• When prescribing doxy-PEP, clinicians should use the dosing regimen of oral doxycycline 200 mg taken ideally within 24 to 72 hours of condomless sex (A1) and counsel patients (A*) on the key points for patient education outlined in Table 1: Considerations for Doxy-PEP Implementation.

• For individuals taking doxy-PEP, clinicians should screen for HIV, chlamydia, gonorrhea, and syphilis at least every 3 months. (A1)

• Clinicians should offer PrEP to individuals who do not have HIV and are initiating or using doxy-PEP. (A*)

• Clinicians should offer HIV treatment to individuals with HIV who are not on antiretroviral therapy and are initiating PrEP and are initiating or using doxy-PEP. (A1)

• Clinicians should engage in shared decision-making with cisgender men who 1) engage in condomless sex with multiple partners assigned female sex at birth and 2) have had a STI diagnosed within the past year and are at ongoing risk of STI exposure. (B3)

Doxy-PEP is not recommended to protect against STI acquisition.

• Evaluation by a clinician after a known or possible STI exposure.

• Evaluation after an STI exposure.

• HIV, chlamydia, gonorrhea, and syphilis at least every 3 months. (A1)

• Doxy-PEP is not recommended to protect against STI acquisition.

• Doxy-PEP is not recommended for use in all bacterial STIs.

• Doxy-PEP is not 100% effective in preventing bacterial STIs and has varying degrees of efficacy in preventing gonorrhea, chlamydia, and syphilis overall and by anatomic site.

• Key Points

○ Doxy-PEP is not 100% effective in preventing bacterial STIs.

○ Doxy-PEP is not 100% effective in preventing bacterial STIs.

○ Doxy-PEP is not recommended in the CDC STI Treatment Guidelines.

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HIV CLINICAL RESOURCE

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ALL RECOMMENDATIONS

• Clinicians should offer doxy-PEP to cisgender men and transgender women who are taking HIV PrEP or receiving HIV care and 1) engage in condomless sex with partner(s) assigned male sex at birth and 2) have had a bacterial STI diagnosed within the past year and are at ongoing risk of STI exposure. (A1)

• Clinicians should offer doxy-PEP to cisgender men and transgender women who are not taking HIV PrEP or receiving HIV care and 1) engage in condomless sex with partner(s) assigned male sex at birth and 2) have had a bacterial STI diagnosed within the past year and are at ongoing risk of STI exposure. (A2†)

• Clinicians should engage in shared decision-making with cisgender men who 1) engage in condomless sex with multiple partners assigned female sex at birth and 2) have had a bacterial STI diagnosed within the past year, offering doxy-PEP on a case-by-case basis. (B3)
<table>
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<th>Consideration(s)</th>
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| Available formulations | • Doxycycline hyclate delayed-release 200 mg oral tablet  
• Doxycycline hyclate or monohydrate immediate-release 100 mg oral capsule or tablet (2 capsules or tablets taken together for a total of 200 mg)  
• The immediate-release formulations are more widely available and usually cost less than the delayed-release formulation. |
| Administration | • As doxy-PEP, 200 mg of doxycycline should ideally be taken within 24 hours after condomless sex, up to 72 hours maximum.  
• No more than 200 mg of doxycycline should be taken in a 24-hour period.  
• Milk and vitamins containing positive cations (e.g., calcium, zinc, magnesium) should be avoided within 2 hours of taking doxycycline, because these interfere with doxycycline absorption and may lower doxycycline levels, potentially reducing efficacy. |
| Contraindications, drug–drug interactions, and dose adjustments | • Doxycycline should not be used as PEP concurrently with other doxycycline therapy (or any other tetracycline-class antibiotic) for treatment or prevention of a health condition (e.g., acne, rosacea, malaria prophylaxis).  
• No significant drug–drug interactions exist between doxycycline and ARVs used for HIV treatment or PrEP.  
• No known drug reactions exist between doxycycline and gender-affirming hormone therapies.  
• No doxycycline dose adjustments are indicated for patients with renal dysfunction.  
• Doxycycline is generally contraindicated during pregnancy because of potential adverse effects on the fetus. |
| Adverse effects | • GI adverse effects are common; taking doxycycline with food may help alleviate nausea or GI upset. Symptoms including nausea, vomiting, and reflux can be severe enough to require cessation of doxycycline.  
• Esophageal injury and irritation can occur. Doxycycline should be taken with an 8–oz glass of water and the individual should remain upright for 30 minutes to 1 hour after dosing.  
• Skin photosensitivity and phototoxicity can occur; wearing sunscreen, limiting sun exposure, and avoiding tanning beds can help prevent sunburn and other skin injury.  
• Intracranial hypertension is a rare but serious adverse effect. Refractory headaches or vision changes should be evaluated promptly by a clinician.  
• Doxycycline use may select for antibiotic-resistant organisms, which can cause infections in some circumstances and can disrupt the microbiome. |
| Supply of doxy-PEP medications | • For patients taking HIV PrEP, consider prescribing a doxy-PEP supply equal to the supply of HIV PrEP medications for patient convenience (e.g., 90 days).  
• For patients not taking HIV PrEP, a 90-day supply is suggested.  
• Regarding dose quantity:  
  - For delayed-release doxycycline 200 mg tablets, the pill quantity dispensed should not exceed 90 per 3 months.  
  - For immediate-release 100 mg capsules or tablets, the quantity dispensed should not exceed 180 per 3 months.  
  - These numbers are the upper limit, and many patients will not need such a large quantity. Shared decision-making can determine the lowest quantity needed based on the frequency of condomless sexual encounters during a 3-month interval. |
| Follow-up and laboratory monitoring | • Engage patients taking doxy-PEP in ongoing comprehensive sexual health services that include STI screening, HIV PrEP, immunizations, and other health promotion strategies as indicated.  
• At least every 3 months:  
  - Screen for syphilis, HIV if not previously diagnosed, gonorrhea, and chlamydia (including extragenital testing when indicated), ensuring tests have been obtained before providing a doxy-PEP prescription refill.  
  - Offer HIV PrEP or HIV treatment as needed.  
  - Assess for ongoing doxy-PEP needs and continue in shared decision-making as new evidence becomes available.  
• The doxycycline package insert advises periodic monitoring of hepatic function, renal function (specifically BUN), and CBC with prolonged therapy. It is currently unclear whether this routine monitoring is necessary for doxy-PEP. The DoxyPEP study protocol included yearly monitoring of these tests, informing the currently recommended strategy. |
| Key points for patient education | • Medication administration instructions and contraindications: See above.  
• Protective effect: Doxy-PEP is not 100% effective and is not effective against all STIs. For cisgender men and transgender women at risk of STIs who were engaged in routine sexual healthcare, doxy-PEP reduced the likelihood of an STI diagnosis by >50%. Evaluation by a clinician after a possible STI exposure is necessary to determine whether treatment is needed.  
• Adverse effects: Doxycycline can cause GI adverse effects, photosensitivity, and esophageal irritation, which can be mitigated using strategies noted above. Long-term doxycycline use may increase the risk of developing an antibiotic-resistant infection. The potential long-term effects of doxy-PEP use are not known at this time.  
• Ongoing screening: Screening for STIs every 3 months is necessary while taking doxy-PEP. Routine HIV testing should continue in individuals at risk of HIV. Yearly blood tests (CBC, liver and kidney tests) are recommended to monitor for potential adverse antibiotic effects. |