IUSTI Europe Position Statement on use of DoxyPEP: June 2024

IUSTI
INTERNATIONAL UNION AGAINST SEXUALLY TRANSMITTED INFECTIONS
EUROPE

Scope

This position statement is aimed at front-line clinical practitioners and public health authorities in WHO European Region providing services for people wishing to reduce their risk of acquiring sexually transmitted infections (STIs), including HIV.

Assurance

This statement was developed by the IUSTI Europe STI Guidelines Editorial Board[§] and agreed by the IUSTI Europe Council at a meeting on 25 June 2024.

Position Statement

1. IUSTI Europe agrees that there is evidence of benefit at the individual level for oral doxycycline 200mg taken 24 to 72 hours after sexual exposure (DoxyPEP) in reducing acquisition of some bacterial STIs in some settings. The most compelling evidence is in reduction of syphilis and chlamydia incidence, with least likely impact on gonorrhoea.
2. IUSTI Europe believes there remain considerable uncertainties over longer-term benefits, population impact, antimicrobial resistance emergence, and scalability to health systems very different to those where DoxyPEP has been intensively studied. Population impact has only been reported to date from a single jurisdiction.
3. Decisions to offer DoxyPEP should therefore be taken in the context of:
    a. **local STI epidemiology and desired outcome:** be clear which infection(s) the DoxyPEP service is intended to impact and how this will be monitored
    b. **capacity of sexual health services**: Provision of DoxyPEP must not be at the expense of maintaining established STI and HIV controls including access to diagnostic testing, treatment, partner notification, vaccination and HIV PrEP.
    c. **capacity of public health systems** to monitor the impact of DoxyPEP on local and regional antimicrobial resistance patterns, both for STI pathogens and other bacterial infections.
    d. **user involvement -** given the complexity of the balance of risk and benefit it is important to have user representation in decision making and in providing local health information. Users may also be able to provide clinical services with information about current use of imported or privately-obtained DoxyPEP.
4. Patient information provided about DoxyPEP needs to:
    - reflect current limitations in evidence, and that this is changing rapidly,
    - ensure users understand that it may only be effective against some STIs.

[§] IUSTI Europe Guidelines Board membership is available at https://iusti.org/wp-content/uploads/2024/05/Editorial-Board-2024.docx [accessed 08/06/2024]

- underscore that even for the infections where there is evidence that DoxyPEP reduces the risk, it is not 100% effective
- explain clearly to users using appropriate locally-sensitive materials the best dose and timings to use,
- explain the importance of testing in a recognised facility / clinic if experiencing symptoms of acute STI to ensure appropriate treatment and to enable antimicrobial resistance monitoring,
- ensure users understand the importance of not using any antibiotic other than doxycycline for prevention of bacterial STIs at this time,
- explain the basis on which any prescription is to be supplied: the prescription is free or co-paid or fully private and whether in that jurisdiction the medication is approved within licensed indication or being used off-label.

Key considerations for individual providers and local public health systems include:

1) **Identifying individuals at the highest risk of preventable bacterial STIs** who are most likely to benefit from DoxyPEP. This will vary between jurisdictions, and criteria for the use of DoxyPEP may therefore differ across the WHO Europe region. Trial evidence is currently limited in populations outside of gay and bisexual men who have sex with men (GBMSM) and transgender women (TGW) so recommendations cannot be made for other populations.
2) **Delivering a DoxyPEP service within an appropriate monitoring framework**. This should include estimating the proportion of service uses and at-risk populations using or being prescribed DoxyPEP, and monitoring side-effects, adherence, and development of on- and off-target antimicrobial resistance.
3) **Ensuring DoxyPEP is delivered as part of a comprehensive and holistic sexual health control strategy** focused on a full range of approaches to reduce the risk of STIs, including reducing health inequalities
4) **Ensure practitioners remain within relevant prescribing** legislation for their jurisdiction. This may include ensuring service users are aware that doxycycline used for this prevention indication may be off-label

A range of broader considerations may be relevant for national programmes including

5) Monitoring for **population-level benefits** and **harms** of DoxyPEP roll-out
6) Monitoring for the **emergence of antimicrobial resistance** both in sexually transmitted pathogens and in other bacterial pathogens
7) Developing **country-level guidance for practitioners**, which should take into account these principles but reflect local epidemiology, legislation and resources

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Background

DoxyPEP is a potentially promising strategy for reducing the burden of some bacterial STIs amongst populations at the highest risk. DoxyPEP entails taking doxycycline 200mg 24-72 hours after sexual activity. Whilst this strategy may potentially help reduce the burden of syphilis, chlamydia and possibly gonorrhoea there remain significant uncertainties in how such an intervention should be delivered in practice and the impact of the strategy on the emergence and spread of antimicrobial resistance.

Evidence to Date

Several organizations and societies have included recommendations in guidelines on DoxyPEP for specific key populations [1,2] with strict criteria but there is not yet a consensus on who would benefit most from DoxyPEP and how they should be selected and managed.

Three individually randomised trials have suggested that DoxyPEP reduces bacterial STIs amongst GBMSM at highest risk[1-3]. In a study from the USA, there was a significant reduction in all three bacterial STIs, whilst in two studies in France, where rates of tetracycline-resistance in Neisseria gonorrhoeae were higher, there were reductions only in syphilis and chlamydia [3-5]. The resistance to tetracycline/doxycycline in *N. gonorrhoeae* in Europe is high[6]

There is limited evidence for the role of DoxyPEP in other high-risk groups. A single study amongst women at higher risk in Kenya showed no impact on the incidence of bacterial STIs, likely due to poor adherence[7]. Whilst in most countries DoxyPEP is not yet officially available through the health system it is estimated that a substantial minority of individuals are already sourcing doxycycline via alternative methods.

The population-level impact of DoxyPEP is uncertain. Early data from San Francisco suggests it may reduce the transmission of STIs at a population level in MSM and TGW[8]. At the same time, data suggest that the introduction of DoxyPEP to populations is likely to result in a substantial overall consumption of antibiotics[9]. This increased exposure is predicted to result in the selection of antibiotic-resistant strains of both STIs and other pathogens [10-12].

References

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