

Syphilis Treatment Recommendations

Stage of Syphilis		Recommended Regimens	Dose/Route
Early Syphilis	Primary, Secondary, and Early Latent Less than 12 months	Benzathine penicillin G	2.4 million units IM in a single dose
Late Syphilis	Late Latent or Unknown Duration Greater than 12 months	Benzathine penicillin G	2.4 million units IM every seven days for three doses, with no fewer than five days between doses.
Any Stage	Neurosyphilis Ocular Syphilis Otosyphilis	Aqueous crystalline penicillin G	18-24 million units per day, administered as 3-4 million units IV every 4 hours or continuous infusion for 10-14 days

Additional Treatment Information

- On the day of treatment, order an RPR test for a "day of treatment titer." This will serve as a benchmark to determine whether patient has adequate treatment response.
- Clinical experience indicates that an interval of 10-14 days between doses of benzathine penicillin for latent syphilis might be acceptable before restarting the sequence of injections (i.e., if dose 1 is administered on day 0, dose 2 is administered on days 10-14).
- **Benzathine penicillin G is the only therapy with documented efficacy for syphilis during pregnancy.** Pregnant people with syphilis in any stage who report penicillin allergy should be desensitized and treated with penicillin.
- Certain evidence indicates that additional therapy is beneficial for pregnant people to prevent congenital syphilis. For a pregnant person who has primary, secondary, or early latent syphilis, a second dose of benzathine penicillin G 2.4 million units IM can be administered 1 week after the initial dose.
- More than 9 days between doses is not acceptable for pregnant people receiving therapy for late syphilis. An optimal interval between doses is 7 days for pregnant people. If a pregnant person does not return for the next dose on day 7, every effort should be made to contact them and link them to immediate treatment within 2 days to avoid retreatment. **If there are >9 days between doses, the pregnant person should repeat the full course of therapy.**
- To consider alternative regimens; see [U.S. CDC 2021 STI Treatment Guidelines](https://www.cdc.gov/std/treatment-guidelines/toc.htm) (https://www.cdc.gov/std/treatment-guidelines/toc.htm)

Assistance

For help interpreting test results and guidance on appropriate staging and treatment, call Maine Disease Reporting at 1-800-821-5821.

Please refer to the complete [U.S. CDC 2021 STI Treatment Guidelines](https://www.cdc.gov/std/treatment-guidelines/toc.htm) for more information.



Syphilis Testing Guidance for Health Care Providers

Who to Test for Syphilis:

- Pregnant Persons:
 - **In Maine, health care providers are required by law, with patient consent, to test all patients at least once during pregnancy.**
 - Maine CDC recommends testing two additional times during pregnancy: at 28 weeks gestation and at delivery.
 - Whenever presenting for care, especially in emergency departments and urgent care centers, jails or other carceral settings, substance use disorder treatment facilities, and labor and delivery units.
- Persons who deliver a stillborn infant
- Birthing parents before being discharged from the hospital with their infant if they haven't been tested at least once during their pregnancy
- Persons who are at high risk* regardless of known pregnancy status
- Persons seeking any sexually transmitted infection (STI) testing

How to Test:

- Two tests are required to diagnose syphilis: a nontreponemal test (i.e. Venereal Disease Research Laboratory [VDRL] or rapid plasma reagin [RPR] test) and a treponemal test (i.e., the T. pallidum passive particle agglutination [TP-PA] assay, various EIAs, chemiluminescence immunoassays [CIAs] and immunoblots, or rapid treponemal assays). **Use of only one type of serologic test (nontreponemal or treponemal) is insufficient for diagnosis.**
- There are two different algorithms (<https://www.std.uw.edu/go/comprehensive-study/syphilis/core-concept/all#laboratory-diagnosis-serologic-testing-algorithms>) frequently used to diagnose syphilis, both of which are acceptable.
- **Order a test that reflexes to the next test in the algorithm rather than a standalone test to minimize venipuncture visits and prevent delays in diagnosis and treatment.**
- Create reminders or alerts in your electronic health record system to order syphilis testing for pregnant patients as required by Maine law.

*Persons at high risk for syphilis include those who live in a community with high syphilis morbidity or and people who are at risk for syphilis acquisition during pregnancy from drug misuse (especially methamphetamine, heroin, xylazine or cocaine by any route), STIs during pregnancy, multiple partners, a new partner, partner with STIs, experiencing homelessness, exchange money or drugs for sex.

