

- Clinician Doxy PEP Factsheet -

Doxy PEP for STI Prevention

Background

Doxy PEP refers to the use of doxycycline for post-exposure prophylaxis (PEP) to prevent bacterial sexually transmitted infections (STIs). In June 2024, the U.S. Centers for Disease Control and Prevention (CDC) published [clinical guidelines](#) for the use of doxy PEP for STI prevention in the United States. Sustained increases in STI incidence make the use of novel approaches to decrease STIs, especially for disproportionately affected populations, a public health priority in Michigan. Doxy PEP 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.

Clinical Recommendations

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

- ✓ A bacterial STI, specifically syphilis, chlamydia or gonorrhea.
- ✓ 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 doxy PEP 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. Clinical data to support doxy PEP in other populations (*i.e.*, cisgender women, cisgender heterosexual men, transgender men, other queer and nonbinary people) are limited. Providers should use their clinical judgement and shared decision-making to inform use of doxy PEP with populations that are not part of CDC recommendations. Doxy PEP should not be used for patients who are pregnant or whose medical history or current medications contraindicate the use of doxycycline.

Discuss: The CDC recommends that providers counsel eligible patients about the benefits and harms of using doxy PEP. When considering doxy PEP initiation, discuss the key points below with patients.

Efficacy Data

Researchers from the University of California recently conducted a [randomized trial](#) of doxy PEP 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 because no significant adverse reactions attributable to doxycycline were noted among participants.*



The efficacy of doxy PEP against other bacterial STIs is not known. Doxy PEP 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.



Dosing and Prescribing

- Providers should write the prescription for self-administration of the recommended dose of 200 mg of doxycycline (any formulation) to be taken as soon as possible within 72 hours (ideally within 24 hours) after having condomless oral, anal or vaginal sex with a maximum dose of 200 mg every 24 hours.
- 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, based on the person's anticipated sexual activity. 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. Ongoing need for doxy PEP should be assessed every three to six months.
- 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 doxy PEP. For patients taking doxy PEP for a prolonged period, clinicians may want to consider periodic or annual liver function tests (LFT), renal function tests and complete blood count (CBC). No severe adverse events were noted in the doxy PEP study.
- To identify and treat existing or breakthrough infections, patients on doxy PEP should be screened at initiation and then every three to six 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 doxy PEP 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. Gastrointestinal side effects were commonly reported in clinical trials of doxy PEP.
- The impacts of long-term use of doxy PEP for STI prevention are unknown, but doxycycline has been previously used safely for long-term prophylaxis of malaria and treatment for acne.
- The long-term impact of doxy PEP 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 doxy PEP 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 PWH are in care and inform patients that undetectable = untransmissible (U=U); maintaining a consistent, undetectable HIV viral load for at least six months prevents transmission of HIV to 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 HPV vaccine.
- Individuals who also have a substance use disorder should be referred to [comprehensive harm reduction services](#).

Additional Resources

U.S. Centers for Disease Control and Prevention: [Doxy PEP for Bacterial STI Prevention](#)

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

Michigan Department of Health & Human Services: [Recommendations for doxy PEP in Adults](#)

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

