

ORAVIG- miconazole tablet
Galt Pharmaceuticals, LLC

HIGHLIGHTS OF PRESCRIBING INFORMATION

HIGHLIGHTS OF PRESCRIBING INFORMATION These highlights do not include all the information needed to use ORAVIG safely and effectively. See full prescribing information for ORAVIG.

ORAVIG (miconazole) buccal tablets Initial U.S. Approval: January 1974

INDICATIONS AND USAGE

ORAVIG is an azole antifungal indicated for the local treatment of oropharyngeal candidiasis in adults. (1)

DOSAGE AND ADMINISTRATION

- Application of one ORAVIG 50 mg buccal tablet to the gum region once daily for 14 consecutive days (2.1).
- Instruct patients not to crush, chew, or swallow tablets (2.2).

DOSAGE FORMS AND STRENGTHS

50 mg buccal tablets (3)

CONTRAINDICATIONS

Known hypersensitivity to miconazole, milk protein concentrate, or any other component of the product. (4)

WARNINGS AND PRECAUTIONS

Hypersensitivity reactions: Anaphylactic reactions have been reported in patients receiving miconazole. Discontinue ORAVIG immediately at the first sign of hypersensitivity (5.1). (5)

ADVERSE REACTIONS

Most common adverse reactions ($\geq 2\%$) are: diarrhea, headache, nausea, dysgeusia, upper abdominal pain, and vomiting (6.1).

To report SUSPECTED ADVERSE REACTIONS, contact Galt Pharmaceuticals, LLC Marietta, GA 30067 at 1-833-757-0904 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch. (6)

DRUG INTERACTIONS

Warfarin: Miconazole may enhance anticoagulant effect. Monitor prothrombin time, INR, and watch for bleeding (7.1). (7)

USE IN SPECIFIC POPULATIONS

- Pregnancy: Based on animal data, may cause fetal harm (8.1).
- Pediatric Use: Safety and efficacy not established in patients less than 16 years of age (8.4).

See 12 for PATIENT COUNSELING INFORMATION and FDA-Approved Patient Labeling

(8)

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 6/2021

FULL PRESCRIBING INFORMATION: CONTENTS*

1 INDICATIONS & USAGE

2 DOSAGE & ADMINISTRATION

2.1 Basic Dosing Information

2.2 Administration Instructions

3 DOSAGE FORMS & STRENGTHS

4 CONTRAINDICATIONS

5 WARNINGS AND PRECAUTIONS

5.1 Hypersensitivity

6 ADVERSE REACTIONS

6.1 Clinical Trial Experience

7 DRUG INTERACTIONS

7.1 Warfarin

7.2 Drugs Metabolized Through CYP 2C9 and 3A4

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

8.2 Lactation

8.4 Pediatric Use

8.5 Geriatric Use

8.6 Hepatic Impairment

8.7 Renal Impairment

10 OVERDOSAGE

11 DESCRIPTION

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

12.3 Pharmacokinetics

12.4 Microbiology

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis & Mutagenesis & Impairment Of Fertility

13.2 Animal Pharmacology & OR Toxicology

14 CLINICAL STUDIES

16 HOW SUPPLIED/STORAGE AND HANDLING

17 PATIENT COUNSELING INFORMATION

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS & USAGE

ORAVIG is indicated for the local treatment of oropharyngeal candidiasis (OPC) in adults.

2 DOSAGE & ADMINISTRATION

2.1 Basic Dosing Information

The recommended dosing schedule for ORAVIG is the application of one 50 mg buccal tablet to the upper gum region (canine fossa) once daily for 14 consecutive days.

2.2 Administration Instructions

ORAVIG should be applied in the morning, after brushing the teeth. The tablet should be applied with dry hands. The rounded side surface of the tablet should be placed against the upper gum just above the incisor tooth (canine fossa) and held in place with slight

pressure over the upper lip for 30 seconds to ensure adhesion. The tablet is round on one side for comfort, but either side of the tablet can be applied to the gum.

Once applied, ORAVIG stays in position and gradually dissolves. [*See Clinical Pharmacology (12.3)*] Subsequent applications of ORAVIG should be made to alternate sides of the mouth. Before applying the next tablet, the patient should clear away any remaining tablet material. In addition,

- ORAVIG should not be crushed, chewed or swallowed.
- Food and drink can be taken normally when ORAVIG is in place but chewing gum should be avoided.
- If ORAVIG does not adhere or falls off within the first 6 hours, the same tablet should be repositioned immediately. If the tablet still does not adhere, a new tablet should be placed.
- If ORAVIG is swallowed within the first 6 hours, the patient should drink a glass of water and a new tablet should be applied only once.
- If ORAVIG falls off or is swallowed after it was in place for 6 hours or more, a new tablet should not be applied until the next regularly scheduled dose. [*see Patient Counseling Information (17)*].

