

# Topical Therapy for the Treatment of Melasma

**Dermatology Times:** *When is topical pharmacologic therapy typically necessary for the treatment of melasma?*

**Pearl E. Grimes, MD, FAAD:** The treatment of melasma is unquestionably challenging. The majority of patients I treat benefit most from pharmacologic treatment combined with aggressive use of sunscreen/photoprotection, including visible light. In addition, I sometimes utilize antioxidants and exfoliants as well as resurfacing procedures, preferably chemical peels.

The most common topical agents used as monotherapy or as part of a combination regimen for the treatment of melasma include hydroquinone, azelaic acid, kojic acid, and niacinamide. Hydroquinone has been around for more than 60 years and is still the most commonly used topical agent either as monotherapy or as part of a combination regimen, especially in patients with moderate-to-severe melasma.

**Dermatology Times:** *Why does hydroquinone remain the go-to drug after all this time? Is it simply that we still haven't found anything that works better in patients with moderate-to-severe melasma?*

**Dr. Grimes:** For those individuals who in particular have moderate-to-severe melasma, because we have the ability to manipulate the dosage of hydroquinone as well as combine it with other agents, it's still our number 1 workhorse drug.

**Dermatology Times:** *What are the primary benefits and potential risks of topical agents commonly used to treat melasma?*

**Dr. Grimes:** In my opinion, the benefits of topical agents used to treat melasma clearly outweigh the risks. Most of the agents that we use are extremely well tolerated and don't have any long-term complications.

The primary benefit of topical therapy is that it lightens dark patches of skin, especially those areas of hyperpigmentation that are typically visible on the forehead, cheeks, upper lip, and around the nose.

The most common safety issue associated with the use of topical therapies is related to irritation. These topicals can cause redness, swelling, and, depending on the level of baseline disease, can be associated with residual or postinflammatory hyperpigmentation. Even if that develops, however, it is something that we can easily treat. I'm not aware in the literature of any reports of long-term complications such as skin cancer or hepatotoxicity associated with topical therapies (in particular, hydroquinone) we use to treat melasma.

**Dermatology Times:** *How long do patients with melasma typically need to use a topical agent?*

**Dr. Grimes:** Given the chronicity of the condition, for the majority of patients with melasma, they probably need to be on something for an extended period of time and perhaps a lifetime. I will sometimes equate melasma with diabetes when I talk to my patients, so that they understand the chronic nature of the condition. Sun protection is key and is going to be a long-term priority. The patient may also need to use some type of exfoliant and antioxidant over the long term.

In regard to topical agents, there are strategies that can be used to successfully navigate the terrain. In my practice, we will typically treat patients with melasma aggressively for 3 to 6 months, but as soon as we achieve an adequate level of clearing, I'll often switch the patient from, for instance, an aggressive hydroquinone-based combination regimen to something less aggressive, often a nonhydroquinone product, that will then serve as their maintenance treatment. This eventually can be tapered to an application 2 to 3 times a week. I find that if we discontinue all therapy, there is a high likelihood that the patient is going to relapse.

**Dermatology Times:** *When you are starting a patient with melasma on topical therapy or a combination of topical agents, what are you telling them they can expect within the course of 2 weeks, 4 weeks, and 2 months?*

**Dr. Grimes:** According to published studies, especially those utilizing triple combination therapy that includes fluocinolone acetonide 0.01%, hydroquinone 4%, and tretinoin 0.05%, patients will typically see clearing within 4 to 8 weeks.<sup>1,2</sup> I was involved in a 6-month trial of that triple combination, branded as Tri-Luma, and we saw patients improving significantly by the 12-week mark, although we did need to put them on a maintenance regimen between weeks 12 and 24 to maintain their level of initial clearance.<sup>3</sup>

If you look at other similarly designed studies around the globe using triple combination therapy, some form of maintenance treatment is typically necessary. In addition, studies show that you can see significant improvement in many patients as early as 4 weeks after initiating triple combination treatment.<sup>1,2,4</sup>

During my initial consultation of patients with melasma, even though I think I can optimize therapy right from the beginning, I don't tell them that they will be totally clear within 4 weeks or even 50% clear by that time. I do,



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however, like to be optimistic, so I tell patients that we should see some evidence of clearing at their 4-week follow-up examination as well as photographically. All agents don't necessarily work at the same speed in all patients, but that's my rule of thumb.

**Dermatology Times:** *Is cost ever an issue for patients with melasma being prescribed topical therapy? If so, how do you manage to help overcome that burden with your patients?*

**Dr. Grimes:** My patient population is perhaps a bit different than the average dermatologist's, in that many of my patients have been through the system a lot before they get to me. In some ways, I run a tertiary care faculty. Many, and perhaps most, of my patients will have seen multiple dermatologists before they end up seeing me at the Vitiligo and Pigmentation Institute.

Having framed it that way, is cost an issue for my patients? Certainly, it's something that I am respectful of, and I think it's something the entire medical community needs to be respectful of in all of our patients, especially when you are dealing with a chronic condition.

My overall experience is that if you can offer patients with melasma a regimen that is effective and relieves their frustration in having this chronic condition, they are willing to pay out of pocket to optimize their treatment outcomes. Now, they aren't going to pay \$1,000 a month for one product or even \$500 a month. But the cost of the topical agents we use to treat melasma and treat it successfully has not been a significant hurdle in my experience.

**Dermatology Times:** *When, if ever, do you consider using higher-strength hydroquinone, such as 8% hydroquinone, as an option in your patients with melasma?*

**Dr. Grimes:** It's not uncommon for me to use higher-strength hydroquinone compounded at my practice, but that is in part because of my patient population. Again, these are often patients who have been around the block. They have seen multiple dermatologists and tried a variety of therapies. Many will have tried 4% hydroquinone, 5% hydroquinone, 6% hydroquinone, and nothing is working. They have tried nonhydroquinone formulations, and nothing is working.

For those patients who have moderate-to-severe melasma, there is a place for these higher concentrations of hydroquinone. I have seen many patients benefit from this higher concentration, and I have not seen any long-term complications beyond treatable skin irritations. I have a number of patients who I start on higher-dose hydroquinone in combination with other topicals. Perhaps they don't see a significant response, but instead of pulling back on the strength of the hydroquinone, I tend to vary the combination of other agents in use and that will often trigger a better response.

**Dermatology Times:** *Are there any unique safety issues associated with higher-dose hydroquinone?*

**Dr. Grimes:** I get the sense in talking to some of my colleagues that there is a general fear of ochronosis associated with higher-strength hydroquinone. However, if you look at cases of ochronosis in Africa, those formulations of hydroquinone were mixed with so many other products that it is hard to tease out the actual cause of ochronosis. Additionally, in almost every reported case, the patient did not use sunscreen, which again could be a contributing factor.<sup>5-7</sup> In the United States, ochronosis is typically associated with low-dose, over-the-counter hydroquinone 2%.<sup>7,8</sup> So based on all that information, I

think the fear of ochronosis with higher-strength hydroquinone has been overblown.

**Dermatology Times:** *Why is compounding topical medications potentially a good idea for the general dermatology community?*

**Dr. Grimes:** Dermatology is such a complex specialty when it comes to treatment. There are some segments within our specialty who believe in compounding and some that don't. I am certainly a proponent of it. It gives us a broader spectrum of medications to offer our patients, especially our more complicated patients such as those with moderate-to-severe melasma. If the conditions we were asked to treat were more straightforward, perhaps compounding would not be necessary, but we have many complicated patients with complex needs. That's why I'm a proponent of compounding medication for the right patients.

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