chemother. 2010 Oct;65(10):2141-8.

Azithromycin: Fayemiwo SA, Muller EE, Gumede L, Lewis DA. Plasmid-mediated penicillin and tetracycline resistance among Neisseria gonorrhoeae isolates in South Africa: prevalence, detection and typing using a novel molecular assay. Sex Transm Dis.2011; 38: 329-333

Azithromycin: de Jongh M, Dangor Y, Adam A, Hoosen AA. Gonococcal resistance: evolving from penicillin, tetracycline to the quinolones in South Africa - implications for treatment guidelines. Int J STD AIDS. 2007;18:697-699.

Azithromycin: Manhart LE, Broad JM, Golden MR. Mycoplasma genitalium: should we treat and how? Clin Infect Dis, 53 Suppl 3, S129-142 (2011).

Azithromycin: Mena LA, Mroczkowski TF, Nsuami M, Martin DH. A randomized comparison of azithromycin and doxycycline for the treatment of Mycoplasma genitalium-positive urethritis in men. Clin Infect Dis. 2009;48:1649-1654.

Azithromycin: Amsden GW, Gray CL. Serum and WBC pharmacokinetics of 1500 mg of azithromycin when given either as a single dose or over a 3 day period in healthy volunteers. J Antimicrob Chemother. 2001 Jan;47(1):61-6.

Azithromycin: Sampson MR, Dumitrescu TP, Brouwer KL, Schmith VD. Population pharmacokinetics of azithromycin in whole blood, peripheral blood mononuclear cells, and polymorphonuclear cells in healthy adults. CPT Pharmacometrics Syst Pharmacol. 2014 Mar 5;3:e103.

Azithromycin: Lewis DA, Maartens GM: Medicine review: The use of azithromycin in the syndromic management algorithms for the management of sexually transmitted infections (STIs) in South Africa, 16 March 2014.

Azithromycin: SAMF, 2012 edition.

v: Azithromycin: Pitsouni E, Iavazzo C, Athanasiou S, Falagas ME. Single-dose azithromycin versus erythromycin or amoxicillin for Chlamydia trachomatis infection during pregnancy: a meta-analysis of randomised controlled trials. Int J Antimicrob Agents. 2007 Sep;30(3):213-21.

vi: Lidocaine 1%: Contract circular HP02-2013AI (1August2013to31July2015): MCC registered package inserts of Kocef® 250 mg, 500 mg, 1 g; Rociject® 500 mg, 1 g; Oframax® 250 mg, 1 g

vii: Azithromycin (LAP): Savaris RF, Teixeira LM, Torres TG, Edelweiss MI, Moncada J, Schachter J. Comparing ceftriaxone plus azithromycin or doxycycline for pelvic inflammatory disease: a randomized controlled trial. Obstet Gynecol. 2007 Jul;110(1):53-60.

Azithromycin (LAP/ SSW/ BUBO): Amsden GW, Gray CL. Serum and WBC pharmacokinetics of 1500 mg of azithromycin when given either as a single dose or over a 3 day period in healthy volunteers. J Antimicrob Chemother. 2001 Jan;47(1):61-6.

Azithromycin (LAP/ SSW/ BUBO): Sampson MR, Dumitrescu TP, Brouwer KL, Schmith VD. Population pharmacokinetics of azithromycin in whole blood, peripheral blood mononuclear cells, and polymorphonuclear cells in healthy adults. CPT Pharmacometrics Syst Pharmacol. 2014 Mar 5;3:e103.

viii: Metronidazole (LAP): Bignell C, Fitzgerald M; Guideline Development Group; British Association for Sexual Health and HIV UK. UK national guideline for the management of gonorrhoea in adults, 2011.Int J STD AIDS. 2011 Oct;22(10):541-7.

Metronidazole (LAP): Workowski KA, Berman S; Centers for Disease Control and Prevention (CDC). Sexually transmitted diseases treatment guidelines, 2010.MMWR Recomm Rep. 2010 Dec 17;59(RR-12):1-110. Erratum in: MMWR Recomm Rep. 2011 Jan 14;60(1):18. Dosage error in article text.

ix: Ceftriaxone 1 g + Azithromycin 2 g (MUS): WHO. Global action plan to control the spread and impact of antimicrobial resistance in Neisseria gonorrhoeae. 2012.

x: Gentamicin: Brown LB, Krysiak R, Kamanga G, Mapanje C, Kanyamula H, Banda B, Mhango C, Hoffman M, Kamwendo D, Hobbs M, Hosseinipour MC, Martinson F, Cohen MS, Hoffman IF. Neisseria gonorrhoeae antimicrobial susceptibility in Lilongwe, Malawi, 2007.Sex Transm Dis. 2010 Mar;37(3):169-72.

xi: Azithromycin (GUS): National STI Surveillance Programme, Centre for HIV & STIs, NICD/NHLS, 2006-2011

Azithromycin (GUS): Lewis D, Newton DC, Guy RJ, Ali H, Chen MY, Fairley CK, Hocking JS. Theprevalence of Chlamydia trachomatis infection in Australia: a systematic review and meta-analysis. BMC Infect Dis. 2012 May 14;12:113.

Azithromycin (GUS): World Health Organization. Guidelines for the management of sexually transmitted infections. WHO, Geneva. 2003.

xii: Pregnancy/ breast feeding (GUS): Adult Hospital level STG, 2012.

xiii: Lidocaine 1% (GUS/ Syphilis): Kingston M, French P, Goh B, Goold P, Higgins S, Sukthankar A, Stott C, Turner A, Tyler C, Young H; Syphilis Guidelines Revision Group 2008, Clinical Effectiveness Group. UK National Guidelines on the Management of Syphilis 2008. Int J STD AIDS. 2008 Nov;19(11):729-40. Erratum in: Int J STD AIDS. 2011 Oct;22(10):613-4.

Lidocaine 1% (GUS/ Syphilis): Amir J, Ginat S, Cohen YH, Marcus TE, Keller N, Varsano I. Lidocaine as a diluent for administration of benzathine penicillin G. Pediatr Infect Dis J. 1998 Oct;17(10):890-3.

xiv: Azithromycin (Bubo): Workowski KA, Berman S; Centers for Disease Control and Prevention (CDC). Sexually transmitted diseases treatment guidelines, 2010.MMWR Recomm Rep. 2010 Dec 17;59(RR-12):1-110. Erratum in: MMWR Recomm Rep. 2011 Jan 14;60(1):18. Dosage error in article text.