

RHOFADE- oxymetazoline hydrochloride cream
Aclaris Therapeutics, Inc.

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use RHOFADE[®] topical cream safely and effectively. See full prescribing information for RHOFADE[®] topical cream.

RHOFADE[®] (oxymetazoline hydrochloride) cream, 1%, for topical use

Initial U.S. Approval: 1964

----- **INDICATIONS AND USAGE** -----

Rhofade cream is an alpha_{1A} adrenoceptor agonist indicated for the topical treatment of persistent facial erythema associated with rosacea in adults. (1)

----- **DOSAGE AND ADMINISTRATION** -----

- Not for oral, ophthalmic, or intravaginal use. (2)
- Prime pump bottle before initial use and discard product from first three pumps. (2)
- Apply a pea-sized amount once daily in a thin layer to cover the entire face (forehead, nose, each cheek, and chin) avoiding the eyes and lips. (2)
- Wash hands after application. (2)

----- **DOSAGE FORMS AND STRENGTHS** -----

Cream, 1%. Each gram of cream contains 10 mg (1%) oxymetazoline hydrochloride, equivalent to 8.8 mg (0.88%) of oxymetazoline free base. (3)

----- **CONTRAINDICATIONS** -----

- None. (4)

----- **WARNINGS AND PRECAUTIONS** -----

- Alpha-adrenergic agonists as a class may impact blood pressure. Advise patients with cardiovascular disease, orthostatic hypotension, and/or uncontrolled hypertension or hypotension to seek medical care if their condition worsens. (5.1)
- Use with caution in patients with cerebral or coronary insufficiency, Raynaud's phenomenon, thromboangiitis obliterans, scleroderma, or Sjögren's syndrome and advise patients to seek medical care if signs and symptoms of potentiation of vascular insufficiency develop. (5.2)
- Advise patients to seek immediate medical care if signs and symptoms of acute narrow-angle glaucoma develop. (5.3)

----- **ADVERSE REACTIONS** -----

Most common adverse reactions (incidence ≥ 1%) are application site dermatitis, worsening inflammatory lesions of rosacea, application site pruritis, application site erythema, and application site pain. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Aclaris Therapeutics, Inc. at 1-833-225-2747 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 11/2018

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

RHOFADE[®] (oxymetazoline hydrochloride) cream, 1% is indicated for the topical treatment of persistent facial erythema associated with rosacea in adults.

2 DOSAGE AND ADMINISTRATION

For topical use only. RHOFADE cream is not for oral, ophthalmic, or intravaginal use.

Prime the RHOFADE cream pump before using for the first time. To do so, with the pump in the upright position, repeatedly depress the actuator until cream is dispensed and then pump three times. Discard the cream from priming actuations. It is only necessary to prime the pump before the first dose.

RHOFADE cream tubes do not require priming.

Apply a pea-sized amount of RHOFADE cream, once daily in a thin layer to cover the entire face (forehead, nose, each cheek, and chin) avoiding the eyes and lips. Wash hands immediately after applying RHOFADE cream.

3 DOSAGE FORMS AND STRENGTHS

RHOFADE[®] (oxymetazoline hydrochloride) cream, 1% is a white to off-white cream. Each gram of cream contains 10 mg (1%) oxymetazoline hydrochloride, equivalent to 8.8 mg (0.88%) of oxymetazoline free base.

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

5.1 Potential Impacts on Cardiovascular Disease

Alpha-adrenergic agonists may impact blood pressure. RHOFADÉ cream should be used with caution in patients with severe or unstable or uncontrolled cardiovascular disease, orthostatic hypotension, and uncontrolled hypertension or hypotension. Advise patients with cardiovascular disease, orthostatic hypotension, and/or uncontrolled hypertension/hypotension to seek immediate medical care if their condition worsens.

5.2 Potentiation of Vascular Insufficiency

RHOFADÉ cream should be used with caution in patients with cerebral or coronary insufficiency, Raynaud's phenomenon, thromboangiitis obliterans, scleroderma, or Sjögren's syndrome. Advise patients to seek immediate medical care if signs and symptoms of potentiation of vascular insufficiency develop.

5.3 Risk of Angle Closure Glaucoma

RHOFADÉ cream may increase the risk of angle closure glaucoma in patients with narrow-angle glaucoma. Advise patients to seek immediate medical care if signs and symptoms of acute angle closure glaucoma develop.

6 ADVERSE REACTIONS

6.1 Clinical Studies Experience

Because clinical trials are conducted under varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

A total of 489 subjects with persistent facial erythema associated with rosacea were treated with RHOFADÉ cream once daily for 4 weeks in 3 controlled clinical trials. An additional 440 subjects with persistent facial erythema associated with rosacea were also treated with RHOFADÉ cream once daily for up to one year in a long-term (open-label) clinical trial. Adverse reactions that occurred in at least 1% of subjects treated with RHOFADÉ cream through 4 weeks of treatment are presented in Table 1 below.

