

**HYDROQUINONE 4% - hydroquinone cream**  
**Nivagen Pharmaceuticals, Inc.**

*Disclaimer: This drug has not been found by FDA to be safe and effective, and this labeling has not been approved by FDA. For further information about unapproved drugs, click here.*

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**HYDROQUINONE 4% CREAM**

**Skin Bleaching Cream**

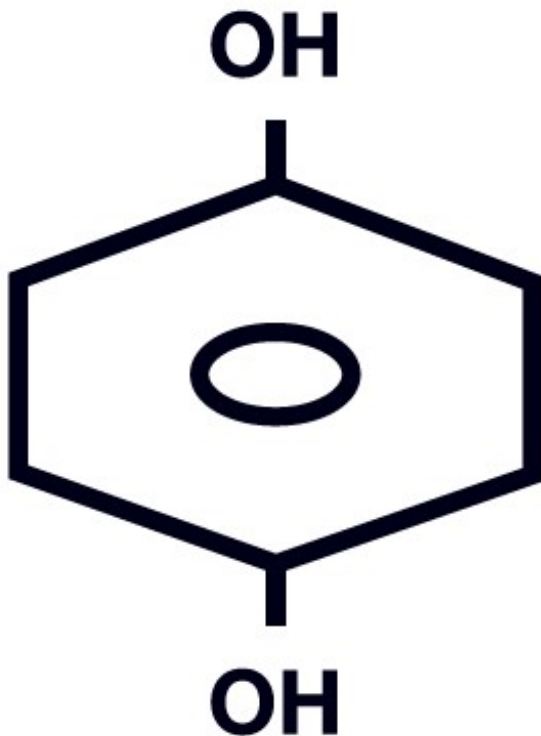
**Rx Only**

**FOR EXTERNAL USE ONLY**

**NOT FOR OPHTHALMIC USE**

**DESCRIPTION**

Each gram of Hydroquinone USP, 4% Skin Bleaching Cream contains 40 mg of hydroquinone USP, in a vanishing cream base of aqua (water), BHT, cetyl alcohol, disodium EDTA, glycerin, glycolic acid, methylparaben, propylparaben, saponins, sodium lauryl sulfate, sodium metabisulfite, stearyl alcohol, tetrahexyldecyl ascorbate, and tocopheryl acetate. Chemically, hydroquinone is  $C_6H_6O_2$  and has a molecular weight of 110.11. The chemical name is 1,4 dihydroxybenzene, and the structural formula of hydroquinone is:



## **CLINICAL PHARMACOLOGY**

Topical application of hydroquinone produces a reversible depigmentation of the skin by inhibition of the enzymatic oxidation of tyrosine to 3,4-dihydroxyphenylalanine (dopa) (Denton, C. et al., 1952)<sup>1</sup> and suppression of other melanocyte metabolic processes (Jimbow, K. et al., 1974)<sup>2</sup>. Exposure to sunlight or ultraviolet light will cause repigmentation of bleached areas (Parrish, J.A. et al., 1978)<sup>3</sup>.

## **INDICATIONS & USAGE**

Hydroquinone USP, 4% Skin Bleaching Cream is indicated for the gradual bleaching of hyperpigmented skin conditions such as chloasma, melasma, freckles, senile lentigines, and other unwanted areas of melanin hyperpigmentation.

## **CONTRAINDICATIONS**

Prior history of sensitivity or allergic reaction to hydroquinone or to any of the ingredients of the product. The safety of topical hydroquinone use during pregnancy or for children (12 years and under) has not been established.

## **WARNINGS**

Contains sodium metabisulfite, a sulfite that may cause allergic-type reactions including anaphylactic symptoms and life-threatening or less severe asthmatic episodes in certain susceptible people. The overall prevalence of sulfite sensitivity in the general population is unknown and probably low. Sulfite sensitivity is seen more frequently in asthmatic than

in non-asthmatic people. Since this product contains no sunscreen, an effective broad spectrum sun blocking agent should be used and unnecessary solar exposure avoided, or protective clothing should be worn to cover bleached skin in order to prevent repigmentation from occurring. Hydroquinone may produce exogenous ochronosis, a gradual blue-black darkening of the skin. If this condition occurs, discontinue treatment and consult your physician. The majority of patients developing this condition are Black, but it may also occur in Caucasians and Hispanics.