3 DOSAGE FORMS & STRENGTHS

ORAVIG is a buccal tablet containing 50 mg of miconazole. ORAVIG tablets are round, off-white tablets, with a rounded side and a flat side. The tablets are marked with an “L” on the flat side.

4 CONTRAINDICATIONS

ORAVIG is contraindicated in patients with known hypersensitivity (e.g., anaphylaxis) to miconazole, milk protein concentrate, or any other component of the product.

5 WARNINGS AND PRECAUTIONS

5.1 Hypersensitivity

Allergic reactions, including anaphylactic reactions and hypersensitivity, have been reported with the administration of miconazole products, including ORAVIG. Discontinue ORAVIG immediately at the first sign of hypersensitivity.

There is no information regarding cross-hypersensitivity between miconazole and other azole antifungal agents. Monitor patients with a history of hypersensitivity to azoles.

6 ADVERSE REACTIONS

The following serious adverse drug reactions are discussed in detail in other sections of labeling:

- Hypersensitivity reactions [see Warnings and Precautions (5.1)]

6.1 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 clinical practice.

The overall safety of ORAVIG was assessed in 480 adult subjects: 315 HIV-infected subjects, 147 subjects with head and neck cancer, and 18 healthy subjects.

HIV Infected Patients

Two trials were conducted in immunocompromised HIV-infected patients: one randomized, double-blind, double-dummy, active-controlled design (N = 290 ORAVIG, 287 control) and one non-comparative trial (N = 25).

In the randomized, double blind trial (Study 1), 290 HIV infected subjects used ORAVIG once daily for 14 days, and 287 subjects used 10 mg clotrimazole troches five times daily for 14 days. Adverse reactions occurring in $\geq 2\%$ of patients in either treatment are presented in Table 1.

Table 1 Adverse Reactions (Treatment-Emergent) Occurring in $\geq 2\%$ of HIV-Infected Patients in the Controlled Clinical Trial

Adverse Reaction (MedDRA v 9.1 System Organ Class and Preferred Term)	ORAVIG N = 290 (%)	Clotrimazole troches N = 287 (%)
Patients with any adverse reaction during the study	158 (54.5)	146 (50.9)
Gastrointestinal disorders	25.9	23.7
Diarrhea	9.0	8.0
Nausea	6.6	7.7
Vomiting	3.8	3.1
Dry mouth	2.8	1.7
Abdominal pain upper	1.7	2.8
Infections and infestations	15.9	17.1
Upper respiratory infection	2.1	2.4
Gastroenteritis	1.4	2.8
Nervous system disorders	13.1	8.4
Headache	7.6	6.6
Ageusia	2.4	0.3
Blood and lymphatic disorders	6.9	8.4
Anemia	2.8	1.7
Lymphopenia	1.7	2.1
Neutropenia	0.7	2.1
General disorders and administration site conditions	6.6	8.0
Fatigue	2.8	2.1
Pain	1.0	2.8
Respiratory/thoracic	5.2	7.7

Cough	2.8	1.7
Pharyngeal pain	0.7	2.4
Investigations	5.5	6.3
Increased GGT	1.0	2.8

Overall local adverse reactions, including oral discomfort, oral burning, oral pain, gingival pain, gingival swelling, gingival pruritis, tongue ulceration, mouth ulceration, glossodynia, dry mouth, application site pain or discomfort, toothache, loss of taste, and altered taste, were reported by 35 (12.1%) patients who received miconazole buccal tablet compared to 27 (9.4%) patients who received clotrimazole troches.

Head and Neck Cancer Patients

In the randomized, open-label comparative trial of oropharyngeal candidiasis in patients with head and neck cancer who had received radiation therapy (Study 2), 147 patients used ORAVIG once daily for 14 days and 147 patients used 125 mg of miconazole oral gel four times daily for 14 days. Adverse reactions occurring in $\geq 2\%$ of patients in either arm are listed in Table 2.