Table 1: Adverse Reactions Reported by $\geq 1\%$ of Subjects through 4 Weeks of Treatment in Controlled Clinical Trials

Adverse Reaction	Pooled Controlled Clinical Trials	
	RHOFADÉ Cream (N = 489)	Vehicle Cream (N = 483)
Application site dermatitis	9 (2%)	0
Worsening inflammatory lesions of rosacea	7 (1%)	1 (<1%)
Application site pruritus	5 (1%)	4 (1%)
Application site erythema	5 (1%)	2 (<1%)
Application site pain	4 (1%)	1 (<1%)

In the long-term (open-label) clinical trial, the rates of adverse reactions over a one-year treatment period were as follows: worsening inflammatory lesions of rosacea (3%), application site dermatitis (3%), application site pruritis (2%), application site pain (2%), and application site erythema (2%). Subjects with persistent erythema along with inflammatory lesions were allowed to use additional therapy for the inflammatory lesions of rosacea.

7 DRUG INTERACTIONS

7.1 Anti-hypertensives/Cardiac Glycosides

Alpha-adrenergic agonists, as a class, may impact blood pressure. Caution in using drugs such as beta-blockers, anti-hypertensives and/or cardiac glycosides is advised.

Caution should also be exercised in patients receiving alpha₁ adrenergic receptor antagonists such as in the treatment of cardiovascular disease, benign prostatic hypertrophy, or Raynaud's disease.

7.2 Monoamine Oxidase Inhibitors

Caution is advised in patients taking MAO inhibitors which can affect the metabolism and uptake of circulating amines.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are no available data on RHOFADÉ cream use in pregnant women to inform a drug-associated risk for major birth defects and miscarriage. A literature article describing intranasal decongestant use in pregnant women identified a potential association between second-trimester exposure to oxymetazoline (with no decongestant exposure in the first trimester) and renal collecting system anomalies [see Data]. In animal reproduction studies, there were no adverse developmental effects observed after oral administration of oxymetazoline hydrochloride in pregnant rats and rabbits at systemic exposures up to 3 times and 73 times, respectively, the exposure associated with the maximum recommended human dose (MRHD) [see Data]. The estimated background risks of major birth defects and miscarriage for the indicated population are unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively.

Clinical Considerations

Fetal/Neonatal Adverse Reactions

Following repeated use of oxymetazoline hydrochloride solution nasal spray for the treatment of nasal congestion at a dose 5 times higher than recommended, one case of fetal distress was reported in a 41-week pregnant patient. The fetal distress resolved hours later, prior to the delivery of the healthy infant. The anticipated exposures for the case are 8- to 18-fold higher than plasma exposures after topical administration of RHOFADÉ cream.

Data

Human Data

No adequate and well-controlled trials of RHOFADÉ cream have been conducted in pregnant women. Across all clinical trials of RHOFADÉ cream, two pregnancies were reported. One pregnancy resulted in the delivery of a healthy child. One pregnancy resulted in a spontaneous abortion, which was considered to be unrelated to the trial medication. A literature article summarizing the results of

exploratory analyses of intranasal decongestant use during pregnancy identified a potential association between second-trimester exposure to oxymetazoline hydrochloride solution (with no decongestant exposure in the first trimester) and renal collecting system anomalies.

Animal Data

Effects on embryo-fetal development were evaluated in rats and rabbits following oral administration of oxymetazoline hydrochloride during the period of organogenesis. Oxymetazoline hydrochloride did not cause adverse effects to the fetus at oral doses up to 0.2 mg/kg/day in pregnant rats during the period of organogenesis (3 times the MRHD on an AUC comparison basis). Oxymetazoline hydrochloride did not cause adverse effects to the fetus at oral doses up to 1 mg/kg/day in pregnant rabbits during the period of organogenesis (73 times the MRHD on an AUC comparison basis). Maternal toxicity, such as decreased maternal body weight, was produced at the high dose of 1 mg/kg/day in pregnant rabbits and was associated with findings of delayed skeletal ossification.

In a rat perinatal and postnatal development study, oxymetazoline hydrochloride was orally administered to pregnant rats once daily from gestation day 6 through lactation day 20. Maternal toxicity was produced at the high dose of 0.2 mg/kg/day (3 times the MRHD on an AUC comparison basis) in pregnant rats and was associated with an increase in pup mortality and reduced pup body weights. Delayed sexual maturation was noted at 0.1 and 0.2 mg/kg/day (2 times the MRHD and 3 times the MRHD on an AUC comparison basis, respectively). Oxymetazoline hydrochloride did not have any adverse effects on fetal development at a dose of 0.05 mg/kg/day (one-half of the MRHD on an AUC comparison basis).