## **PRECAUTIONS**

(see WARNINGS)

## **GENERAL PRECAUTIONS**

Test for skin sensitivity before using by applying a small amount to an unbroken patch of skin; check within 24 hours. Minor redness is not a contraindication, but where there is itching or vesicle formation or excessive inflammatory response further treatment is not advised. Close patient supervision is recommended.

Hydroquinone is a skin bleaching agent which may produce unwanted cosmetic effects if not used as directed. The physician should be familiar with the contents of this insert before prescribing or dispensing this medication.

## **INFORMATION FOR PATIENTS**

Sunscreen use is an essential aspect of hydroquinone therapy because even minimal sunlight sustains melanocytic activity. To prevent repigmentation, during treatment and maintenance therapy, sun exposure on treated skin should be avoided by application of a broad spectrum sunscreen (SPF 15 or greater) or by use of protective clothing. Avoid contact with eyes and mucous membranes.

Keep this and all medications out of reach of children. In case of accidental ingestion, call a physician or a poison control center immediately.

## **DRUG INTERACTIONS**

Patients are cautioned on concomitant use of medications that are known to be photosensitizing.

## **CARCINOGENESIS & MUTAGENESIS & IMPAIRMENT OF FERTILITY**

Studies of hydroquinone in animals have demonstrated some evidence of carcinogenicity. The carcinogenic potential of hydroquinone in humans is unknown. Published studies have demonstrated that hydroquinone is a mutagen and a clastogen. Treatment with hydroquinone has resulted in positive findings for genetic toxicity in the Ames assay in bacterial strains sensitive to oxidizing mutagens, in *in vitro* studies in mammalian cells, and in the *in vivo* mouse micronucleus assay.

## **PREGNANCY**

**Teratogenic Effects: Pregnancy Category C -**

Animal reproduction studies have not been conducted with topical hydroquinone. It is also not known whether topical hydroquinone can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Topical hydroquinone should be given to a pregnant woman only if clearly needed.

## **NURSING MOTHERS**

It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when topical hydroquinone is administered to a nursing woman.

## **PEDIATRIC USE**

Safety and effectiveness for pediatric patients below the age of 12 years have not been established.

## **ADVERSE REACTIONS**

The following adverse reactions have been reported: dryness and fissuring of paranasal and infraorbital areas, erythema, and stinging. Occasional hypersensitivity (localized contact dermatitis) may develop. If this occurs, the medication should be discontinued and the physician notified immediately.

## **OVERDOSAGE**

There have been no systemic reactions reported from the use of topical hydroquinone. However, treatment should be limited to relatively small areas of the body at one time, since some patients experience a transient skin reddening and a mild burning sensation which does not preclude treatment.

## **DOSAGE & ADMINISTRATION**

Hydroquinone USP, 4% Skin Bleaching Cream should be applied to affected areas and rubbed in well twice daily, in the morning and before bedtime, or as directed by a physician. If no improvement is seen after 2 months of treatment, use of this product should be discontinued. There is no recommended dosage for pediatric patients under 12 years of age except under the advice and supervision of a physician.

## **HOW SUPPLIED**

Hydroquinone USP, 4% Skin Bleaching Cream is available as follows:  
1 oz (28.4 g) tube (NDC 75834-137-01)

## **STORAGE**

Hydroquinone USP, 4% Skin Bleaching Cream should be stored at controlled room temperature (20-25°C) (68-77°F). Darkening of this product is normal. This will not affect performance or safety.

All prescription substitutions and/or recommendations using this product shall be made subject to state and federal statutes as applicable. **Please NOTE: This is not an Orange Book product and has not been subjected to FDA therapeutic or other equivalency testing. No representation is made as to generic status or bioequivalency.** Each person recommending a prescription substitution using this product shall make such recommendation based on his/her professional knowledge and opinion, upon evaluating the active ingredients, inactive ingredients, excipients and chemical information provided herein.

## **REFERENCES**

1 DENTON C., LERNER A.B., FITZPATRICK T.B.

Inhibition of Melanin Formation by Chemical Agents

*Journal of Investigative Dermatology* 1952, 18:119-135.

