Description:

Brisdelle® (paroxetine mesylate) is an oral selective serotonin reuptake inhibitor (SSRI) indicated for the treatment of moderate to severe vasomotor symptoms (VMS, also referred to as “hot flashes”) associated with menopause. It is not indicated to treat any psychiatric condition since it contains a low dose of paroxetine and the safety and efficacy of this low dose has not been established for any psychiatric condition. The mechanism of action of Brisdelle (paroxetine) in the treatment of VMS is not known. Paroxetine has been available for many years for treatment of various mental health conditions and it has been used off-label to treat VMS at doses of 10-20 mg daily. Other SSRI agents have been used to treat VMS in a similar manner.

The physiologic mechanism whereby a hot flash occurs is thought to be an elevation in body temperature leading to cutaneous vasodilation, which results in flushing and sweating in association with a subsequent decrease in temperature and chills. Proposed mediators that may be involved in this process include serotonin, norepinephrine, dopamine, and estrogen deprivation.
Classic menopausal symptoms include hot flushes and night sweats, but may also include other symptoms such as sleep disturbance, joint aches, irritability, mood changes, and genitourinary problems. Numerous studies have been conducted that show the efficacy of hormonal replacement therapy in controlling menopausal symptoms. Estrogen-containing products are the most effective FDA approved therapies for treatment of moderate to severe vasomotor symptoms (such as hot flashes and night sweats) associated with menopause and for treatment of moderate to severe symptoms of vulvar and vaginal atrophy (such as dryness, itching, and burning) associated with menopause. Hormonal therapy may also alleviate sleep disturbances and joint symptoms of menopause. Hormonal replacement therapy with Estrogen is also used in the prevention of postmenopausal osteoporosis.

For women who cannot use Estrogen for control of severe vasomotor symptoms, non-estrogen containing medications have been used. Agents that have been shown to be effective in the management of menopausal symptoms include other SSRI such as Citalopram, Escitalopram, Fluoxetine, and Paroxetine. Venlafaxine, a Selective Serotonin Norepinephrine Reuptake Inhibitor, the antihypertensive Clonidine, and the anticonvulsant Gabapentin have also shown efficacy in the management of vasomotor symptoms.

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.
BRISDELLÉ® (paroxetine mesylate) oral capsule (cont.)

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 prescribe 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 Brisdelle® (paroxetine mesylate) oral capsule 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. Incomplete forms will be returned.
Initial therapy FDA-approved product labeling (indication, age, dosage, testing, contraindications, exclusions, etc.) of Brisdelle is considered medically necessary when ALL of the following criteria are met:

1. Individual is female
2. Individual is 18 years of age or older
3. Individual has medical record documentation of a confirmed diagnosis of moderate to severe vasomotor symptoms associated with menopause
4. Individual is unable to use an Estrogen-containing product due to ONE of the following:
   - Estrogen-containing product failed to control moderate to severe vasomotor symptoms
   - Experienced significant adverse drug event from Estrogen-containing product
   - Estrogen-containing product is contraindicated
5. Individual is unable to use ALL of the following generic agents: Citalopram, Escitalopram, Fluoxetine, Paroxetine due to ONE of the following:
   - Generic products failed to control moderate to severe vasomotor symptoms
   - Experienced significant adverse drug event from or intolerance to generic products
   - Generic products are contraindicated
6. Absence of ALL of the following contraindications:
   - Concurrent use with monoamine oxidase inhibitors (MAOI) or use within 14 days of MAOI use
   - Use with thioridazine
   - Use with pimozide
   - History of hypersensitivity to paroxetine or any of the other ingredients in Brisdelle
   - Pregnancy

Continuation of coverage (renewal request): Brisdelle is considered medically necessary with documentation of ALL of the following:

1. The individual has benefited from therapy but remains at high risk
2. The condition has not progressed or worsened while on therapy
3. Individual has not developed any contraindications or other exclusions to its continued use

Brisdelle® (paroxetine) 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.

This includes but is not limited to:
- Depression
- Obsessive compulsive disorder
- Panic disorder
- Generalized anxiety disorder
- Social anxiety disorder
- Post-traumatic stress disorder
- Any other psychiatric condition

Resources:
Brisdelle® (paroxetine) package insert, revised by manufacturer 12/2014, reviewed on 01/31/2017.

Brisdelle™ (paroxetine) package insert, reference ID 3333786, revised by manufacturer on 03-2013, reviewed on 02/13/2014.


FDA-approved indication and dosage:

<table>
<thead>
<tr>
<th>Indication</th>
<th>Recommended Dose</th>
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<tbody>
<tr>
<td>BRISDELLLE is a selective serotonin reuptake inhibitor (SSRI) indicated for the treatment of moderate to severe vasomotor symptoms associated with menopause (VMS)</td>
<td>The recommended dosage of BRISDELLLE is 7.5 mg once daily, at bedtime</td>
</tr>
<tr>
<td>Limitation of Use: BRISDELLLE is not indicated for the treatment of any psychiatric condition</td>
<td>Capsules: 7.5 mg</td>
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