

CHANGES TO AUSTRALIAN STI MANAGEMENT GUIDELINES FOR PRIMARY CARE GUIDELINE FOR TREATMENT OF PHARYNGEAL GONORRHOEA

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In mid-2018, a working group of the Communicable Diseases Network of Australia was established to make recommendations on the prevention, early detection and control of extensively drug resistant (XDR) gonorrhoea in Australia.

The **working group members** were: Christopher Bourne, Marcus Chen, Monica Lahra, David Lewis, Lewis Marshall, David Paterson, Tim Read, David Speers and **secretariat**: Catherine Francis, Christine Selvey.

In December 2018 the recommendations of this working group were considered by the Australian STI Management Guidelines for Primary Care Committee and a change to gonorrhoea treatment recommendations was made. The recommendation was to change the first-line treatment of pharyngeal gonorrhoea to ceftriaxone 500mg IMI and azithromycin orally 2000mg. The azithromycin dose was previously 1000mg.

The recommended treatment for uncomplicated genital gonorrhoea has not changed and remains ceftriaxone 500mg IMI and azithromycin orally 1000mg. This document contains a summary of the rationale for the change to the treatment of pharyngeal gonorrhoea as presented by the working group to the guideline committee.

Background

Ceftriaxone remains the cornerstone of therapy and azithromycin was added in 2014 to theoretically reduce the rate of emergence or onward transmission of ceftriaxone resistant *Neisseria gonorrhoeae* strains after these strains were reported in Japan, France and Spain (Ohnishi et al., 2011; Unemo et al.; Camara et al., 2012). *In vitro* synergy between ceftriaxone and azithromycin was assumed, although there is limited clinical evidence that such synergy exists (Barbee, 2014). One study showed repeat positive oro-pharyngeal *N. gonorrhoeae* tests were reduced when administering azithromycin and ceftriaxone together (7.0%) compared with ceftriaxone alone (9.1%) (Barbee et al., 2013).

In 2017, almost all (> 99.9%) gonococcal isolates cultured in Australia remain fully susceptible to ceftriaxone and most (> 90%) remain susceptible to azithromycin (Lahra et al 2017). Accordingly, the 2018 Australian guideline for the management of uncomplicated gonorrhoea recommends ceftriaxone 500 mg intramuscular injection stat plus single oral dose of azithromycin 1g. The current choice of a 500 mg intramuscular dose of ceftriaxone remains valid as the proportion of gonococcal strains with ceftriaxone MICs of ≥ 0.125 mg/l remains very low in Australia (< 0.05% in 2017). There is no current evidence to support the hypothetical concept that raising the ceftriaxone dose might slow the rise in ceftriaxone MICs for circulating strains, although it is noted that this approach has been recently adopted in Britain.

Whilst the use of dual therapy to treat gonococcal infections in Australia has been associated with a substantial decline in the number of *N. gonorrhoeae* strains with elevated MIC values to ceftriaxone, this has been at the cost of increasing resistance to azithromycin. However most gonococci circulating in Australia remain susceptible to azithromycin, although the [Australian Gonococcal Surveillance Program](#) has reported a rise in the proportion of gonococcal isolates with low-level resistance (LLR) to azithromycin since 2014.

Summary of the rationale for Increasing Azithromycin Dose to Treat Oro-Pharyngeal Gonococcal Infections and unchanged at other sites

We have observed that oro-pharyngeal infections pose a greater challenge to selection for both ceftriaxone and azithromycin resistance because lower mucosal drug penetration levels can occasionally result in treatment failures, even with ceftriaxone and azithromycin susceptible gonococcal strains (Barbee, 2014). The rise in low level resistance to azithromycin among Australian gonococcal isolates is the basis for the recommendation to increase the dose of oral azithromycin from 1 g stat to 2 g stat, as part of dual therapy, for

the treatment of laboratory confirmed oro-pharyngeal gonorrhoea (Table 1). Gonococcal strains determined to have low level azithromycin resistance, where the azithromycin MICs are at or just above the breakpoint for clinical treatment failure, are more likely to respond to a single 2 g oral dose than a single 1 g oral dose. However, it should be appreciated that those gonococcal strains exhibiting high level azithromycin resistance would expect to fail azithromycin monotherapy, regardless of the anatomical site of infection and the dose and regimen used.

TABLE 1. *Recommended treatment for uncomplicated gonorrhoea.*

<p>Recommended Treatment for Uncomplicated Ano-genital Gonorrhoea</p> <ul style="list-style-type: none"> • Ceftriaxone 500 mg i.m. stat.* + Azithromycin 1 g PO stat <p>*dissolve ceftriaxone in 2ml of 1% lignocaine prior to intramuscular injection</p>
<p>Recommended Treatment for Uncomplicated Oro-Pharyngeal Gonorrhoea</p> <ul style="list-style-type: none"> • Ceftriaxone 500 mg i.m. stat.* + Azithromycin 2 g PO stat† <p>*dissolve ceftriaxone in 2ml of 1% lignocaine prior to intramuscular injection †there is no need to re-treat patient with a 2g dose of azithromycin if the patient was already treated for uncomplicated ano-genital gonorrhoea on clinical grounds</p>

PRACTISE POINTS

- For those patients with a STI syndrome treated presumptively for gonorrhoea initially (e.g. men with urethral discharge, contacts of gonorrhoea, or women with pelvic inflammatory disease) in whom oro-pharyngeal gonorrhoea is subsequently detected by nucleic acid amplification testing, an additional 2g single oral dose of azithromycin is NOT considered necessary if ceftriaxone-based dual therapy included azithromycin at an initial dose of 1g. A molecular based test of cure should be undertaken at 3 weeks post-treatment.
- In oro-pharyngeal gonorrhoea cases with positive oro-pharyngeal swab cultures prior to treatment, undertake a culture-based test of cure at seven days post-treatment.
- Gastrointestinal side effects:
 - 2g azithromycin may increase gastrointestinal side effects such as nausea, vomiting and diarrhoea.
 - Advise patients to eat prior to taking azithromycin dose 1g or 2g and provide an anti-emetic for those patients perceived to be at risk of vomiting.
- Azithromycin is available on private prescription in Australia (about \$10-15 for 2x 500mg) and does not have a PBS restricted benefit for gonorrhoea treatment.
- Ceftriaxone 500mg has a PBS restricted benefit for gonorrhoea about \$12.30 (MIMS).
- People having difficulty accessing private treatment can be referred to public sexual health services.

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