

Policy Type:PA/SP

Pharmacy Coverage Policy: EOCCO261

Description

Oteseconazole (Vivjoa) is an orally administered azole antifungal.

Length of Authorization

- Initial: Three months
- Renewal: Cannot be renewed

Quantity Limits

Product Name	Indication	Dosage Form	Quantity Limit
oteseconazole (Vivjoa)	Recurrent vulvovaginal candidiasis (RVVC) in females of non-reproductive potential	150mg capsules	18 capsules/84 days

Initial Evaluation

- I. **Oteseconazole (Vivjoa)** may be considered medically necessary when the following criteria are met:
 - A. Member is 18 years of age or older; **AND**
 - B. A diagnosis of **recurrent vulvovaginal candidiasis (RVVC)** when the following are met:
 1. Member has a history of three or more acute vulvovaginal candidiasis (VVC) episodes within the last 12 months; **AND**
 2. Member is currently experiencing signs and symptoms consistent with an acute episode of VVC (e.g., vulvovaginal pain, pruritis or irritation, abnormal vaginal discharge, etc.); **AND**
 3. Diagnosis of acute VVC has been confirmed by positive KOH or culture; **AND**
 4. Member is of non-reproductive potential, defined as one of the following:
 - i. Postmenopausal; **OR**
 - ii. Member has undergone surgical sterilization (e.g., history of tubal ligation, bilateral salpingo-oophorectomy, or hysterectomy); **OR**
 - iii. Other means of permanent infertility (documentation is verified by a clinical pharmacist at the health plan); **AND**
 5. Member has been treated with weekly oral fluconazole for a period of 6 months; **OR**
 - i. Treatment with fluconazole is not tolerated or contraindicated; **OR**
 - ii. Antifungal susceptibility testing has been conducted and confirms fluconazole resistance; **OR**

- iii. Member has experienced a recurrence during or following maintenance therapy with fluconazole
- II. Oteseconazole (Vivjoa) is considered investigational when used for all other conditions, including but not limited to:
 - A. Acute vulvovaginal candidiasis
 - B. Onychomycosis or other nail fungal infections
 - C. Tinea pedis
 - D. Systemic fungal infections

Renewal Evaluation

- I. See initial evaluation

Supporting Evidence

- I. Oteseconazole (Vivjoa) is an oral azole antifungal that has been FDA-approved to reduce the incidence of recurrent vulvovaginal candidiasis (RVVC). Oteseconazole (Vivjoa) was studied in three Phase 3, randomized, double-blind, placebo-controlled pivotal trials: two VIOLET studies and one ultraVIOLET study. The trial population consisted of a total of 875 post-menarchal females aged 12 years and older who had a diagnosis of RVVC, defined as at least three prior episodes of acute VVC in the past 12 months.
- II. The VIOLET trials consisted of an induction phase with fluconazole 150mg on days one, four, and seven. On day 14 participants were assessed for infection clearance; only participants who had cleared their initial infection were then randomized to receive oteseconazole (Vivjoa) or placebo for the maintenance period. The dosing of oteseconazole (Vivjoa) during the maintenance period was 150mg once daily for one week, followed by 150mg weekly for 11 weeks. The primary efficacy endpoint for both VIOLET trials was the proportion of patients with one or more culture verified acute VVC episodes during the maintenance phase of the study.
- III. In ultraVIOLET, participants were randomized prior to the induction phase to receive oteseconazole (Vivjoa) or fluconazole/placebo. In the oteseconazole (Vivjoa) group, participants received 600mg on day one and 450mg on day two for induction therapy, then oteseconazole (Vivjoa) weekly for 11 weeks starting on day 14 for maintenance therapy. In the fluconazole/placebo group, participants received fluconazole 150mg on days one, four, and seven for induction therapy, then placebo weekly for 11 weeks starting on day 14 for maintenance therapy. Results below:

	Trial 1 (VIOLET)		Trial 2 (VIOLET)		Trial 3 (ultraVIOLET)	
	OTE N = 217	PBO N = 109	OTE N = 218	PBO N = 108	OTE N = 218	FLU/PBO

						N = 108
Induction regimen	FLU		FLU		OTE	FLU
Maintenance regimen	OTE 150mg QD x7 days, then QW x11 weeks	PBO	OTE 150mg QD x7 days, then QW x11 weeks	PBO	OTE 150mg QW x11 weeks	PBO
Proportion of patients with ≥1 culture-verified acute VVC episode (Day 1 – week 48)*	6.7%	42.8%	3.9%	39.4%	10.3%	42.9%
Proportion of patients with ≥1 culture-verified acute VVC episode or received VVC medication (Day 1 – week 48)*	27.3%	50.8%	21.3%	49.7%	43.5%	59.0%
FLU = fluconazole 150mg on days 1, 4, and 7; PBO = matching placebo; OTE = oteseconazole *All results were statistically significant in favor of oteseconazole						

