1. Clinical Trial Experience

Because clinical trials are conducted under widely 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.

The overall safety of ORAVIG has been assessed in 454 adult patients, 174 subjects with head and neck cancer, and 10 healthy subjects.

2. Drug Interactions

Miconazole is a mild inhibitor of CYP2C9 and CYP3A4. Although the systemic absorption of miconazole following the application of ORAVIG buccal tablets was not sufficient to result in detectable plasma concentrations of miconazole, there is a potential for miconazole to interact with other drugs that are metabolized by CYP2C9 or CYP3A4.

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3. Mechanism of Action

Miconazole is active against Candida albicans, C. parapsilosis and C. tropicalis. Miconazole inhibits the enzyme cytochrome P450 1A2-demethylase which leads to inhibition of cholesterol synthesis.

Miconazole is a broad-spectrum antifungal agent. It is effective against a wide range of fungal pathogens, including Candida, Aspergillus, and Cryptococcus.

Miconazole nitrate was not genotoxic when tested in vitro in a bacterial reverse mutation test with a yeast reverse mutation test.

There are no adequate and well-controlled clinical trials of ORAVIG in pregnant women. ORAVIG should not be used during pregnancy unless the potential benefit to the mother justifies the potential risk to the fetus.

4. Pediatric Use

Safety and efficacy of ORAVIG in pediatric patients below the age of 16 years have not been established. The ability of pediatric patients to comply with the application instructions has not been evaluated. Use in younger children is not recommended because of potential risk of choking.

5. Genetic Use

Clinical studies of ORAVIG did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects.

ORAVIG is a buccal tablet containing 50 mg of miconazole. ORAVIG tablets are round and tan. ORAVIG tablets contain the following inactive ingredients: croscarmellose sodium, yellow iron oxide, and sodium saccharin.

6. Nursing Mothers

There are no adequate and well-controlled clinical trials of ORAVIG in nursing women. Caution should be exercised when ORAVIG is administered to a nursing woman.

7. Head and Neck Cancer Patients

Most of the infections were caused by C. albicans and C. parapsilosis. Infections with C. tropicalis were rare. C. krusei and C. glabrata were isolated from a limited number of patients.

8. Drug Interactions

Miconazole is a broad-spectrum antifungal agent. It is effective against a wide range of fungal pathogens, including Candida, Aspergillus, and Cryptococcus.

Miconazole also affects the synthesis of triglyceride and inhibits oxidase and cholesterol synthesis.

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**Clinical and Mycological Cure at the TOC Visit and Relapse at**

<table>
<thead>
<tr>
<th></th>
<th>ORAVIG 5 mg</th>
<th>Microzole gel</th>
<th>p = N/A (NS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cure (N = 176)</td>
<td>N/A (%)</td>
<td>N/A (%)</td>
<td>N/A (%)</td>
</tr>
<tr>
<td>Complete response†</td>
<td>176 (99.4%)</td>
<td>187 (99.2%)</td>
<td></td>
</tr>
<tr>
<td>Clinical relapse‡</td>
<td>48 (27.3%)</td>
<td>32 (20.5%)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>124 (72.7%)</td>
<td>155 (79.5%)</td>
<td></td>
</tr>
<tr>
<td>Missing</td>
<td>12 (7.0%)</td>
<td>7 (9.0%)</td>
<td></td>
</tr>
<tr>
<td>Microscopic cure</td>
<td>71 (40.5%)</td>
<td>60 (33.8%)</td>
<td></td>
</tr>
</tbody>
</table>

**Table 6: Clinical and Mycological Cure at Day 14, in Patients with Head and Neck Cancer who had Received Radiation Therapy**

ORAVIG is a vaginal cream used as an antifungal and antifungal treatment in adults aged 18 years and older with oropharyngeal candidiasis (OPC) who take antiretroviral therapy (ART) and who have persistent and recurrent OPC, or OPC that worsens in the absence of ART. ORAVIG should be used in patients who have already been treated with oral antifungal therapy for OPC and who are considered not to be candidates for further oral antifungal therapy. ORAVIG should be used in patients who have had at least 3 episodes of OPC in the past 6 months. ORAVIG should be used in patients who have had at least 3 episodes of OPC in the past 6 months.

**FDA-Approved Patient Labeling**

**Oravig (ORAVIG) – Buccal Tablets**

Buccal Tablets

Read the Patient Information that comes with ORAVIG before you start taking it and each time you get a refill. There may be new information. This leaflet does not take the place of talking with your doctor or about your medical condition or your treatment.

**What is ORAVIG?**

ORAVIG is a prescription antifungal medicine used in adults to treat fungal (yeast) infections of the mouth and throat. It is not known if ORAVIG is safe and effective in children under the age of 16 years. ORAVIG should not be used in children under the age of 16 years.

**Who should not use ORAVIG?**

Do not use ORAVIG if you:

- are allergic to micafungin (M-Zole, Micafungin, Vystingo)
- are allergic to milk protein concentrate
- are allergic to any of the ingredients in ORAVIG

**What are the possible side effects of ORAVIG?**

ORAVIG may cause serious side effects, including:

Allergic reactions. Tell your doctor or pharmacist if you have any of the symptoms below:

- skin rash
- swelling of your face, eyes, lips, tongue or throat
- trouble breathing or swelling

The most common side effects of ORAVIG include:

- diarrhea
- change in taste
- headache
- upper stomach (abdominal) pain
- nausea
- vomiting

Tell your doctor if you have any side effect that bothers you or that does not go away. These are not all the possible side effects of ORAVIG. For more information, ask your doctor or pharmacist. 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 ORAVIG?**

Store ORAVIG between 68 to 77°F (20 to 25°C). Keep ORAVIG dry.

Keep ORAVIG and all medicine out of the reach of children.

**General information about the safe and effective use of ORAVIG**

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information Leaflet. Do not use ORAVIG for a condition for which it was not prescribed. Do not give ORAVIG to other people, even if they have the same symptoms that you have. It may harm them. This Patient Information Leaflet summarizes the most important information about ORAVIG that is written for health professionals. You can also visit www.oravig.com for more information.

**What are the ingredients in ORAVIG?**

Active ingredient: miconazole

Inactive ingredients: hypromellose, milk protein concentrate, corn starch, tartaric monohydrate, sodium lauryl sulfate, magnesium stearate, and talc.

Manufactured By: Praelia Pharmaceuticals, Inc.

73614 Schorndorf

Manufactured For: Vestig Pharmaceuticals, Inc.

300 Aerial Center Parkway, 160

Morrisville, NC 27560

Distributed By: Pralika Pharmaceuticals, Inc.

100 Tauer View Court

Cary, NC 27513

Revised: 08/2012

US patent numbers: 6,916,495

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