BlueCross BlueShield of Arizona
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PHARMACY COVERAGE GUIDELINES	**ORIGINAL EFFECTIVE DATE: 11/17/16**
SECTION: DRUGS	**LAST REVIEW DATE: 11/16/17**
	LAST CRITERIA REVISION DATE: 11/16/17
	ARCHIVE DATE:

GYNAZOLE•1® (butoconazole nitrate) vaginal cream 2%

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Pharmacy Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Pharmacy Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

This Pharmacy Coverage Guideline does not apply to FEP or other states' Blues Plans.

Information about medications that require precertification is available at www.azblue.com/pharmacy.

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

Precertification for medication(s) or product(s) indicated in this guideline requires completion of the request form in its entirety with the chart notes as documentation. All requested data must be provided. Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602) 864-3126 or emailed to Pharmacyprecert@azblue.com. **Incomplete forms or forms without the chart notes will be returned.**

GYNAZOLE•1® (butoconazole nitrate) vaginal cream 2% (cont.)

Description:

Gynazole•1 (butoconazole nitrate) is an imidazole antifungal agent indicated for the local treatment of vulvovaginal candidiasis (VVC). The diagnosis should be confirmed by potassium hydroxide (KOH) smears and/or cultures.

VVC is usually caused by *C. albicans* but can be caused by other *Candida* species. Prior to use of empirical antifungal therapy, the diagnosis should be confirmed by a wet mount preparation with use of saline and 10% KOH to demonstrate the presence of yeast or hyphae and obtaining vaginal cultures for *Candida*.

Common features of VVC include vulvar pruritus, vulvar burning, soreness, and irritation. These can be accompanied by dysuria or dyspareunia. Symptoms are often worse during the week prior to menses. The intensity of signs and symptoms varies from mild to severe.

VVC can be classified as either uncomplicated (90% of cases) or complicated (10% of cases) on the basis of clinical presentation, microbiological findings, host factors, and response to therapy. Complicated VVC is defined as severe or recurrent disease, infection due to *Candida* species other than *C. albicans*, and/or VVC in an abnormal host.

A variety of topical and systemic oral agents are available for the treatment of VVC. No evidence exists to show the superiority of any topical agent formulation or regimen.

Uncomplicated VVC can be effectively treated with either single-dose or short-course (3 days) therapy, both of which achieve 90% response.

Complicated VVC requires therapy be administered intravaginally with topical agents for 5-7 days or orally with fluconazole (150 mg every 72 hours) for three doses.

Severe VVA (extensive vulvar erythema, edema, excoriation, and fissure formation) is associated with lower clinical response rates in patients treated with short courses of topical or oral therapy. Either 7–14 days of topical azole or 150 mg of fluconazole in two or three sequential oral doses (dosed every 72 hours after initial dose) is recommended.

Episodes of recurrent VVC (≥ 4 symptomatic episodes within one year) is usually caused by *C. albicans* and these infections remain responsive to azole therapy. Treatment of these infections should include induction therapy with a topical agent or oral fluconazole for 10-14 days, followed by a maintenance azole regimen for at least 6 months. The most convenient regimen is fluconazole 150 mg once weekly. If fluconazole is not feasible, options include 10-14 days of a topical azole or alternative oral azole (itraconazole 200 mg once daily for 3 days or 200 mg twice daily for 1 day) followed by topical maintenance therapy for 6 months (clotrimazole 200 mg [10 grams of 2 percent] vaginal cream twice weekly or 500 mg vaginal suppository once weekly).

The exact mechanism of the antifungal action of butoconazole nitrate is unknown; however, it is presumed to function as other imidazole derivatives through inhibition of steroid synthesis. Imidazoles inhibit the conversion of lanosterol to ergosterol, resulting in a change in fungal cell membrane lipid composition. This structural change alters cell permeability and, ultimately, results in osmotic disruption or growth inhibition of the fungal cell. Butoconazole nitrate has fungicidal activity *in vitro* against *Candida* spp. and has been demonstrated to be

GYNAZOLE•1® (butoconazole nitrate) vaginal cream 2% (cont.)

clinically effective against vaginal infections due to *Candida albicans*. *Candida albicans* has been identified as the predominant species responsible for vulvovaginal candidiasis.