Table 2: Adverse Reactions (Treatment-Emergent) Occurring in $\geq 2\%$ of Patients with Head and Neck Cancer who had Received Radiation Therapy (Controlled Clinical Trial)

Adverse Reaction (MedDRA v 9.1 System Organ Class and Preferred Term)	ORAVIG N = 147 (%)	Miconazole gel N = 147 (%)
Patients with at least one adverse reaction	30 (20.4)	32 (21.8)
Gastrointestinal disorders	8.8	13.6
Abdominal pain, upper	1.4	2.0
Oral discomfort	2.7	2.7
Nausea	0.7	2.7
Vomiting	0.7	2.0
Glossodynia	0	2.0
Nervous system disorders	5.4	1.4
Dysgeusia	4.1	0
Skin and subcutaneous	3.4	0.7
Pruritus	2.0	0.7

Overall local adverse reactions, including oral discomfort, oral pain, dry mouth, glossodynia, loss of taste, altered taste, tongue ulceration, mouth ulceration, tooth disorder, and application site discomfort or pain, were experienced by 14 (9.5%) patients who used ORAVIG compared to 16 (10.9%) patients who used miconazole gel.

Overall ORAVIG Safety Experience In Patients and Healthy Subjects

Adverse reactions reported in the overall safety database of 480 subjects who received miconazole buccal tablet is listed in Table 3.

Table 3 Adverse Reactions Reported in $\geq 2\%$ of Patients and Healthy

Subjects who Received ORAVIG in Clinical Trials

Adverse reaction (MedDRA v 9.1 System Organ Class and Preferred Term)	ORAVIG N = 480 (%)
Patients with at least one AE	209 (43.5)
Gastrointestinal disorders	20.6
Diarrhea	6.0
Nausea	4.6
Abdominal pain upper	2.5
Vomiting	2.5
Infections and infestations	11.9
Nervous system disorders	10.6
Headache	5.0
Dysgeusia	2.9

Discontinuation of ORAVIG due to adverse drug reactions occurred in 0.6% overall.

7 DRUG INTERACTIONS

7.1 Warfarin

Concomitant administration of miconazole and warfarin has resulted in enhancement of anticoagulant effect. Cases of bleeding and bruising following the concomitant use of warfarin and topical, intravaginal, or oral miconazole were reported. Closely monitor prothrombin time, International Normalized Ratio (INR), or other suitable anticoagulation tests if ORAVIG is administered concomitantly with warfarin. Also monitor for evidence of bleeding.

7.2 Drugs Metabolized Through CYP 2C9 and 3A4

No formal drug interaction studies have been performed with ORAVIG. Miconazole is a known inhibitor of CYP2C9 and CYP3A4. Although the systemic absorption of miconazole following ORAVIG administration is minimal and plasma concentrations of miconazole are substantially lower than when given intravenously, the potential for interaction with drugs metabolized through CYP2C9 and CYP3A4 such as oral hypoglycemics, phenytoin, or ergot alkaloids cannot be ruled out.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Based on findings from animal data, ORAVIG may cause fetal harm when administered to pregnant women. There are no available data on ORAVIG use in pregnant women to evaluate for a drug-associated risk of major birth defects, miscarriage or adverse maternal or fetal outcomes. In animal reproduction studies, prolonged gestation, dystocia and/or increased number of resorptions were observed after oral administration of miconazole nitrate during organogenesis to pregnant rats and rabbits.

(See Data). Advise pregnant women of the potential risk to a fetus.

The background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the US general population, the estimated background risk of major birth defects and miscarriages in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Data

Animal Data:

Miconazole nitrate administered orally at doses of 80 mg/kg/day or higher to pregnant rats or rabbits crossed the placenta and resulted in embryo- and fetotoxicity, including increased fetal resorptions. These doses also resulted in prolonged gestation and dystocia in rats, but not in rabbits. Embryofetotoxicity was not observed in intravenous studies with miconazole at lower doses of 40 mg/kg/day in rats and 20 mg/kg/day in rabbits, which are approximately 8 times higher than the dose a patient would receive if she swallowed an ORAVIG buccal tablet, based on body surface area comparisons. Teratogenicity was not reported in any animal study with miconazole. _

8.2 Lactation

Risk Summary

There is no available information on the presence of miconazole in human milk, or the effects on the breastfed child, or the effects on milk production following use of ORAVIG.

The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for ORAVIG and any potential adverse effects on the breastfed infant from ORAVIG or from the underlying maternal condition.

8.4 Pediatric Use

Safety and effectiveness 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 due to potential risk of choking.

8.5 Geriatric 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.

8.6 Hepatic Impairment

Miconazole is metabolized by the liver. While miconazole systemic exposure is minimal following the application of ORAVIG, ORAVIG should be administered with caution in patients with hepatic impairment.

8.7 Renal Impairment

Less than 1% of miconazole is excreted as unchanged drug in the urine; therefore, no adjustment to therapy is necessary in patients with renal impairment.

