



## RECURA

### OFFERS IMPROVED DELIVERY OF TOENAIL ANTIFUNGAL MEDICATIONS FOR SUPERIOR OUTCOMES

Toenail fungus affects about 14% of men and women in the U.S. - that's about 42 million cases of onychomycosis, resulting in pain, infection and yellow, brittle, unattractive nails. Without proper treatment, fungal infections can spread to other nails, and widespread discomfort can make even simple things like wearing shoes a very painful experience. Ongoing infections can also eventually cause very unpleasant odors.

Getting rid of toenail fungus can be extremely difficult, primarily because the fungus hides underneath the tough nail which provides a hard, protective barrier preventing most topical antifungal medications from penetrating and reaching the infection. The roots of nail fungus are also exceedingly deep and can extend over large areas of tissue, making them difficult to completely eradicate without ongoing intervention. While there are several antifungal medications available for the treatment of onychomycosis, each comes with its own limitations and issues.

#### TRADITIONAL ANTIFUNGAL MEDICATIONS

Topical antifungal agents like fluconazole and miconazole can be very effective in destroying the fungus that causes toenail infections, and because these agents have been around for some time, they're widely available and very affordable, even on the most modest budget. But they have one significant limitation: they don't penetrate the nail bed as effectively as they need to in order to destroy the fungal infection at its roots. That means that to be effective, they must be used for very long periods of time - often a year or even more - which means patients are exposed to side effects and medical risks associated with long-term antifungal use. Plus, if these agents don't penetrate the tissues at the strength required for fungal eradication, fungal infections can recur.

Even with the affected nail removed to enable creams and ointments greater, unencumbered access to the underlying skin, topical antifungal agents are often unable to penetrate effectively to the entire site of infection, leaving enough fungal bodies in place to cause recurrent symptoms and subsequent infection.

#### ORAL MEDICATIONS

To address the problem of tissue penetration, many physicians have relied on oral medications such as fluconazole and terbinafine to treat fungal infections systemically. While oral antifungal medications can be effective in treating onychomycosis, these medications must travel throughout the body in order to reach the infected toenail, and that means they need to be given at relatively high doses or over a prolonged period of time in order to reach the blood levels necessary to fight off stubborn toenail fungus and to destroy the fungus so recurrence can be prevented.

Long-term use of oral antifungal medications, especially at moderate to high doses, can significantly increase the risks of some very serious side effects including nephrotoxicity, an increased risk of damage to the liver where these drugs are metabolized, and increased risks of drug interactions. Ideally, using a topical helps relieve some of these risks by concentrating the medication in the toe area where the infection is occurring. Plus, topical routes of administration offer an additional advantage over oral medications because they treat the nail structure itself. As a fungal infection progresses, the nail can lift up from the underlying tissue, creating an airspace that prevents oral medications from reaching the fungus systemically. Because topical agents penetrate the nail itself, they can be much more effective in eliminating fungi attached to the underside of the nail - as long as they can reach the fungus at adequate and effective concentration levels (a kind of pharmacological catch-22).

And that's how it remained for years, with topical medications that lacked penetrating capability and risky, long-term use of oral antifungals as the two primary options for onychomycosis treatment.

## NEW TOPICAL AGENTS COME AT A PRICE

In recent years, scientists have discovered novel topical antifungal medications that have proven to be very effective in treating toenail fungal infections, both *in vitro* and *in vivo* - but while they may be more effective in eradicating fungal infections in some patients, there's another problem: cost. In fact, the two newest topical antifungal medications, Jublia (efinaconazole) and Kerydin (tavaborole), come with a pricetag of more than \$500 per bottle in most areas. Considering each bottle contains only about 80 drops and most therapies take nearly a year to complete, here's how those costs would mount up if both big toenails were affected:

$$\begin{aligned}2 \text{ nails} \times 2 \text{ drops per day} &= 4 \text{ drops per day} \\80 \text{ drops} / 4 \text{ drops} &= 20 \text{ days, or almost 3 weeks} \\52 \text{ weeks (one year)} / 3 \text{ weeks} &= 17 \text{ bottles for an average treatment time} \\17 \text{ bottles} \times \$500 &= \$8500 \text{ for treatment}\end{aligned}$$

That's for two big toenails; if additional nails are affected, the cost rises accordingly.

What's more, because novel agents like Jublia and Kerydin are usually considered non-preferred treatments by most insurance and pharmacy coverage policies, that means these plans don't cover them or provide very limited coverage, leaving many patients carrying most or all of the cost of their antifungal medications. For most patients, paying \$8,500 out of pocket to cure their toenail fungus is simply not financially feasible, even with available coupons and incentives from the drug manufacturer. And bear in mind that even with these improved novel agents, there's no guarantee that \$8,500 out-of-pocket cost will bring a 100% cure without the possibility of a future recurrence.

