
DOXYCYCLINE PEP FOR PREVENTION OF SEXUALLY TRANSMITTED INFECTIONS

WRITTEN BY DEVAN NAMBIAR, MSC.
REVIEWED BY JORDAN GOODRIDGE (BHSC, MD, CCFP)

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In Canada, gay, bisexual, and other men-who-have-sex-with-men (gbMSM) and trans women are disproportionately impacted by sexually-transmitted infections (STIs).¹ Doxycycline post-exposure prophylaxis (PEP)—explained below—is a health promotion initiative aimed to reduce and prevent STIs in these populations. Please speak to your healthcare provider for further information about whether doxycycline is right for you.

WHAT IS DOXYCYCLINE?

Doxycycline is an inexpensive antibiotic prescribed to treat acne, malaria, and bacterial STIs. Doxycycline belongs to a class of drugs known as tetracycline antibiotics.² Recent research findings suggest that it can be taken before or after condomless sex to prevent certain bacterial STIs. When doxycycline is taken **after** condomless sex, it is known as ‘doxycycline post-exposure prophylaxis’ or ‘doxy-PEP’ to prevent STIs.

DRUG EFFICACY AND DRUG RESISTANCE

There have been various research studies on doxycycline to prevent STI acquisition in trans women, gbMSM, and cisgender women. The finding from these studies, which have been presented at various large conferences,^{3,4} are summarized below.

In the substudy on doxy-PEP using MSM participants (n=232) enrolled in the ANRS IPERGAY HIV PrEP trial, it was found that chlamydia infection risk reduced by 70% with the use of doxycycline after unprotected sex, while syphilis infection risk decreased by 73%.^{5,7,8}

A separate, more recent doxy-PEP research study (n=501) conducted in gbMSM and trans women found that those who took 200 mg of doxycycline after condomless sex had a reduction in overall STI risk by 65%.^{6,25} Doxycycline has a high oral bioavailability of more than 80%, which is thought to be crucial to ensuring an adequate and persistent concentration of doxycycline in mucosal tissues.²⁰

There are concerns about the development of antibiotic resistance with long-term doxycycline use.^{21,23} The doxy-PEP study from 2023 found a slightly higher rate of new infections with tetracycline-resistant gonorrhea in the group taking doxy-PEP, but the number of gonorrhea cultures that were able to be collected were low (n=39).^{6,25} Longer-term studies are needed to monitor whether, and by what degree, doxycycline as PEP may increase risk for developing tetracycline resistance.^{6,18,19} There is some concern that resistance to doxycycline may build up over time.^{19,21}

Doxycycline also appears to be less effective at treating gonorrhea.^{5,7,19,22} The lower measured efficacy of doxycycline to prevent gonorrhea is thought to be due to pre-existing drug resistance towards tetracycline antibiotics. For instance, the IPERGAY HIV PrEP trial found no significant efficacy of doxycycline to treat gonorrhea and found a high percentage of gonorrhea resistance to tetracyclines (56%).^{5,19,24} The researcher from the IPERGAY study concluded that doxy-PEP is not the long-term solution for gonorrhea infections and recognized that the bacterium could develop resistance to doxycycline with long-term use as doxy-PEP.²⁴

As an alternative method to prevent gonorrhea infection, the DOXYVAC study explored the use of the meningitis B vaccine 4CMenB.⁷ 4CMenB is approved for use against bacterial meningitis.¹¹ In the DOXYVAC study, 4CMenB reduced the incidence of first episode of gonorrhea among gbMSM by about half.^{7,10} The 4CMenB vaccine is not approved for use

against gonorrhea infection. Additional research studies are needed to measure the duration of vaccine effectiveness, determine whether a booster is required, and conduct cost-benefit analysis of using the vaccine to prevent gonorrhea infection.

While doxy-PEP has been found to be effective for preventing certain STIs in gbMSM and transwomen, research studies in cisgender women engaging in vaginal sex found that doxy-PEP was ineffective in preventing chlamydia, gonorrhea, and syphilis.^{9,26} There are many possible reasons for the lack of efficacy of doxy-PEP in cis women, ranging from anatomical differences, suboptimal adherence, and variations in antibiotic resistance.^{9,26} One of the possible explanations is that the mucosal saturation of doxycycline in cervical tissue may be lower than that of urethral, rectal, and throat tissues, but much remains to be further studied.

DOSAGE AND SIDE EFFECTS

Doxycycline is available at various doses. The drug has a long half-life, staying in your body for up to 16-22 hours¹² before it reduces to half of the concentration in your bloodstream. Doxycycline is expected to take approximately five days to be cleared from your body.¹³ The recommended single dose for doxy-PEP for STI prevention is 200mg (given as two 100mg pills) taken as soon as possible after condomless sex. The antibiotic is taken ideally within 24 hours of condomless oral, anogenital, or vaginal sex, but no later than 72 hours after.

If you have sex again within 24 hours of your last dose of doxycycline, take your next dose of doxycycline 24 hours after your last dose. Do not double dose, reduce doses, or share your doses with others. Doxycycline is taken with water and can be taken with food or without food, although taking with food may reduce the risk of gastrointestinal side effects such as nausea. Avoid taking doxycycline within 2 hours of having consumed dairy, calcium, antacids, or multivitamins.^{13,14}

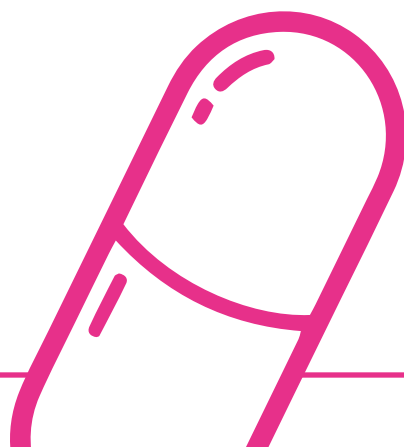
Common side effects of doxycycline can include photosensitivity, esophageal irritation, and an upset stomach. It is recommended to wear sunscreen when taking doxycycline to reduce photosensitivity and risk of sunburn. It is advised not to lie down for 30 minutes after taking doxycycline as it increases the risk of acid reflux and irritation to your throat.¹⁵ Do not take doxycycline if pregnant.¹² Further research is required to have evidence if doxy-PEP affects the gut microbiome—or the balance of healthy/normal bacteria—in the gastrointestinal tract.

ACCESS TO DOXY-PEP

While recent research studies on doxy-PEP point to the effectiveness of doxy-PEP in preventing syphilis and chlamydia infection (and, to a lesser degree, gonorrhea infections), it is not currently prescribed readily by physicians in Canada. The San Francisco Department of Public Health has been the first to readily prescribe doxy-PEP. They recommend its use after oral, anal, or vaginal sex in gbMSM and trans women who are either living with HIV or who are on HIV PrEP.¹⁶

CANADIAN RESEARCH ON DOXYCYCLINE

Currently, the CTN 329: Doxycycline intervention for bacterial STI Chemoprophylaxis (**DISCO**)¹⁷ study is enrolling gbMSM and trans women in various Canadian cities. The inclusion criteria are listed [here](#).



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