10 OVERDOSAGE

Overdose with miconazole in humans has not been reported in the literature.

Miconazole absorption and systemic exposure following application of ORAVIG are minimal [see *Clinical Pharmacology (12.3)*].

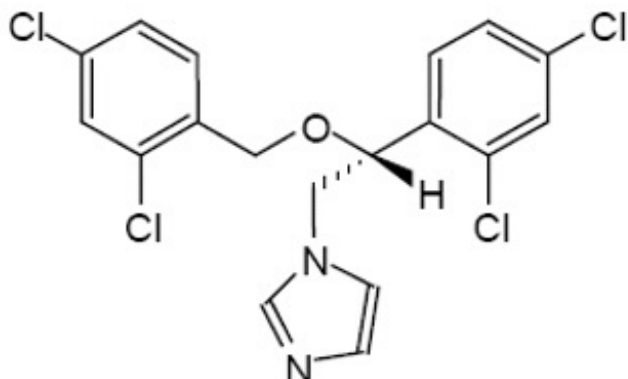
Symptomatic and supportive care is the basis for management.

11 DESCRIPTION

ORAVIG (miconazole) buccal tablets are applied topically to the gum once daily and release miconazole as the buccal tablet gradually dissolves [see *Clinical Pharmacology (12.3)*].

Miconazole is an imidazole antifungal agent and is described chemically as 1-[(2RS)-2-[(2,4-dichlorobenzyl)oxy]-2-(2,4-dichlorophenyl)ethyl]-1H-imidazole with an empirical formula of $C_{18}H_{14}Cl_4N_2O$ and a molecular weight of 416.13. The structural formula is shown in Figure 1.

Figure 1: Structural Formula of Miconazole



Miconazole drug substance is a white to almost white powder.

ORAVIG contains 50 mg of miconazole base, USP and the following inactive ingredients: hypromellose, USP; milk protein concentrate; corn starch, NF; lactose monohydrate, NF; sodium lauryl sulfate, NF; magnesium stearate, NF; and talc, USP.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Miconazole is an antifungal drug [see *Microbiology (12.4)*].

12.3 Pharmacokinetics

Absorption and Distribution

Salivary

Single dose application of ORAVIG containing 50 mg of miconazole to the buccal mucosa of 18 healthy volunteers provided mean maximum salivary concentrations of 15 mcg/mL at 7 hours after application of the tablet. This provided an average saliva exposure to miconazole estimated from the AUC (0-24h) of 55.23 mcg·h/mL. The pharmacokinetic parameters of miconazole in the saliva of healthy volunteers are provided in Table 4.

Table 4: Pharmacokinetic (PK) Parameters of Miconazole in Saliva Following Application of a Single ORAVIG 50 mg Tablet in Healthy Volunteers (N = 18)

Salivary PK Parameters (N = 18)	Mean ±SD (Min - Max)
AUC_{0-24h} (mcg·h/mL)	55.2 ±35.1 (0.5 - 128.3)
C_{max} (mcg/mL)	15.1 ±16.2 (0.5 - 64.8)
T_{max} (hour)	7* (2.0 - 24.1)

*Median

In healthy volunteers, the duration of buccal adhesion was on average 15 hours following a single dose application of ORAVIG 50 mg.

Plasma

Plasma concentrations of miconazole were below the lower limit of quantification (0.4 mcg/mL) in 157/162 (97%) samples from healthy volunteers following single-dose application of ORAVIG 50 mg. Measurable plasma concentrations ranged from 0.5 to 0.83 mcg/mL.

Plasma concentrations of miconazole evaluated after 7 days of treatment in 40 HIV-positive patients were all below the limit of quantification (0.1 mcg/mL).

Metabolism and Excretion

Most of the absorbed miconazole is metabolized by the liver with less than 1% of the administered dose found unchanged in urine. In healthy volunteers, the terminal half-life is 24 hours following systemic administration. There are no active metabolites of miconazole.

Food Effect

There was no formal food effect study conducted with ORAVIG; however, in clinical studies patients were allowed to eat and drink while taking ORAVIG.

12.4 Microbiology

Mechanism of Action

Miconazole inhibits the enzyme cytochrome P450 14 α -demethylase which leads to inhibition of ergosterol synthesis, an essential component of the fungal cell membrane.

Miconazole also affects the synthesis of triglycerides and fatty acids and inhibits oxidative and peroxidative enzymes, increasing the amount of reactive oxygen species within the cell.

Antimicrobial Activity

Miconazole is active against *Candida albicans*, *C. parapsilosis* and *C. tropicalis*. Correlation between minimum inhibitory concentration (MIC) results *in vitro* and clinical outcome has yet to be established.

