

Relevant Research on a Patented Topical Wart Treatment

Studies indicate the effectiveness of a compounded 5-FU/SA plantar wart medication.

BY STEVEN LEON, MS, PA-C

We have had breakthroughs in many difficult-to-treat cutaneous diseases, but the humble wart remains stubbornly defiant to our best treatments, especially plantar warts. A Cochrane meta-analysis on wart treatment found that salicylic acid and cryotherapy were little to no better than placebo. 5-fluorouracil, dinitrochlorobenzene, intralesional bleomycin, intralesional interferon, photodynamic therapy, and

may resolve similarly with or without treatment.⁷ Better technique, improved patient education, and closer follow-up may improve efficacy; however, with treatments that are not very effective to begin with, the needle can be moved only so much.

Tolerability is of paramount importance in the treatment of plantar warts. Although patients with plantar warts do not suffer as much embarrassment as patients with warts in visible areas, plantar wart patients report more pain than those with warts at any other site.⁸ For this reason and due to the infectious nature of warts,⁹ benign neglect is seldom a good option. This is especially true for patients older than 12, where spontaneous regression significantly decreases.¹⁰

Navigating the pain, downtime, and extended treatment times can be difficult, to say the least. Currently there is no commonly accepted algorithm to help navigate plantar wart treatment¹¹, leaving the decisions to be made by providers based on clinical experience. Patient expectations are that we are the experts and should be able to treat warts with little difficulty and that they will be able to continue their normal activities post-treatment. For all warts, but especially plantar warts, there is a need for a medication that has high efficacy, short treatment times (weeks, not months), good tolerability and minimal downtime.

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intralesional antigen were also included. They may be effective but have much less evidence than salicylic acid and cryotherapy. Cantharidin, compounded medications, and surgical removal were not included in the study due to the lack of any RTC for these treatment modalities.² Cantharidin-podophyloxytoxin-salicylic acid formulas have been shown in comparative studies to be superior to both cryotherapy³ and ND:Yag laser.⁴

Multiple in-office treatments are typically required to treat plantar warts⁵, with tolerability and downtime being a major concern. At-home topical treatments have potential for less downtime vs in-office treatments as patients can discontinue or modify treatment when pain or an impaired gait become intolerable; however, low efficacy, long treatment times and likely poor adherence make them yet another imperfect solution for plantar wart. A common rationale for continuing any wart treatment after months of failure is the common belief that even though the treatments are not completely destroying the wart, they are improving our own immune response, thus hastening spontaneous resolution vs non-treatment. This belief should be called into doubt due to the low efficacy of current plantar wart treatment and evidence that warts

New Concepts and Studies

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Before



7 days of Treatment after Curettage



3 Weeks Later: Complete Clearance

Case Study: Warts in a Callus

An 80-year-old female presented with a chief complaint of a longstanding callus which had recently thickened and was now causing discomfort, especially while walking. Examination revealed three warts in the callus. Due to the patient's advanced age, fall risk, and her wish to continue her normal activities, WartPEEL® (2% 5-FU/17% Salicylic Acid) Remedium™ Adhesive Gel was the treatment of choice.

The patient was successfully treated with 10 days of nightly application of WartPEEL. Curettage was performed after the 7th application. The patient had experienced no pain, and reported no skipped days. Skin lines were visible where the warts had been after curettage and I suspected the warts had resolved. The patient was advised to continue for 3 more days since she was not experiencing pain and I wanted to be sure the wart had fully resolved.

Two weeks later, the area was fully healed. The patient reported no disruption of her normal routine during treatment. Mild stinging and discomfort were reported in the last two days of treatment. The patient was examined three months later, and no recurrence was noted. **PM**

Looking for a Better Way

MedCara Pharmaceuticals offers Wartpeel: 5-FU (2%) and Salicylic Acid (17%) in Remedium Adhesive Gel. It is a compounded medication that has been available by prescription since 2004 and has 3 U.S. patents. It is an at-home treatment that is applied nightly for an average of 2-3 weeks for plantar warts. Its estimated cure rate for plantar warts, with proper use and follow-up, is 90%. WartPEEL began as a collaboration between NuCara pharmacists and local podiatrists with the goal of developing a more efficacious plantar wart treatment. It is available by mail order nationwide (wartpeel.com/providers/).