## WHY THE HIGH COST?

The high cost of these newer agents is due in part to their novelty: new drugs are costly to develop and manufacture, at least in their early stages of development and production, and they're protected by patents, which means they don't have generic competitors to keep their costs in check. The higher costs during this early stage help offset the costs associated with researching and developing the drug prior to its release. Fluconazole and miconazole, by comparison, have been on the market for many years; they're no longer protected by patents, and they're widely available, which keeps their costs low and affordable.

But there's more than just research and development costs contributing to the high cost of care - in the case of onychomycosis, treatment can take many months, significantly adding to the high cost of care. Long-term treatment is necessary to enable the topical agents to penetrate the infection site at the levels necessary to eradicate the infection - and that all comes back to how well the drugs are delivered to those target tissues.

## ENTER RECURA: IMPROVED DELIVERY, LOWER COSTS

RECURA topical cream is a compounding vehicle that was developed specifically for improved delivery of more affordable onychomycosis medications like fluconazole and miconazole. RECURA uses a special formulation designed to hold the antifungal medication and to prevent it from dispersing or becoming diluted before it reaches the target treatment zone. That means more medication reaches the fungal bed to destroy the fungal body roots, eliminating the infection and destroying the fungi to prevent recurrent infections.

### References

Turner R et al., A Novel Vehicle for Enhanced Drug Delivery Across the Human Nail for the Treatment of Onychomycosis, *International Journal of Pharmaceutical Compounding* 2016;20(1):71-80

How effective is RECURA? In a clinical study using fungal toenail models, RECURA significantly improved the delivery of fluconazole 10% and miconazole 10%, achieving or surpassing efficacy levels of more costly novel treatments. In the study, two models were used: one to determine how well the RECURA-enhanced fluconazole and miconazole preparations penetrated nail tissue and how well the enhanced agents fought off and destroyed the fungal bodies (*dermatophytes*) that cause toenail fungal infections. In both of the study models, the results of RECURA-enhanced treatments were compared with treatments using more costly Jublia and Penlac, a generic antifungal medication. At the end of the study, the researchers found RECURA increased penetration of both fluconazole and miconazole to help them achieve clinically-effective levels equivalent or superior to the more costly agents. According to the study authors, such a topically applied system has the possibility of overcoming the systemic side effects of antifungals when taken orally.

What does this mean for patients? By improving the delivery of readily-available, low-cost options like fluconazole and miconazole, patients can enjoy the same benefits of novel topical antifungal medications or oral medications but without the increased risks associated with long-term use of oral antifungal medications or the exorbitant and prohibitive costs of new topical agents.

|                                      | Clinically Effective | Cost     | Covered by insurance |
|--------------------------------------|----------------------|----------|----------------------|
| Penlac topical solution (ciclopirox) | *                    | \$       | Yes                  |
| Lamisil tablets (terbinafine)        | *                    | \$       | Yes                  |
| Diflucan tablets (fluconazole)       | *                    | \$       | Yes                  |
| Kerydin (tavaborole)                 | ****                 | \$\$\$\$ | Most likely not      |
| Jublia (efinaconazole)               | ****                 | \$\$\$\$ | Most likely not      |
| Miconazole 10% in Recura cream       | ***                  | \$\$     | Maybe                |
| Fluconazole 10% in Recura cream      | ***                  | \$\$     | Maybe                |

Another benefit of RECURA: Because it's a compounded formulation, it enables prescribers to customize the dosing based on each patient's needs for a more patient-centered approach to care that can take each patient's individual health profile into account. And of course, because fluconazole and miconazole have been used for many years to treat toenail fungal infections, there's a large body of research and data concerning potential side effects and safety issues, which means patients can have the peace of mind that comes from using medications that have been fully vetted rather than relying on medications that have been only recently introduced and have a far more limited clinical history and background.

## THE ROLE OF RECURA

Toenail fungal infections can cause considerable discomfort and embarrassment, and finding a treatment that works is the key to resolving infections as quickly as possible (as well as preventing recurrence). As clinicians and researchers learn more about the toenail fungal infection process and the lifecycle of the fungus itself, new, more advanced medications and delivery systems may be developed that offer greater efficacy in shorter timeframes, without increasing the potential side effects. Until then, RECURA provides an effective treatment option for many of the million of men and women dealing with the painful symptoms and cosmetic effects of hard-to-treat toenail fungal infections.

If you would like to write a prescription for an antifungal drug compounded in Recura cream, please prescribe one of the following:

- Miconazole 10% in Recura cream
- Fluconazole 10% in Recura cream

Apply to affected toenails once to twice daily  
#30 grams x \_\_\_\_ refills

**Phone: (949) 642-0106**  
**Fax: (949) 642-5039**