Resistance

In vitro studies have shown that some *Candida* strains that demonstrate reduced susceptibility to one antifungal azole may also exhibit reduced susceptibility to other azoles suggesting cross-resistance.

Clinically relevant resistance to systemically utilized triazoles may occur in *Candida* species. Resistance may occur by multiple mechanisms such as changes in amino acids and/or in the regulation of the target enzyme and of a variety of efflux pump proteins. Multiple mechanisms may co-exist in the same isolate. Resistance breakpoints, correlating *in vitro* activity with clinical efficacy, have not been established for miconazole.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis & Mutagenesis & Impairment Of Fertility

Carcinogenicity studies with miconazole have not been conducted. Miconazole nitrate was not genotoxic when tested *in vitro* in a bacterial reverse mutation (Ames) assay or in an *in vivo* mouse bone marrow micronucleus test. Intraperitoneal injections of miconazole to mice induced chromosomal aberrations in spermatocytes and bone marrow cells, and morphologic abnormalities in sperm at doses similar to or below clinical doses. However, no impairment of fertility was observed in intravenous studies with miconazole at 40 mg/kg/day in rats or 20 mg/kg/day in rabbits, which are approximately 8 times higher than the dose a patient would receive if she swallowed an ORAVIG buccal tablet, based on body surface area comparisons.

13.2 Animal Pharmacology & OR Toxicology

Local tolerance studies (LLNA sensitization test and tolerance study on the jugal mucosa of hamster) did not reveal any toxicity.

14 CLINICAL STUDIES

Study in HIV Infected Patients

The efficacy and safety of ORAVIG in the treatment of OPC was evaluated in a randomized, double-blind, double-dummy, multicenter trial comparing ORAVIG 50 mg once daily for 14 consecutive days (n = 290) with clotrimazole troches 10 mg 5 times per day for 14 days (n = 287) in HIV-positive patients with OPC. Seventy-five percent of patients were not receiving highly active antiretroviral treatment, 5% had CD4+ cell count < 50 cells/mm³, and 17% had a history of previous OPC. The mean viral load was

117,000 copies/mL. Patients were required to have symptoms and microbiological documentation of OPC for study entry. Most of the infections were caused by *C. albicans* (85%), followed by *C. tropicalis* (9%), and *C. parapsilosis* (3%). About 2% of the subjects were infected with more than one *Candida* species.

Clinical cure [defined as a complete resolution of both signs and symptoms of OPC at the test of cure (TOC) visit (days 17-22)], and clinical relapse by days 35-38 (21-24 days after end of therapy) are presented in Table 5. Mycological cure [defined as eradication (i.e., no yeast isolates) of *Candida* species] at the TOC visit (days 17-22) is also reported in the table.

Table 5: Clinical Cure and Mycological Cure at the TOC Visit and Relapse at Days 35-38 in HIV Infected Patients

	ORAVIG 50 mg N=290 ^a (%)	Clotrimazole troches N=287 ^a (%)
Clinical cure†	176 (60.7%)	187 (65.2%)
Clinical relapse‡		
Yes ^b	48 (27.3%)	52 (27.8%)
No	124 (70.5%)	133 (71.1%)
Missing	4 (2.3%)	2 (1.1%)
Mycological cure	79 (27.2%)	71 (24.7%)

^a Analysis population includes all randomized patients who took at least 1 dose of study medication. One randomized subject excluded from the ORAVIG arm.

^b In those subjects who relapsed, the mean time to relapse was 15.3 days (SD 4.6) and 15.7 days (SD 6.6), in the ORAVIG and Clotrimazole treatment arms, respectively.

† Difference in clinical cure rates (ORAVIG-clotrimazole troche) was -4.5%, with a 95% CI: (-12.4%, 3.4%).

‡ Percentage based on those who had clinical cure.

Study in Head and Neck Cancer Patients

The efficacy and safety of ORAVIG 50 mg was evaluated in an open-label, randomized, multicenter trial comparing ORAVIG 50 mg once daily for 14 days to miconazole oral gel 125 mg four times daily for 14 days in head and neck cancer patients who had received radiation therapy. Most of the infections were caused by *C. albicans* (71%), and *C. tropicalis* (8%). About 7% of the subjects were infected with more than one *Candida* species. Success rates of treatment at day 14 [defined as a complete (complete disappearance of candidiasis lesions) or partial response (improvement by at least 2 points of the score for extent of oral lesion compared with the score at day 1) based on a blind assessment] are shown in Table 6. Also reported in Table 6 are relapse rate at day 30, and mycologic cure assessed at day 14.