Definitions:

Vulvovaginal candidiasis:
A disorder characterized by signs and symptoms of vulvovaginal inflammation in the presence of *Candida* species

Recurrent vulvovaginal candidiasis
Four or more episodes of symptomatic infection within one year, due to relapse from a persistent vaginal reservoir of organisms or endogenous reinfection with the identical strain of susceptible *C. albicans*

Risk Factors that may predispose to symptomatic infection:
Diabetes mellitus — Women with diabetes mellitus who have poor glycemic control are more prone to VVC

Antibiotic use — Use of broad spectrum antibiotics significantly increases the risk of developing VVC either during or after taking antibiotics

Increased estrogen levels — Vulvovaginal candidiasis appears to occur more often in the setting of increased estrogen levels, such as oral contraceptive use (especially when estrogen dose is high), pregnancy, and estrogen therapy

Immunosuppression — Candidal infections are more common in immunosuppressed patients, such as those taking glucocorticoids or other immunosuppressive drugs, or with human immunodeficiency virus (HIV) infection

Contraceptive devices — Vaginal sponges, diaphragms, and intrauterine devices have been associated with VVC, but not consistently

Behavioral factors —Infection may be linked to orogenital and, less commonly, anogenital sex. Evidence of a link between VVC and hygienic habits (douching, use of tampons/menstrual pads) or wearing tight or synthetic clothing is weak and conflicting

Uncomplicated infection — Criteria include all of the following:
Sporadic, infrequent episodes (≤ 3 episodes/year)
Mild to moderate signs/symptoms
Probable infection with *Candida* albicans
Healthy, non-pregnant woman

Complicated infections — Criteria include one or more of the following criteria:
Severe signs/symptoms
Candida species other than *C. albicans*, particularly *C. glabrata*
Pregnancy, poorly controlled diabetes, immunosuppression, debilitation
History of recurrent (≥ 4/year) culture-verified vulvovaginal candidiasis

GYNAZOLE•1® (butoconazole nitrate) vaginal cream 2% (cont.)

Gynazole•1 (butoconazole nitrate)

Medication class:
Antifungal agent, imidazole derivative, vaginal

FDA-approved indication(s):
- Local treatment of vulvovaginal candidiasis due to Candida albicans.

Recommended Dose:
- Insert 1 applicatorful (delivers approximately 5 g of cream with 100 mg butoconazole) intravaginally as a single dose.

Maximum dosage
- One application

Available Dosage Forms:
- 2% vaginal cream in a carton with one single-dose prefilled disposable applicator

Warnings and Precautions:
- Contains mineral oil that may weaken latex or rubber (condoms or diaphragms); use of these products within 72 hours of treatment is not recommended.
- HIV infection should be considered in sexually active women with difficult to eradicate recurrent vaginal yeast infections.

Criteria:

- **Criteria for initial therapy:** Gynazole•1 (butoconazole nitrate) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Individual is 18 years of age or older

  2. A confirmed diagnosis of vulvovaginal candidiasis

  3. Individual has failure, contraindication or intolerance to **at least 2** the following preferred antifungals:
     - Preferred antifungal products:
       - Clotrimazole vaginal product
       - Miconazole vaginal product
       - Terconazole vaginal product
       - Tioconazole vaginal product
       - Fluconazole oral product

  4. There are **NO** contraindications:
     - Contraindications include:
       - Individuals with a history of hypersensitivity to any of the components of the product

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Initial approval duration: 1 month

- **Criteria for continuation of coverage (renewal request):** Gynazole•1 (butoconazole nitrate) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Individual experienced a recurrent episode (a relapse or reinfection) of symptomatic confirmed diagnosis of vulvovaginal candidiasis

  2. The indication for use is one that requires a longer duration than the usual duration and the other alternatives as listed in the criteria for initial therapy section cannot be used

  3. Individual has not developed any contraindications or other significant level 4 adverse drug effects that may exclude continued use
     - Contraindications as listed in the criteria for initial therapy section

  4. There are no significant interacting drugs

  Renewal duration: 6 month

Resources:

Gynazole•1. Package Insert. Revised by manufacturer 6/2014. Accessed 9/16/16.