8.2 Lactation

No clinical data are available to assess the effects of oxymetazoline on the quantity or rate of breastmilk production, or to establish the level of oxymetazoline present in human breastmilk post-dose. Oxymetazoline was detected in the milk of lactating rats. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for RHOFADÉ cream and any potential adverse effects on the breastfed child from RHOFADÉ cream or from the underlying maternal condition.

8.4 Pediatric Use

Safety and effectiveness of RHOFADÉ cream have not been established in pediatric patients below the age of 18 years.

8.5 Geriatric Use

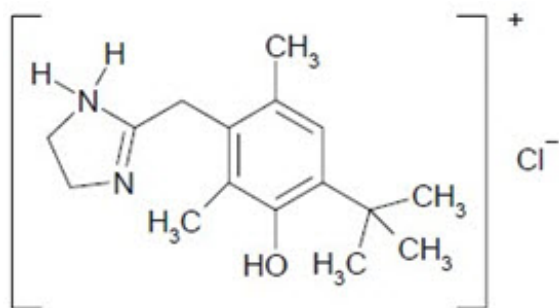
One hundred and ninety-three subjects aged 65 years and older received treatment with RHOFADÉ cream (n = 135) or vehicle (n = 58) in clinical trials. No overall differences in safety or effectiveness were observed between subjects \geq 65 years of age and younger subjects, based on available data. Clinical studies of RHOFADÉ cream did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects.

10 OVERDOSAGE

RHOFADÉ cream is not for oral use. If oral ingestion occurs, seek medical advice. Monitor patient closely and administer appropriate supportive measures as necessary. Accidental ingestion of topical solutions (nasal sprays) containing imidazoline derivatives (e.g., oxymetazoline) in children has resulted in serious adverse events requiring hospitalization, including nausea, vomiting, lethargy, tachycardia, decreased respiration, bradycardia, hypotension, hypertension, sedation, somnolence, mydriasis, stupor, hypothermia, drooling, and coma. Keep RHOFADÉ cream out of reach of children.

11 DESCRIPTION

RHOFADE[®] (oxymetazoline hydrochloride) cream, 1% contains oxymetazoline hydrochloride, an α_{1A} adrenoceptor agonist. RHOFADE is a white to off-white cream. It has a chemical name of 3-[(4,5-Dihydro-1H-imidazol-2-yl)methyl]-6-(1,1-dimethylethyl)-2,4-dimethyl-phenol hydrochloride and a molecular weight of 296.8. It is freely soluble in water and ethanol and has a partition coefficient of 0.1 in 1-octanol/water. The molecular formula of oxymetazoline HCl is $C_{16}H_{25}ClN_2O$ and its structural formula is:



Each gram of RHOFADE[®] (oxymetazoline hydrochloride) cream contains 10 mg (1%) oxymetazoline hydrochloride, equivalent to 8.8 mg (0.88%) of oxymetazoline free base. The cream contains the following inactive ingredients: sodium citrate dihydrate, citric acid anhydrous, disodium edetate dihydrate, butylated hydroxytoluene, anhydrous lanolin, medium chain triglycerides, diisopropyl adipate, oleyl alcohol, polyethylene glycol 300, PEG-6 stearate, glycol stearate, PEG-32 stearate, cetostearyl alcohol, cetareth-6, stearyl alcohol, cetareth-25, methylparaben, propylparaben, phenoxyethanol, and purified water.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Oxymetazoline is an α_{1A} adrenoceptor agonist. Oxymetazoline acts as a vasoconstrictor.

12.2 Pharmacodynamics

The pharmacodynamics of RHOFADE cream has not been studied.

12.3 Pharmacokinetics

Absorption

The pharmacokinetics of oxymetazoline was evaluated following topical administration of RHOFADE cream in a thin layer to cover the entire face in adult subjects with erythema associated with rosacea. The median weight of cream for each dose administration was 0.3 g. Plasma oxymetazoline concentrations were measurable in most of the subjects. Following the first dose application, the mean \pm standard deviation (SD) peak concentrations (C_{max}) and area under the concentration-time curves from time 0 to 24 hours (AUC_{0-24hr}) were 60.5 ± 53.9 pg/mL and 895 ± 798 pg*hr/mL, respectively. Following once daily applications for 28 days, the mean \pm SD C_{max} and AUC_{0-24hr} were 66.4 ± 67.1 pg/mL and 1050 ± 992 pg*hr/mL, respectively. Following twice daily applications (twice the recommended frequency of application) for 28 days, the mean \pm SD C_{max} and AUC_{0-24hr} were 68.8 ± 61.1 pg/mL and 1530 ± 922 pg*hr/mL, respectively.

Distribution

An *in vitro* study demonstrated that oxymetazoline is 56.7% to 57.5% bound to human plasma proteins.

