HYDROQUINONE TIME RELEASE- hydroquinone cream
TWi 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.

Hydroquinone USP, 4% Time Release Cream

Skin Lightening Moisturizing Cream

Rx Only

FOR EXTERNAL USE ONLY

NOT FOR OPHTHALMIC USE

DESCRIPTION

Each gram of Hydroquinone USP, 4% Time Release Cream contains 40 mg hydroquinone USP and retinyl palmitate (vitamin A) incorporated into microspheres composed of acrylates/C10-30 alkyl acrylate crosspolymer. This polymeric system provides gradual release of active ingredient into the skin. Other ingredients include ascorbic acid (vitamin C), ascorbyl palmitate, ascorbyl tetraisopalmitate, benzyl alcohol, bisabolol, butylated hydroxytoluene, cetyl alcohol, cyclopentasiloxane, edetate disodium, ethylhexyl palmitate, glycerin, glyceryl monostearate, light mineral oil, phenoxyethanol, poloxamer 188, polyoxyl 40 stearate, propyl gallate, purified water, *Simmondsia chinensis* (Jojoba) seed oil, sodium metabisulfite, sorbitan tristearate, tocopheryl acetate (vitamin E), tricontanyl PVP, and trolamine. 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)[1] and suppression of other melanocyte metabolic processes (Jimbow, K. et al., 1974)[2]. Exposure to sunlight or ultraviolet light will cause repigmentation of the bleached areas (Parrish, J.A. et al., 1978)[3].

INDICATIONS AND USAGE

Hydroquinone USP, 4% Time Release Cream is indicated for the gradual treatment of ultraviolet induced dyschromia and discoloration (such as chloasma, melasma, freckles, and senile lentigines) resulting from the use of oral contraceptives, pregnancy, hormone replacement therapy, or skin trauma.

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 on 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 in 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% Time Release 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. Promptly tighten cap after each use. 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% Time Release Cream is available as follows:

30 g tube (NDC 24979-**144**-29)

Store at 20-25°C (68-77°F) [see USP Controlled Room Temperature].

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.A., 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:

TWi Pharmaceuticals USA, Inc.

Paramus, NJ 07652

Manufactured by:

Perrigo, Bronx, NY 10457

Rev 04-17

: 5H700 84 J1

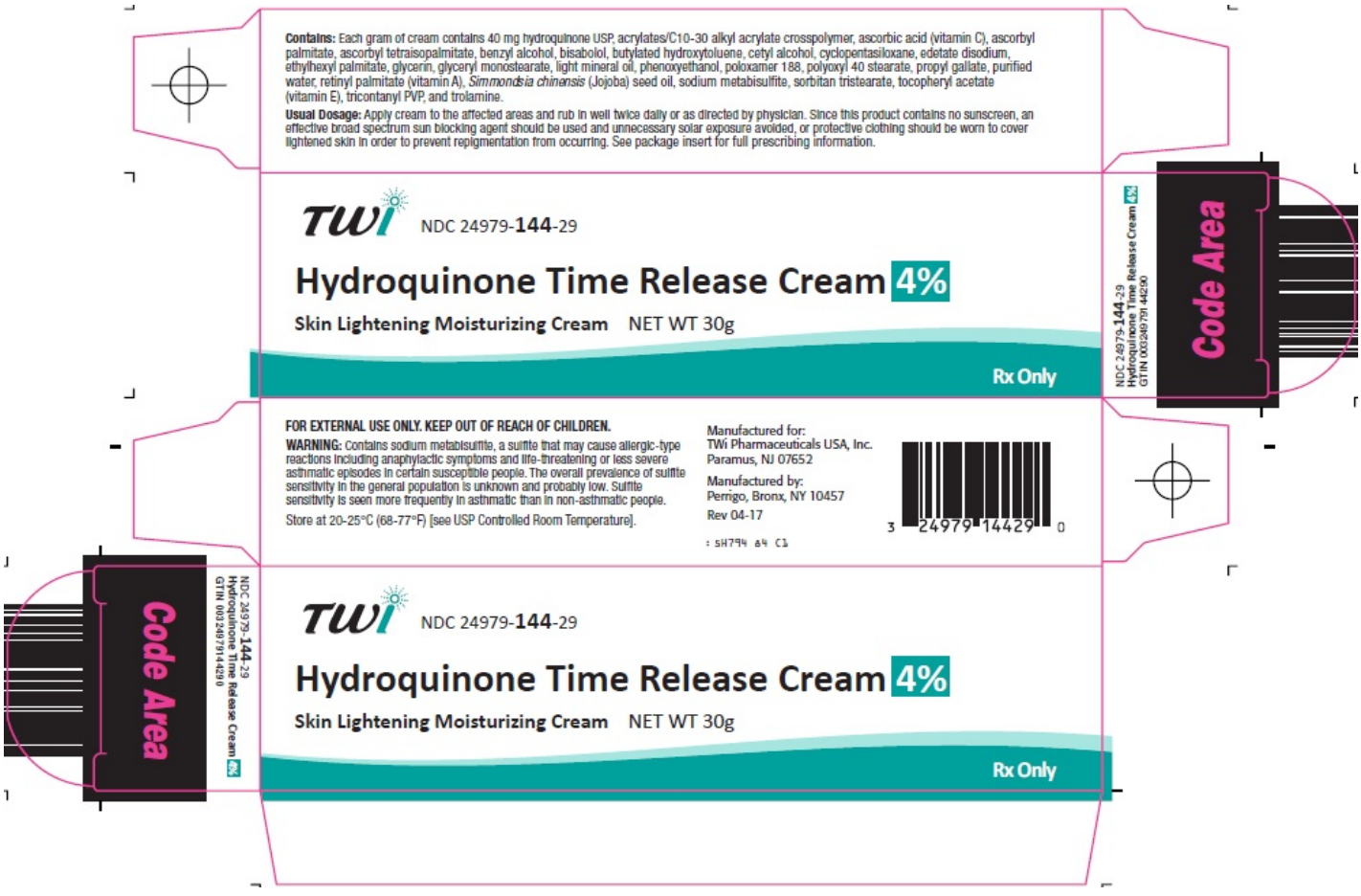
PACKAGE/LABEL PRINCIPAL DISPLAY PANEL

Rx Only

Hydroquinone Time Release Cream 4%

Skin Lightening Moisturizing Cream

NET WT 30 g



HYDROQUINONE TIME RELEASE
hydroquinone cream

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:24979-144
Route of Administration	TOPICAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
HYDROQUINONE (UNII: XV74C1N1AE) (HYDROQUINONE - UNII:XV74C1N1AE)	HYDROQUINONE	40 mg in 1 g

Inactive Ingredients

Ingredient Name	Strength
VITAMIN A PALMITATE (UNII: 1D1K0N0VVC)	
ASCORBIC ACID (UNII: PQ6CK8PD0R)	
ASCORBYL PALMITATE (UNII: QN83US2B0N)	
ASCORBYL TETRAISOPALMITATE (UNII: 47143LT58A)	
BENZYL ALCOHOL (UNII: LKG8494WBH)	
LEVOMENOL (UNII: 24WE03BX2T)	
BUTYLATED HYDROXYTOLUENE (UNII: 1P9D0Z171K)	
CETYL ALCOHOL (UNII: 936JST6JCN)	
CYCLOMETHICONE 5 (UNII: 0THT5PCI0R)	
EDETATE DISODIUM (UNII: 7FLD91C86K)	
ETHYLHEXYL PALMITATE (UNII: 2865993309)	
GLYCERIN (UNII: PDC6A3C0OX)	
GLYCERYL MONOSTEARATE (UNII: 230OU9XXE4)	
LIGHT MINERAL OIL (UNII: N6K5787QVP)	
PHENOXYETHANOL (UNII: HIE492ZZ3T)	
POLOXAMER 188 (UNII: LQA7B6G8JG)	
POLYOXYL 40 STEARATE (UNII: 13A4J4NH9I)	
PROPYL GALLATE (UNII: 8D4SNN7V92)	
WATER (UNII: 059QF0KO0R)	
SODIUM METABISULFITE (UNII: 4VON5FNS3C)	
SORBITAN TRISTEARATE (UNII: 6LUM696811)	
.ALPHA.-TOCOPHEROL ACETATE (UNII: 9E8X80D2L0)	
TRICONTANYL POVIDONE (UNII: N0SS3Q238D)	
TROLAMINE (UNII: 9O3K93S3TK)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:24979-144-29	1 in 1 CARTON	06/16/2017	
1		30 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		06/16/2017	

Labeler - TWi Pharmaceuticals, Inc. (658402052)

Registrant - TWi Pharmaceuticals, Inc. (658402052)

Establishment

Name	Address	ID/FEI	Business Operations
Perrigo New York Inc		078846912	manufacture(24979-144) , analysis(24979-144) , pack(24979-144)

Revised: 6/2017 TWi Pharmaceuticals, Inc.