Pappas PG, Kauffman CA, Andes DR, et al.: Clinical Practice Guideline for the Management of Candidiasis: 2016 Update by the Infectious Diseases Society of America. CID 2015. DOI:10.1093/cid/civ933 http://www.idsociety.org/uploadedFiles/IDSA/Guidelines-Patient_Care/PDF_Library/Candidiasis.pdf

UpToDate: Approach to women with symptoms of vaginitis. Current through Sep, 2017. https://www-uptodate-com.mwu.idm.oclc.org/contents/approach-to-women-with-symptoms-of-vaginitis?source=search_result&search=vulvovaginal%20candidiasis&selectedTitle=2~150

UpToDate: Candida vulvovaginitis. Current through Sep, 2017. https://www-uptodate-com.mwu.idm.oclc.org/contents/candida-vulvovaginitis?source=search_result&search=vulvovaginal%20candidiasis&selectedTitle=1~150

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Fax completed prior authorization request form to 602-864-3126 or email to pharmacyprecert@azblue.com.
Call 866-325-1794 to check the status of a request.
All requested data must be provided. **Incomplete forms or forms without the chart notes will be returned.**
Pharmacy Coverage Guidelines are available at www.azblue.com/pharmacy.

Pharmacy Prior Authorization Request Form

Do not copy for future use. Forms are updated frequently.
REQUIRED: Office notes, labs, and medical testing relevant to the request that show medical justification are required.

Member Information

Member Name (first & last):	Date of Birth:	Gender:	BCBSAZ ID#:
Address:	City:	State:	Zip Code:

Prescribing Provider Information

Provider Name (first & last):	Specialty:	NPI#:	DEA#:
Office Address:	City:	State:	Zip Code:
Office Contact:	Office Phone:	Office Fax:	

Dispensing Pharmacy Information

Pharmacy Name:	Pharmacy Phone:	Pharmacy Fax:

Requested Medication Information

Medication Name:	Strength:		Dosage Form:
Directions for Use:	Quantity:	Refills:	Duration of Therapy/Use:

☐ Check if requesting **brand** only ☐ Check if requesting **generic**

☐ Check if requesting continuation of therapy (prior authorization approved by BCBSAZ expired)

Turn-Around Time For Review

☐ Standard ☐ Urgent. Sign here: _____ ☐ Exigent (requires prescriber to include a written statement)

Clinical Information

1. **What is the diagnosis? Please specify below.**

   ICD-10 Code: _____ **Diagnosis Description:** _____

2. ☐ Yes ☐ No **Was this medication started on a recent hospital discharge or emergency room visit?**

3. ☐ Yes ☐ No **There is absence of ALL contraindications.**

4. **What medication(s) has the individual tried and failed for this diagnosis? Please specify below.**
Important note: Samples provided by the provider are not accepted as continuation of therapy or as an adequate trial and failure.

Medication Name, Strength, Frequency	Dates started and stopped or Approximate Duration	Describe response, reason for failure, or allergy

5. **Are there any supporting labs or test results? Please specify below.**

Date	Test	Value

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Pharmacy Prior Authorization Request Form

6. Is there any additional information the prescribing provider feels is important to this review? Please specify below.
For example, explain the negative impact on medical condition, safety issue, reason formulary agent is not suitable to a specific medical condition, expected adverse clinical outcome from use of formulary agent, or reason different dosage form or dose is needed.

Signature affirms that information given on this form is true and accurate and reflects office notes

Prescribing Provider's Signature: Date:

Please note: Some medications may require completion of a drug-specific request form.

Incomplete forms or forms without the chart notes will be returned.

Office notes, labs, and medical testing relevant to the request that show medical justification are required.