2 JIMBOW K., OBATA H., PATHAK M., FITZPATRICK T.B.

Mechanism of Depigmentation by Hydroquinone

*Journal of Investigative Dermatology* 1974, 62:436-449.

3 PARRISH J.A., ANDERSON R.R., URBACH F., PITTS D.

*UVA, Biological Effects of Ultraviolet Radiation with Emphasis on Human Responses to Longwave Ultraviolet*

Plenum Press, New York and London, 1978, p. 151.

## **Manufactured for:**

**Nivagen Pharmaceuticals, Inc.**

**Sacramento, CA 95827 USA**

**Toll free number: 1-877-977-0687**

Rev. 02/2022

Hydroquinone USP, 4%

Skin Bleaching Cream

## **PACKAGE LABEL.PRINCIPAL DISPLAY PANEL**

**28.4 g Tube Carton**



NDC 75834-137-01

# Hydroquinone USP, 4%

## Skin Bleaching Cream

Net Wt. 1 oz (28.4 g)

Rx Only

**Contains:** Each gram of cream contains 40 mg of hydroquinone USP, in a vanishing cream base of aqua (water), BHT, cetyl alcohol, disodium EDTA, glycerin, glycolic acid, methylparaben, propylparaben, saponins, sodium lauryl sulfate, sodium metabisulfite, stearyl alcohol, tetrahexyldecyl ascorbate, and tocopheryl acetate.

**Usual Dosage:** Apply cream to the affected area and rub in well twice daily or as directed by physician. See package insert for complete product information.

**FOR EXTERNAL USE ONLY.**

**Keep out of reach of children.**

**Warnings:** Contains sodium metabisulfite, a sulfite that may cause allergic-type reactions including anaphylactic symptoms and life-threatening or less severe asthmatic episodes in certain susceptible people. The overall prevalence of sulfite sensitivity in the general population is unknown and probably low. Sulfite sensitivity is seen more frequently in asthmatic than in non-asthmatic people. Store at 20-25°C (68-77°F) [See USP; Controlled Room Temperature]

Manufactured for:  
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### HYDROQUINONE 4%

hydroquinone cream

#### Product Information

<b>Product Type</b>	HUMAN PRESCRIPTION DRUG	<b>Item Code (Source)</b>	NDC:75834-137
<b>Route of Administration</b>	TOPICAL		

#### Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
<b>Hydroquinone</b> (UNII: XV74C1N1AE) (Hydroquinone - UNII:XV74C1N1AE)	Hydroquinone	40 mg in 1 g

## Inactive Ingredients

Ingredient Name	Strength
<b>Water</b> (UNII: 059QF0KO0R)	
<b>Butylated Hydroxytoluene</b> (UNII: 1P9D0Z171K)	
<b>Cetyl Alcohol</b> (UNII: 936JST6JCN)	
<b>Glycerin</b> (UNII: PDC6A3C00X)	
<b>Glycolic Acid</b> (UNII: 0WT12SX38S)	
<b>Methylparaben</b> (UNII: A2I8C7HI9T)	
<b>Propylparaben</b> (UNII: Z8IX2SC1OH)	
<b>Sodium Lauryl Sulfate</b> (UNII: 368GB5141J)	
<b>Sodium Metabisulfite</b> (UNII: 4VON5FNS3C)	
<b>Stearyl Alcohol</b> (UNII: 2KR89I4H1Y)	
<b>Tetrahexyldecyl Ascorbate</b> (UNII: 9LBV3F07AZ)	
<b>.ALPHA.-TOCOPHEROL ACETATE, DL-</b> (UNII: WR1WPI7EW8)	
<b>EDETATE DISODIUM</b> (UNII: 7FLD91C86K)	

## Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:75834-137-01	1 in 1 CARTON	08/17/2022	
1		28.4 g in 1 TUBE; Type 0: Not a Combination Product		

## Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
UNAPPROVED DRUG OTHER		08/17/2022	

**Labeler** - Nivagen Pharmaceuticals, Inc. (052032418)

Revised: 2/2024

Nivagen Pharmaceuticals, Inc.