Metabolism

In vitro studies using human liver microsomes showed that oxymetazoline was minimally metabolized, generating mono-oxygenated and dehydrogenated products of oxymetazoline. The percentage of parent drug oxymetazoline remaining was 95.9% after a 120-minute incubation with human liver microsomes.

Excretion

The excretion of oxymetazoline following administration of RHOFADÉ cream has not been characterized in humans.

Drug Interaction

In vitro studies using human liver microsomes demonstrated that oxymetazoline up to the tested concentration of 100 nM had no inhibition on the activities of the cytochrome P450 (CYP) isoenzymes 1A2, 2B6, 2C8, 2C9, 2C19, 2D6, and 3A4/5. Treatment of cultured human hepatocytes with up to 100 nM oxymetazoline did not induce CYP1A2, CYP2B6, or CYP3A4.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Oxymetazoline hydrochloride was not associated with an increased incidence of neoplastic or proliferative changes in transgenic mice given oral doses of 0.5, 1.0, or 2.5 mg/kg/day oxymetazoline hydrochloride for 6 months.

Oxymetazoline hydrochloride revealed no evidence of mutagenic or clastogenic potential based on the results of two *in vitro* genotoxicity tests (Ames assay and human lymphocyte chromosomal aberration assay) and one *in vivo* genotoxicity test (mouse micronucleus assay).

Effects on fertility and early embryonic development were evaluated in rats following oral administration of 0.05, 0.1, or 0.2 mg/kg/day oxymetazoline hydrochloride prior to and during mating and through early pregnancy. Decreased number of corpora lutea and increased post-implantation losses were noted at 0.2 mg/kg/day oxymetazoline hydrochloride (3 times the MRHD on an AUC comparison basis). However, no treatment related effects on fertility or mating parameters were noted at 0.2 mg/kg/day oxymetazoline hydrochloride (3 times the MRHD on an AUC comparison basis).

14 CLINICAL STUDIES

RHOFADÉ cream was evaluated for the treatment of persistent erythema associated with rosacea in two identical, randomized, double-blind, vehicle-controlled, parallel-group clinical trials. The trials enrolled 885 subjects aged 18 years and older. Overall, 90% of subjects were Caucasian and 79% were female. Subjects applied either RHOFADÉ cream or vehicle once daily for 29 days.

Disease severity was graded by the clinician using a 5-point clinician erythema assessment (CEA) scale and by the subject on a similar 5-point subject self-assessment (SSA) scale, on which subjects scored either "moderate" or "severe" on both scales.

CEA and SSA were measured over a 12-hour period at equally-spaced timepoints (hours 3, 6, 9, and 12) post dose on Days 1, 15, and 29. The primary efficacy endpoint was defined as the proportion of subjects with at least a 2-grade reduction in erythema (improvement) from baseline (pre-dose on Day 1) on both the CEA and SSA measured at hours 3, 6, 9, and 12 on Day 29. The results from both trials on the composite endpoint for Day 29 are presented in Table 2.

Table 2: Proportion of Subjects Achieving Composite Success* on Day 29

Time-point (Hour)	Trial 1		Trial 2	
	RHOFADÉ Cream (N=222)	Vehicle Cream (N=218)	RHOFADÉ Cream (N = 224)	Vehicle Cream (N=221)
3	12%	6%	14%	7%
6	16%	8%	13%	5%

9	18%	6%	16%	9%
12	15%	6%	12%	6%

* Composite success is defined as the proportion of subjects achieving at least a 2-grade improvement on both CEA and SSA.

16 HOW SUPPLIED/STORAGE AND HANDLING

RHOFADE[®] (oxymetazoline hydrochloride) cream, 1%, is a white to off-white cream. The product is available in a laminated tube and an airless pump polypropylene bottle in the following packaging configurations, each with a child-resistant closure:

NDC 71180-003-30	30 gram tube
NDC 71180-003-60	60 gram tube
NDC 71180-003-35	30 gram pump
NDC 71180-003-65	60 gram pump

Storage: Store at 20°C-25°C (68°F-77°F); excursions permitted to 15°C-30°C (59°F-86°F) [see USP Controlled Room Temperature].

17 PATIENT COUNSELING INFORMATION

Advise the patient and/or caregiver to read the FDA-approved patient labeling (*Patient Information and Instructions for Use*).

Important Administration Instructions

Advise patients of the following:

- RHOFADE cream is for topical use only.
- RHOFADE cream pumps require priming before initial use and discard product from the first three pumps.
- Do not apply RHOFADE cream to irritated skin or open wounds.
- Avoid contact with the eyes and lips.
- Wash hands immediately after application.
- Keep RHOFADE cream out of reach of children.