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

	ORAVIG	Miconazole oral
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	50 mg N=148 ^a (%)	gel N=146 ^a (%)
Success rate (CR+PR) ^b	79 (53.4%)	69 (46.6%)
CR †	74 (50.0%)	64 (43.8%)
Clinical relapse‡		
Yes ^c	14 (18.9%)	8 (12.5%)
No	59 (79.7%)	56 (87.5%)
Missing	1 (1.4%)	0
Mycological cure	66 (44.6%)	78 (53.4%)

^a Analysis population includes all subjects who received at least one dose of study medication. Reasons for not receiving treatment included negative mycological culture, informed consent withdrawn, or lost during screening. Six patients excluded per arm.

^bCR: complete response; PR: partial response

^cIn those subjects who relapsed, the mean time to relapse was 18.8 days (SD 16.3) and 20.6 days (SD 13.5), in the ORAVIG and Miconazole oral gel group, respectively.

†Difference in clinical complete response rates (ORAVIG-Miconazole oral gel) was 6.2%, with a 95% CI: (-5.2%, 17.6%).

‡Percentage based on those who had complete response.

16 HOW SUPPLIED/STORAGE AND HANDLING

ORAVIG 50 mg buccal tablets are supplied as off-white tablets containing 50 mg of miconazole. ORAVIG tablets have a rounded side and a flat side. ORAVIG tablets are packaged in bottles of 14 tablets (NDC 61825-303-14).

ORAVIG should be stored at 20 to 25 °C (68 to 77 °F) [see USP controlled room temperature]; excursions between 15 and 30 °C permitted at room temperature. Protect from moisture, and keep out of reach of children.

17 PATIENT COUNSELING INFORMATION

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

Important Administration Instructions

The tablet should be used immediately after removal from the bottle.

- Instruct patients not to crush, chew, or swallow the tablet.
- The rounded side of the tablet should be applied to the upper gum above the incisor tooth in the morning, after brushing the teeth.
- The tablet should be held in place for 30 seconds with a slight pressure of the finger over the upper lip to make the tablet stick to the gum.
- The tablet may be used if it sticks to the cheek, inside of the lip or the gum.

- If the tablet does not adhere, it should be repositioned.
- As the ORAVIG tablet absorbs moisture from the mouth, it will slowly dissolve over time and should be left in place – there is no need to remove the tablet.
- Subsequent applications of ORAVIG should be made to alternate sides of the gum.
- If ORAVIG does not stick or falls off within the first 6 hours, the same tablet should be repositioned immediately. If the tablet does not adhere, a new tablet should be placed.
- If ORAVIG is swallowed within the first 6 hours, the patient should drink a glass of water and a new tablet should be applied only once.
- If ORAVIG falls off or is swallowed after it was in place for 6 hours or more, a new tablet should not be applied until the next regularly scheduled dose.

Patients should avoid situations that could interfere with the sticking of the tablet including:

- touching or pressing the tablet after placement
- wearing upper denture
- chewing gum
- hitting tablet when brushing teeth
- rinsing mouth too vigorously

Hypersensitivity and Other Adverse Reactions

Patients who develop hives, skin rash, or other symptoms of an allergic reaction, and patients who develop swelling or pain, at the tablet application site should stop ORAVIG and contact a healthcare provider. Patients may experience other adverse reactions including diarrhea, headache, nausea, and change in taste.

Potential Embryo-fetal Toxicity

Advise pregnant women and females of reproductive potential of the potential risk to a fetus. Advise females to inform their healthcare provider of a known or suspected pregnancy [see Use in Specific Populations (8.1)].

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US patent numbers: 6,916,485; 7,651,698; 8,518,442.

PATIENT INFORMATION

Oravig (OR-a-vig)
(miconazole)
buccal tablets

Read this Patient Information Leaflet 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 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 the throat.
- It is not known if ORAVIG is safe and effective in children under the age of 16 years.
- **It is not known if children can follow the instructions on what to do with the buccal tablet. In younger children, there is a possible risk of choking.**

Who should not use ORAVIG?

Do not use ORAVIG if you are allergic to:

- miconazole (M-Zole, Monistat, Vusion).
- milk protein concentrate.
- any of the ingredients in ORAVIG. See the end of this Patient Information Leaflet for a complete list of ingredients in ORAVIG.

What should I tell my doctor before using ORAVIG?

Before taking ORAVIG, tell your doctor about all of your medical conditions, including if you:

- have liver problems
- are pregnant or plan to become pregnant. Talk to your doctor if you are pregnant or plan to become pregnant.
- are breastfeeding or plan to breastfeed. It is not known if ORAVIG passes into your breast milk. Talk to your doctor about the best way to feed your baby if you use ORAVIG.

