Dear Healthcare Professional,

At MPR we strive to bring you important drug information in a concise and timely fashion. In keeping with this goal, we are pleased to bring you this PRESCRIBING ALERT introducing Oravig™ (miconazole) 50 mg buccal tablets for the treatment of oropharyngeal candidiasis (OPC) in adults, from Strativa Pharmaceuticals.1

OPC is an oral fungal infection that can be common in immunocompromised patients, including those with HIV/AIDS and cancer.2,3 OPC can be associated with lesions, inflammation, pain, and burning in the mouth.4 In clinical studies, Oravig provided relief to patients with mild-to-severe oral thrush signs and symptoms, including those with reduced salivary flow.1 Oravig is the first and only orally dissolving buccal tablet, for the local treatment of OPC, with convenient once-daily dosing.1 Once applied, Oravig sticks to the gum when moistened, allowing for an immediate and sustained release of miconazole at the site of infection, with minimal systemic absorption.1,5,* The most common adverse events reported with Oravig are diarrhea, headache, nausea, dysgeusia, upper abdominal pain, and vomiting.1

*Although the systemic absorption and exposure of miconazole after Oravig administration is minimal, caution should be used in patients with hepatic impairment and in patients taking drugs metabolized through CYP2C9 and CYP3A4, such as oral hypoglycemics, phenytoin, or ergot alkaloids as the potential interaction cannot be ruled out.

More information regarding the use of Oravig is available in the current edition of MPR or at www.oravig.com.

Sincerely,

Grace L. McBride
Editorial Director
MPR Custom Programs

Please see full Prescribing Information and Important Safety Information on next page for Oravig.

(continued on next page)
Indication

- Oravig is indicated for the local treatment of oropharyngeal candidiasis (OPC) in adults

Important Safety Information

- Oravig is contraindicated in patients with a known hypersensitivity to miconazole, milk protein concentrate, or any other component of the product. Allergic reactions, including anaphylactic reactions and hypersensitivity, have been reported with the administration of miconazole

- Discontinue Oravig immediately at the first sign of hypersensitivity. There is no information regarding cross-hypersensitivity between miconazole and other azole agents. Monitor patients with a history of hypersensitivity to azoles

- The potential for interaction with drugs metabolized through CYP2C9 and CYP3A4 cannot be ruled out. Concomitant administration of miconazole and warfarin has resulted in enhancement of anticoagulant effect. Closely monitor patients if Oravig is administered concomitantly with warfarin

- During clinical trials, the most common adverse events (≥2%) reported with Oravig were diarrhea (6.0%), headache (5.0%), nausea (4.6%), dysgeusia (2.9%), upper abdominal pain (2.5%), and vomiting (2.5%)

Please see full Prescribing Information for Oravig.

REFERENCES


Oravig is a trademark of Par Pharmaceutical Companies, Inc.
©2010 Strativa Pharmaceuticals, a division of Par Pharmaceutical, Inc.
**Company:** Strativa Pharmaceuticals, a division of Par Pharmaceutical, Inc.  
**Pharmacologic Class:** Azole antifungal  
**Active Ingredient:** Miconazole 50 mg; buccal tablet  
**Indication:** Local treatment of oropharyngeal candidiasis in adults.  
**Adults:** Do not crush, chew, or swallow. Alternate application site. Apply to upper gum region, hold in place for 30 seconds.  
≥16yrs: 50 mg once daily in the AM for 14 consecutive days.  
**Children:** <16yrs: not recommended.  
**Contraindications:** Allergy to milk protein concentrate or any other component of the product.  
**Precautions:** History of hypersensitivity to azoles; monitor and discontinue if allergic reactions develop. Hepatic Impairment.  

**Pregnancy (Cat. C). Nursing mothers.**  
**Interactions:** May potentiate anticoagulant effect with warfarin (monitor PT, INR, evidence of bleeding). Caution with drugs metabolized by CYP2C9 and CYP3A4 (eg, oral hypoglycemics, phenytoin, ergot alkaloids).  
**Adverse Reactions:** Diarrhea, headache, nausea, dysgeusia, upper abdominal pain, vomiting.  
**How Supplied:** Buccal tabs–14 count

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**First and only orally-dissolving buccal tablet for the local treatment of oral thrush**

- Oravig is indicated for the local treatment of oropharyngeal candidiasis (OPC) in adults

**INNOVATIVE, BUCCAL TABLET FORMULATION**

- Immediate and sustained release of miconazole
- Proven efficacy in a local treatment
- Minimal systemic absorption
- Flavorless, odorless, and convenient once-daily dosing

*Although the systemic absorption and exposure of miconazole after Oravig administration is minimal, caution should be used in patients with hepatic impairment and in patients taking drugs metabolized through CYP2C9 and CYP3A4, such as oral hypoglycemics, phenytoin, or ergot alkaloids as the potential interaction cannot be ruled out.