Manufactured for Aclaris Therapeutics, Inc., Wayne, PA 19087, U.S.A. by DPT Laboratories, Ltd, San Antonio, TX 78215

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Patented. U.S. Patent Numbers: U.S. 7,812,049; U.S. 8,420,688; U.S. 8,815,929; U.S. 8,883,838 and U.S. 9,974,773. Made in the U.S.A.

<p>PATIENT INFORMATION RHOFADE[®] (roe' fayd) (oxymetazoline hydrochloride) cream</p>

<p>Important: RHOFADE cream is for skin (topical) use on the face only. Do not use RHOFADE cream</p>

in your eyes, mouth, or vagina.

Keep RHOFADE cream out of the reach of children.

Get medical help right away if you, a child, or anyone else swallows RHOFADE cream.

What is RHOFADE cream?

RHOFADE cream is a prescription medicine used on the skin (topical) to treat facial redness due to rosacea that does not go away (persistent) in adults.

It is not known if RHOFADE cream is safe and effective in children under 18 years of age.

Before you use RHOFADE cream, tell your healthcare provider about all of your medical conditions, including if you:

- have heart, blood vessel, or blood pressure problems. Call your healthcare provider or get medical help if these conditions worsen.
- have problems with blood circulation or have had a stroke
- have Sjögren's Syndrome
- have scleroderma
- have Raynaud's phenomenon
- have thromboangiitis obliterans
- have narrow-angle glaucoma. Call your healthcare provider or get medical help if your glaucoma worsens.
- have irritated skin or open sores on the face
- are pregnant or plan to become pregnant. It is not known if RHOFADE cream will harm your unborn baby.
- are breastfeeding. It is not known if RHOFADE cream passes into your breast milk. Talk to your healthcare provider about the best way to feed your baby if you use RHOFADE cream.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, skin products, vitamins, and herbal supplements. Using RHOFADE cream with certain other medicines may affect each other and can cause serious side effects.

How should I use RHOFADE cream?

- See the detailed Instructions for Use that comes with your RHOFADE cream tube or pump for information about how to apply RHOFADE cream correctly.
- Use RHOFADE cream exactly as your healthcare provider tells you. Do not use more RHOFADE cream than prescribed.
- RHOFADE cream is for use on your skin only. **Do not** use RHOFADE cream in your eyes, mouth, or vagina. Avoid contact with your lips and eyes.
- **Do not** apply RHOFADE cream to irritated skin or open wounds.

What are the possible side effects of RHOFADE cream?

The most common side effects of RHOFADE cream include application site reactions of:

- skin reactions (dermatitis)
- worsening of rosacea pimples
- itching
- redness
- pain

These are not all the possible side effects of RHOFADE cream.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store RHOFADE cream?

- Store RHOFADE cream at room temperature between 68°F to 77°F (20°C to 25°C).

Keep RHOFADE cream and all medicines out of the reach of children.

General information about the safe and effective use of RHOFADE cream

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use RHOFADE cream for a condition for which it was not prescribed. Do not give RHOFADE cream to other people, even if they have the same symptoms that you have. It may harm them. You can ask your pharmacist or healthcare provider for information about RHOFADE cream that is written for health professionals.

What are the ingredients in RHOFADE cream?

Active ingredient: oxymetazoline hydrochloride

Inactive ingredients: sodium citrate dihydrate, citric acid anhydrous, disodium edetate dihydrate, butylated hydroxytoluene, anhydrous lanolin, medium chain triglycerides, diisopropyl adipate, oleyl alcohol, polyethylene glycol 300, PEG-6 stearate, glycol stearate, PEG-32 stearate, cetostearyl alcohol, cetareth-6, stearyl alcohol, cetareth-25, methylparaben, propylparaben, phenoxyethanol, and purified water

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This Patient Information has been approved by the U.S. Food and Drug Administration

Approved: 11/2018

INSTRUCTIONS FOR USE

RHOFADE® (roe' fayd)

(oxymetazoline hydrochloride) cream

Tube

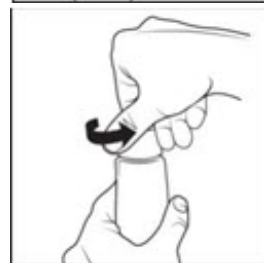
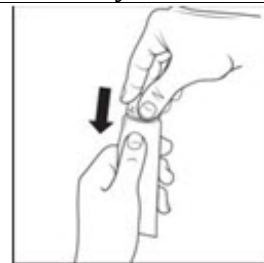
Important:

- RHOFADE cream is for skin (topical) use on the face only. Do not use RHOFADE cream in your eyes, mouth, or vagina.
- **Keep RHOFADE cream out of the reach of children.**
- **Get medical help right away if you, a child, or anyone else swallows RHOFADE cream.**

Read and follow the steps below so that you use your tube of RHOFADE cream correctly:

Step 1: Open the tube of RHOFADE cream by gently pressing down on the child-resistant cap and twisting it counterclockwise until the cap is removed. Do not squeeze the tube while opening or closing.