Tell your doctor about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

ORAVIG may affect the way other medicines work, and other medicines may affect how ORAVIG works.

Especially tell your doctor if you take:

- the blood thinner medicine warfarin (Coumadin, Jantoven).
- a diabetes medicine.
- phenytoin (Dilantin, Phenytek).
- an ergot alkaloid medicine. Ask your doctor or pharmacist if you are not sure if your medicine is an ergot alkaloid medicine.

Know the medicines you take. Keep a list of them to show your doctor and pharmacist when you get a new medicine.

How should I use ORAVIG?

- Read the detailed Instructions for Use that come with ORAVIG.
- Always use ORAVIG exactly as your doctor tells you.
- You should apply ORAVIG in the morning after you brush your teeth.
- ORAVIG is placed 1 time each day to your upper gum for 14 days.
- You should use ORAVIG right away after you remove it from the bottle.
- You may eat and drink normally while ORAVIG is in place.
- Do not crush, chew or swallow ORAVIG.
- You should change where you place ORAVIG, between the left and right side of your upper gum with each use.
- It is okay if ORAVIG sticks to your cheek, the inside of your lip or your gum.
- If ORAVIG does not stick, re-apply it to the other side of your upper gum.
- If ORAVIG does not stick or falls off of your gum within the first 6 hours, re-apply the same tablet to the other side of your upper gum right away. If it still does not stick, replace it with a new tablet.
- If you swallow ORAVIG within the first 6 hours of placing it, drink a glass of water and place a new ORAVIG to your upper gum only 1 time.
- If ORAVIG falls off your gum or is swallowed after it was in place for 6 hours or more, do not apply a new ORAVIG. Just place your next dose at your regularly scheduled time.
- Check to see if ORAVIG is still in place after you brush your teeth, rinse your mouth, eat, or drink.

<p>What should I avoid while using ORAVIG? You should avoid activities that may prevent ORAVIG from sticking to your gum, including:</p> <ul style="list-style-type: none"> • touching or pressing ORAVIG after placement • wearing an upper denture that interferes with placement of the tablet • chewing gum • hitting tablet when brushing your teeth • rinsing your mouth too vigorously 						
<p>What are the possible side effects of ORAVIG? ORAVIG may cause serious side effects, including: Allergic reactions. Stop using ORAVIG and tell your doctor right away or get emergency medical help if you have any of the symptoms below:</p> <ul style="list-style-type: none"> • skin rash or hives • swelling of your face, eyes, lips, tongue or throat • trouble swallowing or breathing <p>Stop using ORAVIG and tell your doctor if you develop swelling or pain at the tablet application site. The most common side effects of ORAVIG include:</p> <table border="0"> <tr> <td>• diarrhea</td> <td>• change in taste</td> </tr> <tr> <td>• headache</td> <td>• upper stomach (abdominal) pain</td> </tr> <tr> <td>• nausea</td> <td>• vomiting</td> </tr> </table> <p>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.</p>	• diarrhea	• change in taste	• headache	• upper stomach (abdominal) pain	• nausea	• vomiting
• diarrhea	• change in taste					
• headache	• upper stomach (abdominal) pain					
• nausea	• vomiting					
<p>How should I store ORAVIG?</p> <ul style="list-style-type: none"> • Store ORAVIG at room temperature between 68°F to 77°F (20°C to 25°C). • Keep ORAVIG dry. <p>Keep ORAVIG and all medicines out of the reach of children.</p>						
<p>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. If you would like more information, talk with your doctor. You can ask your pharmacist or doctor for information about ORAVIG that is written for health professionals. You can also visit www.oravig.com for more information.</p>						
<p>What are the ingredients in ORAVIG? Active ingredient: miconazole Inactive ingredients: hypromellose, milk protein concentrate, corn starch, lactose monohydrate, sodium lauryl sulfate, magnesium stearate, and talc.</p>						
<p><small>Manufactured By: Catalent Germany Schorndorf GmbH Steinbeisstraße 1-2 73614 Schorndorf Germany Distributed by: Galt Pharmaceuticals, LLC 1090 Northchase Pkwy., Suite 140, Marietta, GA 30067 Address medical inquiries to: Galt Pharmaceuticals, LLC 1-833-757-0904 US patent numbers: 6,916,495; 7,651,698; 8,518,442. ©2021 Galt Pharmaceuticals, LLC</small></p>						

This Patient Information has been approved by the U.S. Food and Drug Administration Revised: 06/2021

INSTRUCTIONS FOR USE

Oravig (OR-a-vig)
(miconazole)
buccal tablets

Read this Instructions for Use before you start using ORAVIG and each time you get a refill. There may be new information. This information does not take the place of talking to your doctor about your medical condition or treatment. Talk to your doctor or pharmacist if you have any questions about how to use ORAVIG.