- IV. Although the trial was designed to allow providers to treat participants with fluconazole for episodes of recurrence, other VVC medications were used during the trial to treat suspected acute VVC infections. The investigators did not initially consider all instances where participants used other VVC medications as incidence of recurrence. A post-hoc sensitivity analysis conducted by the FDA considered the use of other VVC medications as recurrence shows a slightly different efficacy profile, and results are reported in the second endpoint in the table above. Although the post-hoc analysis cannot formally be considered for statistical significance, this shows a more realistic efficacy profile that remains clinically meaningful.
- V. The most commonly reported adverse events consisting of headache (7.4%) and nausea (3.6%). Although the clinical trials included participants who were of reproductive potential, oteseconazole (Vivjoa) is contraindicated in females of reproductive potential and in pregnant and lactating women due to embryo-fetal toxicity risks, including ocular abnormalities based on data from animal trials, that cannot be adequately mitigated given the drug exposure window of approximately 690 days.
- VI. The FDA label defines ‘non-reproductive potential’ as follows: persons who are biological females who are postmenopausal or have another reason for permanent infertility (e.g., tubal ligation, hysterectomy, salpingo-oophorectomy). Although contraception is highly effective at preventing pregnancy, there is always a chance of contraceptive failure with any contraceptive method. Additionally, because the effects of contraception are reversible, use of various contraceptive methods, including abstinence, are not considered ‘permanent infertility’.
- VII. Although the pivotal clinical trials enrolled post-menarchal patients aged 12 years and older, the majority of participants were between age 18 and 34 years and only two total patients under

- age 18 years participated. Due to the small population size, the true safety and efficacy profile of oteseconazole (Vivjoa) has not been established in patients under the age of 18 years.
- VIII. Clinical guidelines, including those published by the Centers for Disease Control and Prevention (CDC) and Infectious Disease Society of America (IDSA), indicate that diagnosis of VVC can typically be made via the presentation of infection signs/symptoms: pruritis, irritation, vaginal soreness, external dysuria, and dyspareunia accompanied by signs of vulvar edema, erythema, excoriation, fissures and white, thick, curd-like vaginal discharge. For complicated VVC and RVVC, diagnosis should be confirmed with a wet-mount preparation with use of saline and 10% potassium hydroxide (KOH). If KOH is negative, a culture for *Candida* should be obtained.
- IX. RVVC is usually defined as having at least three episodes of acute VVC within one year and are typically caused by azole-susceptible *C. albicans*. Clinical guidelines recommend beginning treatment with induction therapy with a 10-to-14-day course of a topical azole or oral fluconazole, followed by maintenance therapy with fluconazole 150mg once weekly for six months. If oral fluconazole is not feasible, topical clotrimazole (200mg cream twice weekly or 500mg vaginal suppository once weekly) or other intermittent oral or topical antifungal treatment is recommended. After cessation of maintenance therapy, IDSA approximates a 40-50% recurrence rate. Oteseconazole (Vivjoa) may be considered medically necessary if oral fluconazole has been not tolerated, is contraindicated, fluconazole resistance is confirmed, or if members experience recurrence of acute VVC symptoms anytime during or after maintenance therapy with fluconazole.
- X. According to results of an extension trial reported by the manufacturer, 85% of participants who completed the maintenance regimen with oteseconazole (Vivjoa) did not experience a recurrent episode for up to 96 weeks (approximately two years). However, rates of recurrence beyond two years or safety and efficacy of retreatment with oteseconazole (Vivjoa) has not been established. Due to lack of adequate safety and efficacy data to establish an appropriate timeline for retreatment, renewal requests will be evaluated against initial policy criteria.

Investigational or Not Medically Necessary Uses

- I. Oteseconazole (Vivjoa) has not been FDA-approved, or sufficiently studied for safety and efficacy for the conditions or settings listed below:
- A. Acute vulvovaginal candidiasis
- i. One Phase 2, randomized, double-blind, active-controlled, parallel-group, dose-ranging trial evaluated oteseconazole (Vivjoa) at various doses (300mg once daily, 600mg daily or 600mg twice daily) for three days against a single dose of fluconazole 150mg in the setting of acute VVC. The primary endpoint was the proportion of participants with therapeutic cure at the test-of-care (TOC) day 28 visit. This study was not appropriately powered for statistical analysis and

statistical significance could not be evaluated. However, the nominal data indicate that no difference in therapeutic cure was identified between any of the oteseconazole (Vivjoa) groups and the fluconazole group.

- B. Onychomycosis or other nail fungal infections
- C. Tinea pedis
- D. Systemic fungal infections

References

1. Brand SR, Sobel JD, Nyirjesy P, et al. A Randomized Phase 2 Study of VT-1161 for the Treatment of Acute Vulvovaginal Candidiasis. *Clinical Infectious Diseases*. 2021;73(7):e1518-24.
2. Sobel JD, Nyirjesy P. Oteseconazole: an advance in treatment of recurrent vulvovaginal candidiasis. *Future Microbiol.* (2021) 16(18), 1453-1461.
3. New Drug Review: oteseconazole (Vivjoa). IPD Analytics. May 2022.
4. Centers for Disease Control and Prevention (CDC). 2015 Sexually Transmitted Diseases Treatment Guideline: Vulvovaginal candidiasis. Accessed July 19, 2021.
5. Pappas PG, et al. Clinical Practice Guideline for the Management of Candidiasis: 2016 Update by the Infectious Diseases Society of America. *Clinical Infectious Diseases*. 2016;62(4):e1-50.
6. Vivjoa [Prescribing Information]. Mycovia Pharmaceuticals: Durham, NC. April 2022.
7. Kotch LE. Integrated Review - Application number: 211288Orig1s000. Center for Drug Evaluation and Research. August 26, 2021.

Policy Implementation/Update:

Action and Summary of Changes	Date
Updated wording to reflect standard policy language; Added criteria for fluconazole resistance	03/2023
Policy created	08/2022