Note: When the cap is removed, the tube is not child-resistant.



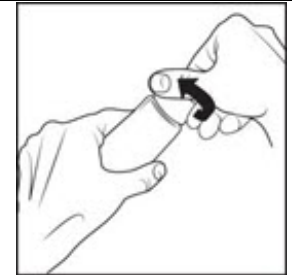
Step 2: To apply RHOFADÉ cream to your face, squeeze a pea-sized amount of RHOFADÉ cream from the tube onto your fingertip.



Step 3: Apply the pea-sized amount of RHOFADÉ cream to cover your entire face (forehead, nose, each cheek, and chin) 1 time each day. Spread the cream smoothly and evenly in a thin layer over your face.

- Avoid contact with your eyes and lips.
- **Do not** apply cream to irritated skin or open wounds.

Step 4: To close your RHOFADÉ cream tube, place the cap back on the tube. Press down on the child-resistant cap and twist clockwise until it stops. The tube is child-resistant again.



Step 5: Wash your hands right away after applying RHOFADÉ cream.

How do I store RHOFADÉ cream?

- Store RHOFADÉ cream at room temperature between 68°F to 77°F (20°C to 25°C). **Keep RHOFADÉ cream and all medicines out of the reach of children.**

This Instructions for Use has been approved by the U.S. Food and Drug Administration.

Manufactured for Aclaris Therapeutics, Inc., Wayne, PA 19087, U.S.A. by DPT Laboratories, Ltd, San Antonio, TX 78215

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Approved: 11/2018

INSTRUCTIONS FOR USE

RHOFADÉ® (roe' fayd)

(oxymetazoline hydrochloride) cream

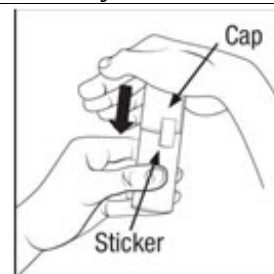
Pump

Important:

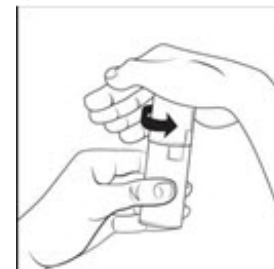
- RHOFADÉ cream is for skin (topical) use on the face only. Do not use RHOFADÉ cream in your eyes, mouth, or vagina.
- **Keep RHOFADÉ cream out of the reach of children.**
- **Get medical help right away if you, a child, or anyone else swallows RHOFADÉ cream.**

Read and follow the steps below so that you use your RHOFADÉ cream pump correctly:

Step 1: Open the RHOFADÉ cream pump by pushing down on the child resistant cap and twisting it counterclockwise until the cap is removed. The clear sticker will break when opening for the first time.



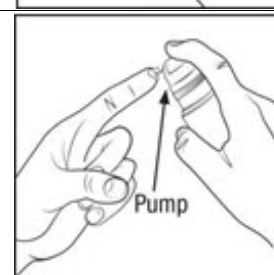
Note: When the cap is removed, the pump is not child-resistant.



Prime your RHOFADÉ cream pump before the first use only. Hold the pump upright and press down several times until the cream is dispensed onto a tissue. Pump 3 more times onto the tissue and throw away (discard) the tissue. Your pump is now ready to use.



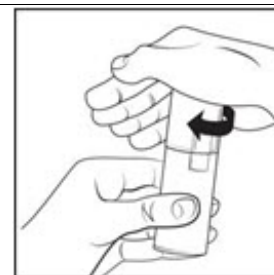
Step 2: To apply RHOFADÉ cream to your face, press down on the pump one time to dispense a pea-sized amount of RHOFADÉ cream onto your fingertip.



Step 3: Apply the pea-sized amount of RHOFADÉ cream to cover your entire face (forehead, nose, each cheek, and chin) 1 time each day. Spread the cream smoothly and evenly in a thin layer over your face.

- Avoid contact with your eyes and lips.
- **Do not** apply RHOFADÉ cream to irritated skin or open wounds.

Step 4: To close your RHOFADÉ cream pump, place the cap back on the pump. Push down on the child-resistant cap and turn the cap clockwise until it stops. The pump is child-resistant again.



Step 5: Wash your hands right away after applying RHOFADÉ cream.

How do I store RHOFADÉ cream?

- Store RHOFADÉ cream at room temperature between 68°F to 77°F (20°C to 25°C). **Keep RHOFADÉ cream and all medicines out of the reach of children.**

This Instructions for Use has been approved by the U.S. Food and Drug Administration.

Manufactured for Aclaris Therapeutics, Inc., Wayne, PA 19087, U.S.A. by DPT Laboratories, Ltd, San Antonio, TX 78215

RHOFADE and its design are registered trademarks of Aclaris Therapeutics, Inc.

