5.2 Potentiation of Vascular Insufficiency

Beta-blockers, calcium channel blockers, or nitrate therapy should be used 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 potential vascular insufficiency develop.

5.3 Risk of Angle Closure Glaucoma

Alpha-adrenergic agonists may impact blood pressure. Caution in using drugs such as cyclosporine, mitotane, metoprolol, nifedipine, oxymetazoline, or pseudoephedrine. Severe or uncontrolled hypertension or hypotension. Advise patients with cardiovascular disease, orthostatic hypotension, and/or uncontrolled hypertension or hypotension to seek medical care if their condition worsens. (5.1)

6 ADVERSE REACTIONS

6.1 General Reactions

Due to the nature of the disease, all patients with persistent facial erythema associated with rosacea were also treated with RHOFADE cream once daily in a thin layer applied to cover the entire face. (3%)

6.2 Adverse Reactions, by System Organ Class

Adverse reactions that occur with greater frequency are listed in Table 1. Adverse reactions that are at least twice as frequent in treated compared to placebo are shown in Table 2. Use of RHOFADE cream can result in serious adverse events requiring hospitalization, including nausea, vomiting, lethargy, tachycardia, decreased respiration, bradycardia, hypertension, hypotension, sedation, somnolence, mydriasis, myosis, myalgia, and headache. (5.3)

6.3 Laboratory Abnormalities

The laboratory results of tests were 10 mg (1%) oxymetazoline hydrochloride cream containing the following inactive ingredients: sodium citrate dihydrate, citric acid anhydrous, disodium edetate, sodium chloride, polyethylene glycol 400, purified water, and phenoxyethanol. (2)

6.4 Postmarketing Experience

Subjects with persistent erythema along with inflammatory lesions of rosacea, application site pruritis, application site erythema, and application site pain. (6.1)

7 DRUG INTERACTIONS

7.1 Anti-hypertensives/Cardiac Glycosides

Application site erythema

Application site pruritus

Worsening inflammatory

Adverse Reaction

Pooled Controlled Clinical Trials

Table 1: Adverse Reactions by System Organ Class

<table>
<thead>
<tr>
<th>System Organ Class</th>
<th>RHOFADE Cream</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Application site allergic</td>
<td>2 (1%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Application site dermatitis</td>
<td>9 (1%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Application site irritate</td>
<td>10 (2%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Application site skin</td>
<td>10 (2%)</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

In the long-term (open-label) clinical trials, the rates of adverse reactions over a one-year treatment period were similar to those following six weeks of treatment. (5.2)

8.2 Lactation

None. (4)

8.3 Pediatric Use

None. (4)

8.4 Genitourinary Use

None. (4)

9 CLINICAL STUDIES

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

<table>
<thead>
<tr>
<th>Time (Hour)</th>
<th>RHOFADE Cream (N=222)</th>
<th>Vehicle Cream (N=218)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>17%</td>
<td>13%</td>
</tr>
<tr>
<td>3</td>
<td>21%</td>
<td>17%</td>
</tr>
<tr>
<td>6</td>
<td>25%</td>
<td>18%</td>
</tr>
<tr>
<td>12</td>
<td>28%</td>
<td>19%</td>
</tr>
<tr>
<td>24</td>
<td>30%</td>
<td>22%</td>
</tr>
</tbody>
</table>

*Composite success is defined as the proportion of subjects achieving at least a 2-grade improvement on both CEA and SFA.
INSTRUCTIONS FOR USE
RHOFADE® (roxofadine) (oxymetazoline hydrochloride) cream

Important:
• RHOFADE cream is for skin (topical) use on the face only. Do not use RHOFADE cream in your eyes, mouth, or vagina.

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

INSTRUCTIONS FOR USE
RHOFADE® (roxofadine) (oxymetazoline hydrochloride) cream

Step 1: Open the RHOFADE 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.

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

Step 3: Apply the pea-sized amount of RHOFADE 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.

Step 4: To close your RHOFADE 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 RHOFADE cream.

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

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