Hydroquinone USP, 4%
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 hydroquinone USP, in a vanishing cream base of aqua (water), ascorbic acid, BHT, cetyl alcohol, disodium EDTA, glycerin, glycolic acid, methylparaben, propylparaben, saponins, sodium lauryl sulfate, sodium metabisulfite, stearyl alcohol and tocopheryl acetate. Chemically, hydroquinone is C₆H₄O₂ and has a molecular weight of 110.11. The chemical name is 1,4 dihydroxybenzene, and the structural formula of hydroquinone is:

\[
\begin{align*}
\text{C} & \text{H} \\
\text{OH} & \text{OH}
\end{align*}
\]

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)¹ and suppression of other melanocyte metabolic processes (Jimbow, K. et al., 1974)². Exposure to sunlight or ultraviolet light will cause repigmentation of bleached areas (Parrish, J.A. et al., 1978)³.

INDICATIONS AND 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
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 AND 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 (28.35 g) tube (NDC 72056-060-01)

STORAGE
Hydroquinone USP, 4% Skin Bleaching Cream should be stored at controlled room temperature (15-30°C) (59-86°F). Darkening of this product is normal.
This will not affect performance or safety.

REFERENCES
1 DENTON C., LERNER A.B., FITZPATRICK T.B.
Inhibition of Melanin Formation by Chemical Agents

2 JIMBOW K., OBATA H., PATHAK M., FITZPATRICK T.B.
Mechanism of Depigmentation by Hydroquinone

3 PARRISH J.A., ANDERSON R.R., URBACH F., PITTS D.
Hydroquinone USP, 4% Skin Bleaching Cream

PRINCIPAL DISPLAY PANEL - 28.35 g Tube Carton

SYNTENZA

NDC 72056-060-01
Hydroquinone USP, 4% Skin Bleaching Cream
Net Wt. 1 oz. (28.35 g)
Rx Only

Warnings: Contains sodium metabsulphite, a sulfite that may cause allergic-type reactions including asthma in certain susceptible people. The overall prevalence of sulfite sensitivity in the general population is unknown but probably low. Sulfite sensitivity is seen more frequently in asthmatics than in non-asthmatic people.

To Open: Remove cap and peel off seal away from product. Can be stored at 20-25°C (68-77°F) [See USP, Controlled Room Temperature].

Hydroquinone USP, 4% Skin Bleaching Cream

Manufactured for:
Syntenza Pharmaceuticals LLC
Edina, MN 55436, USA

Rx Only
# Product Information

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## Active Ingredient/Active Moiety

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## Product Characteristics

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## Marketing Information

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**Labeler** - Syntenza Pharmaceuticals LLC (080999747)