Aclaris and its design are trademarks of Aclaris Therapeutics, Inc.

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Patented. U.S. Patent Numbers: U.S. 7,812,049; U.S. 8,420,688; U.S.

8,815,929; U.S. 8,883,838 and U.S. 9,974,773. Made in the U.S.A.

Approved: 11/2018

PRINCIPAL DISPLAY PANEL - 30 g Tube Carton

NDC 71180-003-30

Rhofade[®]

(oxymetazoline

hydrochloride) cream, 1%*

*Each gram of RHOFADE[®] cream contains 10 mg
of oxymetazoline hydrochloride, equivalent to
8.8 mg of oxymetazoline free base

For Topical Use Only

Keep Out of Reach of Children

aclaris[™]

THERAPEUTICS

Rx only

30 g

NDC 71180-003-30

Rhofade[®]
(oxymetazoline
hydrochloride) cream, 1%*

*Each gram of RHOFADÉ[®] cream contains 10 mg of oxymetazoline hydrochloride, equivalent to 8.8 mg of oxymetazoline free base

For Topical Use Only
Keep Out of Reach of Children

aclaris
THERAPEUTICS

Rx only
30 g

Not for oral, ophthalmic, or intravaginal use.

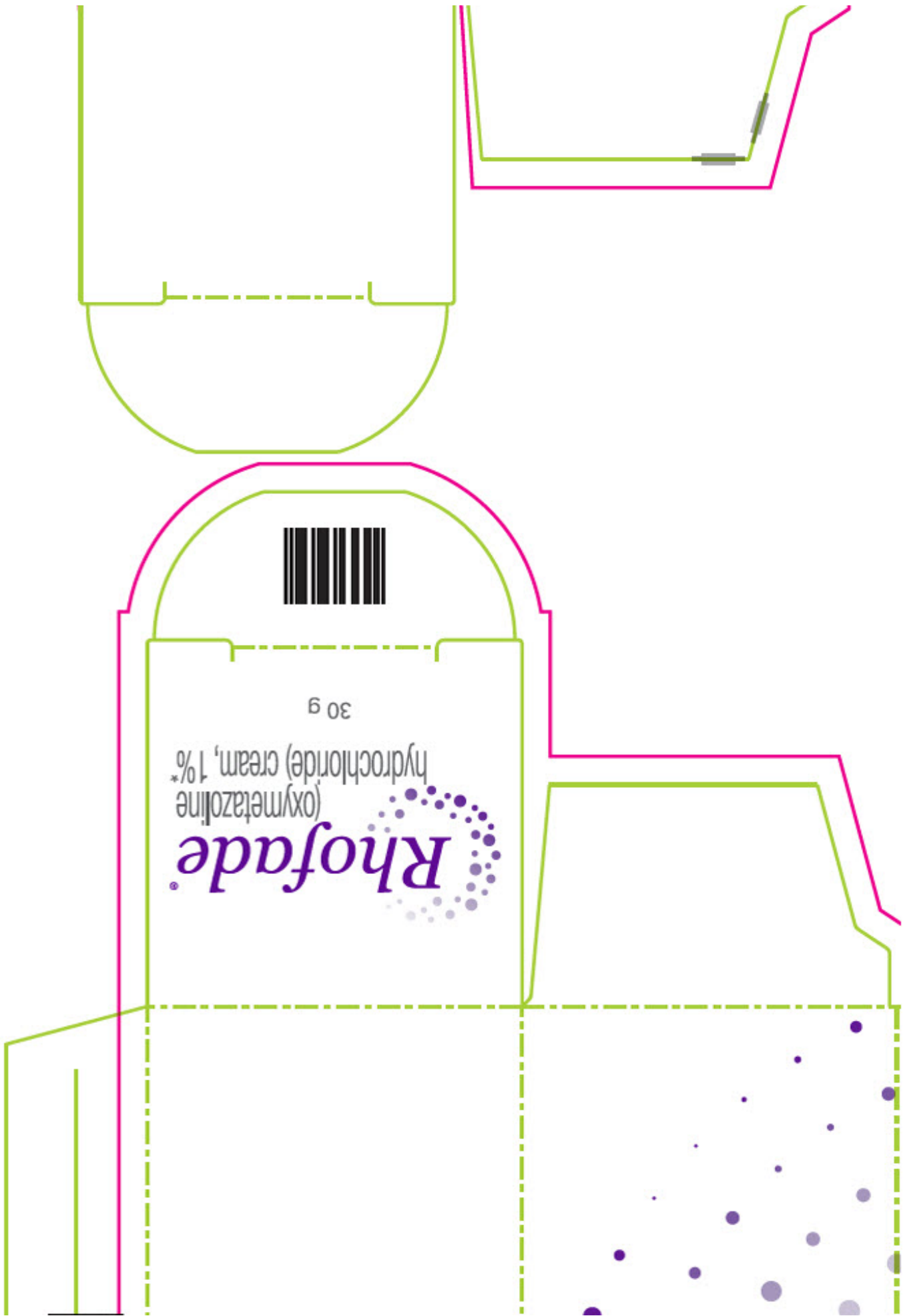
To Open Tube: Push cap in and turn counterclockwise, a quarter of a turn, and remove cap.