**Studied in almost 900 patients with oral thrush**

- Oravig was evaluated in clinical trials for treatment of oral thrush in HIV/AIDS patients
- Studied in head and neck cancer patients who underwent radiotherapy and had reduced salivary flow

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*Please see full Prescribing Information and Important Safety Information on last page.*

*(continued on next page)*
Proven once-daily efficacy against oral thrush in HIV/AIDS patients

Figure 1

RATE OF CLINICAL CURE IN HIV/AIDS PATIENTS

HIV/AIDS (SMILES)—Primary Efficacy Results in ITT Population

<table>
<thead>
<tr>
<th></th>
<th>Oravig (n=290)</th>
<th>Clotrimazole troches (n=287)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical Cure</td>
<td>61%</td>
<td>65%</td>
</tr>
</tbody>
</table>

SMILES—study design

A randomized, double-blind, double-dummy, multicenter study with a total of 577 HIV/AIDS patients treated with once-daily Oravig or clotrimazole troches 5 times per day for 14 days. Seventy-five percent of patients were not receiving highly active antiretroviral treatment.

Clinical cure

Complete resolution of oral thrush signs (lesions) and symptoms (burning and soreness) at the test of cure (TOC) visit (Day 17-22).

71% of HIV/AIDS patients were relapse-free

Figure 2

RELAPSE-FREE RATES IN HIV/AIDS PATIENTS

HIV/AIDS (SMILES)—Relapse-free Rates at Days 35-38 in ITT Population

<table>
<thead>
<tr>
<th></th>
<th>Oravig (n=176)</th>
<th>Clotrimazole troches (n=187)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>71%</td>
<td>71%</td>
</tr>
</tbody>
</table>

Post-treatment follow-up

After 14-day treatment, clinically cured patients were followed for 21 days to evaluate relapse of oral thrush.

In the patients who experienced relapse, the mean time to relapse was 15.3 days and 15.7 days for Oravig and clotrimazole troches, respectively.

Please see full Prescribing Information and Important Safety Information on last page.
Established efficacy in patients with head and neck cancer

- In a study of patients who underwent radiation therapy for head and neck cancer, Oravig was effective in reducing the extent of candidiasis lesions (Figure 3)
- Efficacy of Oravig was not compromised in the majority of patients with reduced salivary flow (>90% of patients had reduced salivary flow at baseline)\(^3\)

Figure 3

<table>
<thead>
<tr>
<th>Head and Neck Cancer Study—Primary Efficacy Results in ITT Population(^1)</th>
<th>Head and neck cancer—study design(^3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oravig (n=148)</td>
<td>An open-label, multicenter, randomized trial of 294 head and neck cancer patients with oral thrush who had previously undergone radiation therapy. Seventy-one percent of the infections were caused by (C.) (a)l(b)ic(a)ns.</td>
</tr>
<tr>
<td>Miconazole oral gel(^2) (n=146)</td>
<td><strong>Clinical success</strong> Complete response (disappearance of candidiasis lesions) or partial response (improvement by (\geq)2 points in lesion score compared to baseline). Lesion score ranged from 0 (none) to 3 (extensive/confluent).</td>
</tr>
</tbody>
</table>

ITT = Intent to treat.
\(^1\)Clinical success was the primary end point.
\(^2\)Not currently available in the United States.

\(\text{ITT} = \text{Intent to treat.}\)

80% of head and neck cancer patients were relapse free\(^1\)

Figure 4

<table>
<thead>
<tr>
<th>Head and Neck Cancer Study—Relapse-free Rates at Day 30 and Day 60 in ITT Population(^1,4)</th>
<th>Post-treatment follow-up(^1,4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oravig (n=74)</td>
<td>After 14-day treatment, patients who showed complete response (disappearance of lesions) were evaluated for relapse at Day 30 and 60. In the patients who experienced relapse, the mean time to relapse was 18.8 days and 20.6 days for Oravig and miconazole oral gel, respectively.</td>
</tr>
<tr>
<td>Miconazole oral gel (n=64)</td>
<td></td>
</tr>
</tbody>
</table>

ITT = Intent to treat.

\(\text{ITT} = \text{Intent to treat.}\)

Please see full Prescribing Information and Important Safety Information on last page.
Safe once-daily treatment option\(^1\)
- Adverse events reported in ≥2% of patients and healthy subjects (n=480) who received Oravig included diarrhea, headache, nausea, dysgeusia, upper abdominal pain, and vomiting\(^1\)

Oravig utilizes an innovative buccal tablet formulation\(^1,2\)

4 APPLICATION STEPS

**Step 1**—Oravig tablets are flat on one side and rounded on the other. The flat side of the tablet is marked with the letter “L.” Place the “L” side of the tablet on a clean and dry fingertip.\(^3\)

**Step 2**—Apply the rounded side of the tablet directly to the upper gum, “L” side facing the inside of the lip, into the small depression above either the left or right incisor tooth. Remind patients to alternate the side of their gum each day.\(^1\)

**Step 3**—Once in place under the lip, hold the tablet by applying a slight pressure with a finger placed outside the upper lip for 30 seconds.\(^1\)

**Step 4**—As the Oravig tablet absorbs moisture, it will slowly dissolve during the day.\(^1\)

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REFERENCES