



Improving lives through the prevention and treatment of anogenital & HPV-related diseases

PATIENT RESOURCES

Treatment of Genital Warts (Condyloma)

Medication Treatments

Imiquimod (Aldara, Zyclara)

Imiquimod works by stimulating your own immune system to fight the virus. Two formulations are available, Aldara (5% imiquimod) and Zyclara (3.75% imiquimod), for treatment of external genital warts, but the manufacturers recommend against using the medication inside the vagina. There is not enough information regarding the safety of imiquimod in pregnancy; therefore, it is not recommended for pregnant people. The choice between the two formulations should be made based on patient preference, cost and convenience.



Handwashing before and after cream application is recommended. The patient applies imiquimod cream directly to the clean, dry, warty tissue at bedtime, rubbing it in until the cream is no longer visible. This area is washed with mild soap and water 6 to 10 hours later. Sexual contact should be avoided while the cream is on the skin. The cream can weaken condoms and diaphragms.

Aldara is applied three days per week (e.g. Monday-Wednesday-Friday) for 4 to 16 weeks. **Zyclara** is applied daily for up to 8 weeks.

A mild, local inflammatory reaction (redness, swelling or firmness, ulceration/erosion, itching, burning, blisters) should occur, which is a sign the drug is working. It is generally not so severe as to need a break

in treatment. If severe inflammation occurs, use of the drug should be stopped until the inflammation clears and then it can be restarted using it less often.

About half of patients will have complete clearance of the warts and most others will have partial clearance, but up to 1/3 will experience a recurrence within 12 weeks.

A retrospective observational study by Planned Parenthood Federation of America concluded imiquimod alone or in combination with TCA was the most cost-effective initial approach to management of patients with warts in multiple locations or recurrent warts. In addition, it was the most cost-effective second-line approach to warts that had not completely cleared after three clinic visits in which cryotherapy or monotherapy TCA was employed.

Trichloroacetic acid and bichloroacetic acid (TCA, BCA)

Both trichloroacetic acid (TCA) and bichloroacetic acid (BCA) are caustic acids that destroy the wart tissue. TCA is used most commonly, and must be applied by a doctor, nurse practitioner, or other medical provider. It can be used on the cervix and vagina, and it can be used during pregnancy. TCA solution is applied sparingly to the wart tissue with a cotton swab; the wart turns white as the solution dries. Application of an ointment or gel (such as petroleum or lidocaine jelly) to the normal tissue surrounding the wart can help prevent spreading of acid to unaffected



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areas. Excessive application of medication can be neutralized by washing with sodium bicarbonate solution, otherwise the patient may experience pain or burning of adjacent healthy tissue. The patient should not sit, stand or dress until the treatment area has dried. Repeated weekly application is required for four to six weeks, or until the lesions have cleared. Thick, large lesions may not respond because the acid may not penetrate to treat the entire lesion. The only trial that evaluated use of TCA in people assigned female at birth (AFAB) reported a 70 percent clearance rate.

Interferon injection

Injectable interferon is given in the office. Experience with these agents is more limited than for other medical therapies. Interferons are contraindicated in pregnancy. The medicine is injected directly into the wart two to three times per week for up to nine weeks. Local anesthesia is used before the injection. Patients receiving interferons by any route commonly experience flu-like symptoms, fatigue, loss of appetite, and local pain. Given the frequency of bothersome side effects, variable rates of effectiveness, and inconvenience of administration, we suggest avoiding interferon therapy for primary treatment of anogenital warts. Interferon may be used as an additional therapy to surgical and destructive treatments, especially in patients with lesions that do not respond well to other treatments.

Podophyllotoxin

Podophyllotoxin (podofilox) and podophyllum resin (podophyllin) are related. Neither drug should be used by pregnant patients because of potential fetal risks.

Podophyllotoxin (podofilox) is recommended for initial therapy of external genital warts, as long as the patient can comply with home therapy. Podophyllotoxin (podofilox) has very minimal absorption into the bloodstream, can



be self-administered, and is more effective than podophyllum resin (podophyllin). Using a cotton swab, the patient applies a 0.5 percent gel or solution to external genital warts twice daily for three consecutive days. No more than 0.5 mL of podofilox should be applied in one day. The patient then withholds treatment for four days, and repeats this cycle weekly up to four times. Large areas (10 cm² or more) should not be treated in a single application because pain is likely when the area becomes necrotic.

