

- Clinician DoxyPEP Factsheet -

DoxyPEP for STI Prevention

Background

DoxyPEP is the use of doxycycline for post-exposure prophylaxis to prevent bacterial sexually transmitted infections (STIs). Recent increases in STIs make the use of new approaches to decrease STIs a public health priority in Virginia. DoxyPEP is the first biomedical prevention tool for bacterial STIs that has been shown to be effective and well-tolerated.

While it remains an off-label indication, doxycycline is inexpensive and has a history of off-label long-term use for other conditions. National guidance for DoxyPEP is pending. The CDC has published [considerations](#) for patients and clinicians considering DoxyPEP for bacterial STI prevention.

Clinical Recommendations

Conduct a thorough [sexual health history](#) with patients who are sexually active. Consider offering DoxyPEP using a shared decision-making model to adult **men who have sex with men** and **transgender women** who report having any of the following in the past year:

- ✓ a bacterial STI
- ✓ condomless anal or oral sex with at least one male or transgender female partner
- ✓ multiple sex partners in the past year
- ✓ sex with anonymous partners or under the influence of drugs or alcohol

Consider prescribing DoxyPEP to adult men and transgender women who ask for it, even if they do not disclose any of the risks noted above. Stigma, distrust, or shame may prevent patients from talking about sex with you.

Note: Current efficacy data only applies to gay/bisexual men and transgender women. DoxyPEP efficacy in other populations (i.e., cisgender women, cisgender heterosexual men, transgender men, other queer and nonbinary people) remains unclear. Given the lack of supporting data and the contraindications for doxycycline during pregnancy, there is not currently enough evidence to recommend DoxyPEP for people who have receptive vaginal sex or who may become pregnant. DoxyPEP should not be used for patients whose medical history or current medications contraindicate the use of doxycycline.

Discuss: When considering DoxyPEP initiation, discuss the following key points with patients:

Efficacy Data

Researchers from the University of California recently conducted a [randomized trial](#) of DoxyPEP for the prevention of syphilis, chlamydia, and gonorrhea. Study participants included cisgender men who have sex with men (MSM) and transgender women who were either taking HIV pre-exposure prophylaxis (PrEP) or living with HIV (PLWH). All had been diagnosed with an STI in the past year. Participants in the intervention arm received a single dose of 200 mg doxycycline administered within 24–72 hours after condomless sex. The trial ended early due to the high efficacy observed, and no significant adverse reactions attributable to doxycycline were noted among trial participants.*



The efficacy of DoxyPEP against other bacterial STIs is not known. DoxyPEP does not prevent HIV, mpox, or other viral infections such as human papillomavirus (HPV) or herpes simplex virus (HSV).

* Source: Luetkemeyer et al. Postexposure Doxycycline to Prevent Bacterial Sexually Transmitted Infections. N Engl J Med 2023 Apr; 388:1296-1306.

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Dosing and Prescribing

- 200 mg of doxycycline should ideally be taken within 24 hours (for highest effectiveness) but no later than 72 hours after condomless oral, anal, or vaginal sex.
- Either doxycycline hyclate delayed release 200 mg (one tablet) *OR* doxycycline hyclate or monohydrate immediate release 100 mg (two tablets taken at the same time) are acceptable options. Immediate release doxycycline may be less expensive than delayed release and should be equivalently bioavailable.
- Prescribe enough doses (or refills) of doxycycline to last until the next follow-up visit (3-6 months). This will increase the likelihood that patients can take a dose within 24 hours of having sex, reduce the number of trips to and potential questions from their local pharmacy, and still allow opportunities for STI screening.
- Doxycycline can be taken as often as once per day, depending on frequency of sexual activity, but individuals should not take more than 200 mg within a 24-hour period.
- Use ICD-10 diagnosis code Z20.2 “Contact with and (suspected) exposure to infections with a predominantly sexual mode of transmission.” Another option is ICD-10 code Z79.2 “Long term (current) use of antibiotics.”

Monitoring

- Monitor how frequently patients take DoxyPEP. For patients taking DoxyPEP for a prolonged period, consider periodic or annual liver function tests (LFT), renal function tests, and complete blood count (CBC). No severe adverse events were noted in the DoxyPEP study.
- To identify and treat existing or breakthrough infections, patients on DoxyPEP should be screened at initiation and then every 3-6 months for gonorrhea and chlamydia at all anatomic sites of exposure (urogenital/urine, pharyngeal, and rectal), syphilis, and HIV (if not known to be living with HIV).
- Patients who get an STI while using DoxyPEP should be treated according to standard [CDC STI Treatment Guidelines](#).

Counseling Messages

- Counsel patients about possible drug interactions, risk of sun sensitivity, remaining upright for 30 minutes after taking doxycycline to reduce the risk of pill esophagitis, and the (rare) risk of benign intracranial hypertension.
- Encourage patients to take doxycycline with a glass of water; take with food if gastric upset occurs. Avoid taking with antacids or dairy products.
- The impacts of long-term use of DoxyPEP for STI prevention are unknown, but doxycycline has been previously used safely for long-term prophylaxis of malaria and treatment for acne.
- The impact of DoxyPEP on the gut microbiome and on antibiotic resistance at the individual and population level remains unknown. Some studies have associated changes in the gut microbiome with chronic illnesses such as diabetes and inflammatory bowel disease. The extent and clinical significance of any microbiome changes attributable to DoxyPEP requires more study.

Provide Comprehensive Sexual Health Services

- Counsel all HIV-negative patients on their HIV PrEP options, including daily oral PrEP and long-acting injectable PrEP (cabotegravir).
- Ensure PLWH are in care and inform patients that U=U (undetectable = untransmissible); maintaining a consistent, undetectable HIV viral load for at least six months prevents transmission of HIV to sexual partners during sex.
- Recommend and offer the following vaccines, which protect against sexually transmitted or sexually associated infections, based on local eligibility and [ACIP Guidance](#): Mpox vaccine (Jynneos), meningococcal vaccine (MenACWY), Hepatitis A / Hepatitis B vaccines, and human papillomavirus (HPV) vaccine.
- Individuals who also have a substance use disorder should be referred to [comprehensive harm reduction services](#).

Additional Resources

Virginia Department of Health:
[Updates and Clinical Resources for Health Professionals](#)

National Coalition of STD Directors:
[Doxycycline as STI PEP Implementation Toolkit](#)

Centers for Disease Control and Prevention: [STI Treatment Guidelines](#)

Centers for Disease Control and Prevention: [PrEP for the Prevention of HIV Guidelines](#)