How should I store ORAVIG?

- Store ORAVIG at room temperature between 68°F to 77oF (20°C to 25oC).
- Keep ORAVIG dry.

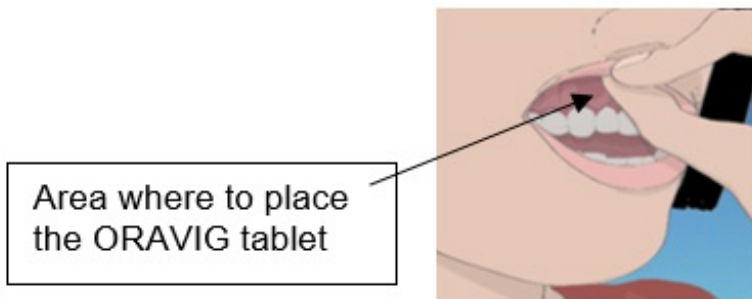
Keep ORAVIG and all medicines out of the reach of children.

How to use ORAVIG?

Before applying the ORAVIG tablet

Step 1. Locate the area on the upper gum, just above the left or the right incisor tooth.

The incisor tooth is the tooth just to the right or left of your two front teeth (See Figure A).

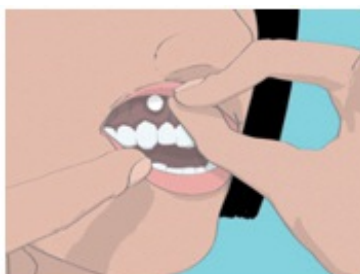


Step 2. With dry hands, take 1 ORAVIG tablet out of the bottle. ORAVIG is round on one side and flat on the other side (See Figure B). The tablet is marked with an “L” on the flat side.



Applying the ORAVIG tablet

Step 3. Place the flat side of the ORAVIG tablet on your dry fingertip. Gently push the round side of the tablet against your upper gum in the area shown in Figure C. Push the ORAVIG tablet up as high as it will go on your gum. The flat side will be facing the inside of your lip.



Step 4. Hold the ORAVIG tablet in place by applying a slight pressure with your finger on the outside of your upper lip for 30 seconds (See Figure D). This will make the tablet stick to your gum.



Step 5. Leave the ORAVIG tablet in place until it dissolves. Do not remove the tablet.

Step 6. Before applying your next dose, be sure to clear away any remaining ORAVIG tablet material on your gum.

Manufactured By: Catalent Germany Schorndorf GmbH Steinbeisstraße 1-2 73614 Schorndorf Germany

Distributed by: Galt Pharmaceuticals, LLC 1090 Northchase Pkwy., Suite 140, Marietta, GA 30067

Address medical inquires to: Galt Pharmaceuticals, LLC 1-833-757-0904

US patent numbers: 6,916,485; 7,651,698; 8,518,442.

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PACKAGE LABEL.PRINCIPAL DISPLAY PANEL

NDC 61825-303-14

once-daily
ORAVIG®
(miconazole) buccal tablets 50 mg

50 mg

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
MICONAZOLE (UNII: 7NNO0D7S5M) (MICONAZOLE - UNII:7NNO0D7S5M)	MICONAZOLE	50 mg

Inactive Ingredients

Ingredient Name	Strength
HYPROMELLOSE, UNSPECIFIED (UNII: 3NXW29V3WO)	
STARCH, CORN (UNII: O8232NY3SJ)	
LACTOSE MONOHYDRATE (UNII: EWQ57Q8I5X)	
SODIUM LAURYL SULFATE (UNII: 368GB5141J)	
MAGNESIUM STEARATE (UNII: 70097M6I3O)	
TALC (UNII: 7SEV7J4R1U)	
CASEIN (UNII: 48268V50D5)	

Product Characteristics

Color	white (Off-White)	Score	no score
Shape	ROUND (rounded side / flat side marked with "L")	Size	8mm
Flavor		Imprint Code	L
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:61825-303-14	14 in 1 BOTTLE; Type 0: Not a Combination Product	12/31/2021	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA022404	12/31/2021	

Labeler - Galt Pharmaceuticals, LLC (079214973)

Revised: 1/2022

Galt Pharmaceuticals, LLC