Podophyllum resin is a plant-based resin that blocks cell division and leads to cell death. The clinician applies the solution directly to the warts with a cotton swab (or similar device). No more than 0.5 mL should be applied during each treatment session and large areas (10 cm² or more) should not be treated in a single application because of potential pain when the area becomes necrotic. The area should air-dry before the patient dresses.



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In contrast to podophyllotoxin, systemic absorption (absorption into the bloodstream) and side effects have been documented. For this reason, a weaker solution (10 percent) should be used when treating large, and application to open lesions/wounds should be avoided.

We instruct the patient to wash the area one to four hours after application of the drug, otherwise excessive skin irritation and systemic absorption can occur. The treatment is repeated weekly for four to six weeks, or until the lesions have cleared. Adverse effects range from mild skin irritation to ulceration and pain, depending upon the concentration used and the length of time it is left on the skin.

Sinecatechins

Sinecatechins (Veregen) is a botanical drug product for self-administered topical treatment of external anogenital warts. The active ingredient is kunecatechins, which is a mixture of catechins and other components of green tea. The exact mechanism of action of catechins is unknown, but they have both antioxidant and immune enhancing activity.

A 0.5 cm strand of ointment is placed on each wart and a finger is used to cover the wart with a thin layer of the ointment, three times each day for up to 16 weeks. It should not be used in the vagina or anus and should be washed off of the skin before sexual contact or before inserting a tampon into the vagina. It can weaken the latex in condoms and diaphragms.

Sinecatechins should be avoided in immunocompromised patients and patients with active genital herpes lesions because safety and efficacy have not been established. There is minimal information on the risk of use during pregnancy. Of note, Veregen costs about \$257 for one 15 gram tube.

Cryotherapy

Cryotherapy with liquid nitrogen destroys wart tissue by breaking down cells. Liquid nitrogen is most commonly used, and is applied directly to the lesion with a cotton swab or a fine spray. The treatment is applied for 30 to 60 seconds, until an ice ball forms and encompasses the lesion and 1 to 2 mm surrounding area. Repeated weekly application is required.



Cryotherapy causes pain during application and variable localized inflammation afterward. Providing local anesthesia for the procedure is especially important when the area undergoing cryotherapy is large. Adverse reactions include skin irritation, edema (swelling), blistering, and ulceration.



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Post-treatment hypopigmentation (skin discoloration) is also relatively common.

For these reasons, we suggest a course of at least four applications of a medical therapy, such as podophyllotoxin, TCA, or imiquimod before resorting to cryotherapy. Cryotherapy can be used during pregnancy.

Electrocautery

Electrocautery can also be used for ablation of lesions. In contrast to cryotherapy, electrocautery requires administration of anesthesia and use of an operating room. Bleeding and discomfort following the procedure are more common than with other types of treatment, and may be prolonged. Advantages of this approach are that a single treatment session is usually adequate for eliminating all of the warts and it can be used to treat vaginal lesions.

Excision

We recommend excisional (removing), rather than ablative (destroying), therapy when underlying intraepithelial neoplasia (VIN, pre-cancer) is suspected and a specimen is required for histopathological examination. Excision is appropriate for both single and extensive lesions. Excision may require administration of anesthesia and use of an operating room. For a highly motivated patient, however, small lesions can be excised or cauterized with sedation and anesthetic.



Combination Therapy

A number of trials have examined various combinations of cytotoxic therapies, immune-mediated therapies, and surgical therapies to improve cure rates or minimize recurrence rates, particularly in patients with refractory disease. Theoretically, the immune-mediated therapies may help reduce the viral load, while the cytotoxic and surgical therapies can debulk and eradicate the wart tissue. To date, no combination therapy has been proven to be more effective than a single treatment type. For particularly difficult cases, we suggest combining intralesional interferon and a non-immune-mediated medical therapy (such as TCA or liquid nitrogen).