Traditional vehicles like creams, ointments and pastes were abandoned early in the development process. Even with tape occlusion, these vehicles were observed to spread the 5-fu/SA to perilesional skin, causing irritation and early discontinuation. Dilution of the active ingredients as it spread off the wart to perilesional skin was also thought to play a significant

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role in the high rate of treatment failures. Due to the poor results with standard vehicles, which were better suited to rashes than warts, it was determined that a new vehicle needed to be created specifically for warts. This vehicle needed to dry and concentrate rather than spread and dilute. The goal was to penetrate the thick, compacted and dry compact stratum corneum of the wart and consistently deliver 5-FU to the level of wart replication.

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WartPEEL in Remedium Adhesive gel formulation highlights:

- Adheres to the wart: Adhesive gel Formulation dries in 15 minutes and does not migrate to perilesional skin.
- Water based formula: Unlike anhydrous vehicles, Remedium concentrates as it dries and donates water moisture to the dry compact stratum corneum of the wart, facilitating drug release and penetration.
- Penetration: The synergistic action of water, salicylic acid and DMSO increase the 5-FU penetration to the level of wart replication.

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- 3M Blenderm tape: This tape is included with the prescription. It is applied after WartPEEL has dried to reduce transepidermal water loss and improve penetration.

Since WartPEEL is a unique topical medication, proper patient education is crucial for optimal results. Below are some keys to successful patient education:

- Let it dry: WartPEEL is not a cream or a gel—it's a glue, so you need to let it fully dry before you apply the tape. WP dries completely within 10 to 15 minutes. This point is stressed in the instructions but should be reinforced by the prescriber as it is the most common reason for treatment failure. Inappropriate spreading of wartpeel not only causes irritation to perilesional skin but also dilutes its potency.
- Avoid skipping days: Warts grow quickly and need to be completely destroyed so they do not recur. If a patient forgets to apply it at night, they should put it on in the morning.
- Schedule a follow-up: Most health care providers expect topical wart medications to take months to work and typically schedule a follow-up in 2-3 months. The average treatment time for WartPEEL for plantar warts is 2-3 weeks and a three-week follow-up is recommended. At the follow up, curettage may be performed.

Relevant Research Studying Topical Preparation of 5-FU/SA

WartPEEL is a compounded medication which does not require FDA approval and no studies have been done specifically using WartPEEL. More extensive studies have been conducted using a prescription wart treatment widely available in Europe. It is a combination of .05% 5-FU/10% SA in a film-forming solution (Verrumal). The concentration of active ingredients in Verrumal is significantly lower than in WartPEEL but the two vehicles have

some similarities. Meta-analysis of the randomized-controlled studies (RCTs) included a total of 625 patients, including 101 patients with plantar warts. The plantar wart group had complete healing of 63% vs. 11% for the 5-FU free control group, showing significant superiority of 5-FU/SA over SA alone.¹² Additional studies with this formula have shown efficacy for warts of the nail unit^{13,14} and anogenital warts.¹⁵

Two studies have shown efficacy with 5-FU/Salicylic compounds with different levels of active ingredients and different vehicles than WartPEEL. One case study was a treatment-resistant case of severe, widespread facial filiform warts. The patient had over 50 warts initially and showed near-complete resolution with only two warts remaining at his final visit.¹⁶ A second study on the treatment of plantar warts had all 20 participants achieving complete resolution.¹⁷ There are also studies with the use of standard prescription 5% 5-FU cream for the treatment of warts in children and adults.^{18,19}

Safety

The two ingredients, 5-FU and SA, are commonly used both separately and combined, and their side effects are well documented. With WartPEEL, there is no specific safety data for the product to supplement what we know about 5-FU and SA from the literature. For patients, proper education and appropriate follow-up is key to prevent excessive irritation and erythema caused by improper use or overuse. Patients typically discontinue

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WartPEEL when it is applied directly to exposed dermis due to increased irritation. Post-Inflammatory hyperpigmentation is common but temporary and consistent with other topical or destructive treatments. There has been no reported scarring to date. All topical 5-FU medication should be avoided during pregnancy due to risk of teratogenicity based on conflicting human data with systemic 5-FU. Risk of fetal harm is low based on expected limited systemic absorption.

Conclusion

The low efficacy, prolonged treatment times and potential downtime have motivated health care providers across multiple specialties to consider compounded medications to improve treatment outcomes for warts. This is especially true of the treatment of plantar warts, where a short treatment duration, good tolerability and minimal down time are desirable. Many patients who

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present with warts have already failed multiple treatments and are looking for new, more effective treatment options. Due to its speed, effectiveness, and tolerability, WP has become a vital first-line treatment for cutaneous warts in my practice. **PM**

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