

Support:

- State policy on drug availability which mirrors FDA findings
- Evidence-based decisions on the availability of drugs
- The safe use of hydroquinone products and formulations
- Continued studies to assess possibilities of carcinogenic risks and exogenous ochronosis from topical use

Oppose:

- Additional restrictions placed on hydroquinone that are not supported by clinical evidence
- The use of hydroquinone products which have not been manufactured under safe, regulated conditions
- Illegal import and use of unapproved hydroquinone products
- Use of prescription-grade hydroquinone without a physician's oversight

Hydroquinone is a drug which has been used for many years to lessen the appearance of sun-related skin discolorations and other undesired hyperpigmentation disorders. Hydroquinone predates the formation of the Food and Drug Administration (FDA)'s Drug Efficacy Study Implementation program, and thus some formulations currently on the market have never been studied for safety and efficacy. However, without proactive action by the FDA to the contrary triggered by safety concerns, products containing hydroquinone which contain the same basic features as those which were on the market prior to November 13, 1984 may remain on the market.

Hydroquinone is available at lower concentrations for over-the-counter (OTC) use and at higher concentrations for prescription use. The maximum concentration allowed in OTC preparations is currently 2 percent hydroquinone whereas 4 percent hydroquinone formulations, for example, are only available by prescription. There are also compounded increased concentrations available by prescriptions at specialty pharmacies. Newer proprietary preparations of hydroquinone-containing drugs have undergone FDA evaluation through the investigational new drug pathway and have proven safe and effective.

In 2006, the FDA proposed a change to over-the-counter (1.5%-2% concentrations) hydroquinone's previous status as generally recognized as safe and effective (GRASE) and recommended that the drug be studied further by the National Toxicology Program (NTP)ⁱ. The FDA's primary concerns were that hydroquinone may cause cancer and that it has been linked to ochronosis (skin darkening and disfiguration) in humans.ⁱⁱ In the interim, the FDA recommended that hydroquinone remain available for OTC use.

The FDA's 2006 actions were based on studies in which hydroquinone was taken orally. At that time, the FDA stated that hydroquinone cannot be ruled out as a potential carcinogen. This conclusion was centered on a two-year study of the oral administration of hydroquinone on rats.ⁱⁱⁱ

There have been no reported incidences of cancer from topical application of hydroquinone in humans. Though health concerns are related to oral ingestion of hydroquinone, concerns over topical toxicity and carcinogenesis have been raised but not validated when the product is used correctly as directed under the supervision of an appropriately trained, licensed physician.^{iv}

There has been an increase in privately dispensed or physician-based lies of various hydroquinone formulations and these products have not undergone clinical study or FDA evaluation. It is this genre of hydroquinone products that have raised safety and health concerns. Such compounded medications are not regulated in their formulation or preparation and therefore may pose potential safety concerns. In these settings ASDSA promotes the proper acquisition and use of safely prepared and dispensed formulations. Limiting the availability of properly prepared hydroquinone formulations may lead to an increase of other preparations containing non-hydroquinone ingredients that may pose risks to patients.

The causal effect of products containing hydroquinone and skin darkening and disfiguration (cutaneous ochronosis) is unclear. It is yet to be established whether cutaneous onchronosis is a direct result of the effect of hydroquinone alone, or other substances present in formulations, or higher concentrations of hydroquinone present in many countries around the world.^v

One of the primary concerns with relation to the topical application of hydroquinone is depigmentation. However, this is not widespread, nor does hydroquinone induce vitiligo. Patients may have vitiligo, but additionally have hypermelanosis, post-inflammatory hyper pigmentation and/or melasma. In these cases, even though the patient has vitiligo, which is an autoimmune mediated disease that destroys the melanocytes, hydroquinone is still prescribed for treating hyperpigmentation.

Serious and fatal side effects have not been reported with hydroquinone with higher concentrations, such as 4 percent. Rather, such side effects have either resulted from feeding rats oral doses of hydroquinone and/or such side effects are purely speculative rather than a result of any reported adverse events. Hydroquinone has been used for decades topically in the 4% or other higher and lower concentrations in the United States without such serious and fatal side effects.

*Approved by the ASDSA Board of Directors: July 2015
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ⁱ United States Food and Drug Administration (2006). Skin Bleaching Drug Products for Over-the-Counter Product Use; Proposed Rule (Report). 1978N-0065

ⁱⁱ United States Food and Drug Administration (2010), Hydroquinone Studies Under the National Toxicology Program (NTP). Retrieved from: <http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ucm203112.htm>

ⁱⁱⁱ Levitt J. The safety of hydroquinone: A dermatologist's response to the 2006 Federal Register. J Am Acad Dermatol. 2007;57:854–72.

^{iv} Lawrence N, Bligard CA, Reed R, et al. Exogenous ochronosis in the United States. J Am Acad Dermatol 1988; 18: 1207–1211.

^v Levitt, Jacob. The safety of hydroquinone: A dermatologist's response to the 2006 Federal Register. J Am Acad Dermatol. 2007 Nov;57(5):854-72.