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.

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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*.

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.
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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. Episodes of recurrent VVC caused by *C. albicans* remain responsive to short duration oral or topical azole therapy. However, some recommend a longer duration of initial therapy (such as 7–14 days of topical therapy or a 100 mg, 150 mg, or 200 mg oral dose of fluconazole every third day for a total of 3 doses [day 1, 4, and 7]) to attempt to maintain remission before initiating a maintenance regimen. Oral fluconazole (100 mg, 150 mg, or 200 mg dose) weekly for 6 months is the first line maintenance regimen. Alternatively, topical treatments used intermittently can also be considered. 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 sequential oral doses (second dose 72 hours after initial dose) is recommended.

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

**Definitions:**

**Drug related events:**

- **Ineffective / failure**
  Use of a drug employing optimal doses (FDA-recommended doses) for optimal duration; where the condition being treated has not improved or worsened

  A request for branded agent due to generic drug failure or ineffectiveness will be assessed for potential approval with documentation of use of optimal dose / duration of the generic product and meeting other criteria within the coverage guideline. When the drug in question is a combination product, there must be documentation of failure / ineffectiveness of concurrent use (each ingredient used at the same time) of individual generic components. When the drug in question is a low dose formulation, there must be documentation of failure / ineffectiveness of low dose generic formulation.

- **Adverse Drug Event:** Allergic reaction / Hypersensitivity / Intolerance
  Use of a drug produced a significant reaction where continued use of the drug places the individual at risk for either lack of improvement or worsening of the condition being treated or at risk for harm and the concern is documented in medical record. A significant adverse drug event is when an individual's outcome is death, life-threatening, hospitalization (initial or prolonged), disability resulting in a significant, persistent, or permanent change, impairment, damage or disruption in the individuals' body function/structure, physical activities or quality of life, or requires intervention to prevent permanent impairment or damage.

  **Allergic reaction / hypersensitivity** – may or may not involve the active ingredient. When the active ingredient is involved, use of same or a chemically similar agent places the individual at risk for harm when the same or chemically similar agent is used. The subsequent reaction may be the same as the original
reaction or a more exaggerated response may be seen, potentially placing the individual at even greater risk for harm.

If the reaction occurred from the active/main generic ingredient; request for branded agent with same active ingredient will not be considered unless it is proven (documented) that active ingredient did not cause reaction and the request meets other criteria within the coverage guideline

*Intolerance* – these events represent circumstance(s) where use of a drug produced a significant reaction and continued use may result in non-adherence to proposed therapy and this concern is documented in medical record

**Contraindication**
Use of a drug that is not recommended by the manufacturer or FDA labelling

Use of any drug in the face of a contraindication is outside of the FDA and manufacturer’s labelled recommendation and is considered investigational or experimental

**Non-adherence**
Individual does not follow prescribed regimen that places the individual at risk for lack of improvement or worsening of the condition being treated and this concern is documented in medical record

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**Precertification:**

Precertification (Prior Authorization) is required for members with a Blue Cross Blue Shield of Arizona (BCBSAZ) pharmacy benefit for medication(s) or product(s) indicated in this guideline.

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](http://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.

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**Criteria:**

See “Resources” section for FDA-approved dosage.

- Precertification for Gynazole•1® (butoconazole nitrate) requires completion of the specific request form in its entirety. 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](mailto:Pharmacyprecert@azblue.com). Incomplete forms will be returned.
PHARMACY COVERAGE GUIDELINES

SECTION: DRUGS

ORIGINAL EFFECTIVE DATE: 11/17/16
LAST REVIEW DATE: 11/17/16
LAST CRITERIA REVISION DATE: 

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- FDA-approved product labeling (indication, age, dosage, testing, contraindications, exclusions, etc.) of Gynazole•1 (butoconazole nitrate) is considered medically necessary when ALL of the following criteria are met:
  1. Individual is 18 years of age or older
  2. Medical record documentation of a confirmed diagnosis of vulvovaginal candidiasis
  3. ALL of the following baseline tests have been completed before initiation of treatment:
     - Positive KOH examination OR positive culture for Candida spp
  4. Medical record documentation that the individual is unable to use ALL of the following antifungals due to a failed response, significant adverse drug event or contraindication:
     - Clotrimazole vaginal product
     - Miconazole vaginal product
     - Terconazole vaginal product
     - Tioconazole vaginal product
     - Fluconazole oral product
  5. Absence of ALL of the following contraindications:
     - Individuals with a history of hypersensitivity to any of the components of the product
  6. Absence of ALL of the following exclusions:
     - Individual is male

- Gynazole•1 (butoconazole nitrate) for all other indications not previously listed is considered experimental or investigational based upon:
  1. Lack of final approval from the Food and Drug Administration, and
  2. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes, and
  3. Insufficient evidence to support improvement of the net health outcome, and
  4. Insufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives, and
  5. Insufficient evidence to support improvement outside the investigational setting.

Resources:

FDA-approved indication and dosage:
GYNAZOLE® (butoconazole nitrate) vaginal cream 2% (cont.)

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<tr>
<th>Indication</th>
<th>Recommended Dose</th>
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<td>Gynazole•1 Butoconazole Nitrate Vaginal Cream USP, 2% is indicated for the</td>
<td>The recommended dose of Gynazole•1 Butoconazole Nitrate Vaginal Cream USP, 2% is one applicatorful of cream (approximately 5 grams of the cream) intravaginally. This amount of cream contains approximately 100 mg of butoconazole nitrate.</td>
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<td>local treatment of vulvovaginal candidiasis (infections caused by Candida). The diagnosis should be confirmed by KOH smears and/or cultures.</td>
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<td>Note: Gynazole•1 Butoconazole Nitrate Vaginal Cream USP, 2% is safe and effective in non-pregnant women; however, the safety and effectiveness of this product in pregnant women has not been established.</td>
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