Dosage: Apply a pea-sized amount once daily in a thin layer to cover the entire face (forehead, nose, each cheek, and chin), avoiding the eyes and lips.

Storage: Store at 20°C-25°C (68°F-77°F), excursions permitted to 15°C-30°C (59°F-86°F) [see USP Controlled Room Temperature].

Each gram contains the **active** ingredient oxymetazoline hydrochloride 10 mg (1%) with the **inactive** ingredients sodium citrate dihydrate, citric acid anhydrous, disodium edetate dihydrate, butylated hydroxytoluene, anhydrous lanolin, medium chain triglycerides, diisopropyl adipate, oleyl alcohol, polyethylene glycol 300, PEG-6 stearate, glycol stearate, PEG-32 stearate, cetostearyl alcohol, cetareth-6, stearyl alcohol, cetareth-25, methylparaben, propylparaben, phenoxyethanol, and purified water.

Manufactured for Aclaris Therapeutics, Inc.
Wayne, PA 19087, U.S.A.
By DPT Laboratories, Ltd
San Antonio, TX 78215
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US Patents 7812049, 8420688, 8883838, 8815929, 9974773
Made in U.S.A.



Parke-Davis



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[\$CFPG_RT#]
[\$OutputMonthYear]

RHOFADE

oxymetazoline hydrochloride cream

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:71180-003
Route of Administration	TOPICAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
oxymetazoline Hydrochloride (UNII: K89MJ0S5VY) (oxymetazoline -	oxymetazoline	1g in 100g

UNII:8VLN5B44ZY)

Hydrochloride

18 III 100 g

Inactive Ingredients

Ingredient Name	Strength
TRISODIUM CITRATE DIHYDRATE (UNII: B22547B95K)	
ANHYDROUS CITRIC ACID (UNII: XF417D3PSL)	
EDETATE DISODIUM (UNII: 7FLD91C86K)	
butylated hydroxytoluene (UNII: 1P9D0Z171K)	
lanolin (UNII: 7EV65EAW6H)	
medium-chain triglycerides (UNII: C9H2L21V7U)	
diisopropyl adipate (UNII: P7E6YFV72X)	
oleyl alcohol (UNII: 172F2WN8DV)	
polyethylene glycol 300 (UNII: 5655G9Y8AQ)	
PEG-6 stearate (UNII: 8LQC57C6B0)	
glycol stearate (UNII: 0324G66D0E)	
cetostearyl alcohol (UNII: 2DMT128M1S)	
ceteareth-6 (UNII: 2RJS3559D3)	
stearyl alcohol (UNII: 2KR89I4H1Y)	
ceteareth-25 (UNII: 8FA93U5T67)	
methylparaben (UNII: A2I8C7HI9T)	
propylparaben (UNII: Z8IX2SC1OH)	
phenoxyethanol (UNII: HIE492ZZ3T)	
water (UNII: 059QF0K00R)	
PEG-32 stearate (UNII: 33GX5WQC0M)	

Product Characteristics

Color	WHITE (White to off-white)	Score	
Shape		Size	
Flavor		Imprint Code	
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:71180-003-30	1 in 1 CARTON	01/18/2017	
1		30 g in 1 TUBE; Type 0: Not a Combination Product		
2	NDC:71180-003-45	1 in 1 CARTON	01/18/2017	
2		45 g in 1 TUBE; Type 0: Not a Combination Product		
3	NDC:71180-003-60	1 in 1 CARTON	01/18/2017	
3		60 g in 1 TUBE; Type 0: Not a Combination Product		
4	NDC:71180-003-35	1 in 1 CARTON	01/18/2017	
4		30 g in 1 BOTTLE, PUMP; Type 0: Not a Combination Product		
5	NDC:71180-003-65	1 in 1 CARTON	01/18/2017	
5		60 g in 1 BOTTLE, PUMP; Type 0: Not a Combination		

	Product		
6	NDC:71180-003-15	3 g in 1 TUBE; Type 0: Not a Combination Product	01/18/2017
Marketing Information			
Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA208552	01/18/2017	

Labeler - Aclaris Therapeutics, Inc. (032365882)

Registrant - DPT Laboratories, Ltd. (832224526)

Establishment			
Name	Address	ID/FEI	Business Operations
DPT Laboratories, Ltd.		832224526	MANUFACTURE(71180-003)

Revised: 10/2019

Aclaris Therapeutics, Inc.