BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

BONJESTA® (doxylamine-pyridoxine) oral tablet extended release 20-20 mg
DICLEGIS® (doxylamine-pyridoxine) oral tablet delayed release 10-10 mg
Doxylamine-Pyridoxine oral tablet delayed release 10-10 mg
Generic Equivalent (if available)

This Pharmacy Coverage Guideline (PCG):
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope
- This PCG applies to Commercial and Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require prior authorization is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Criteria:

➢ **Criteria for therapy:** Bonjesta (doxylamine-pyridoxine) extended release, Diclegis (doxylamine-pyridoxine) delayed release, or generic doxylamine-pyridoxine delayed release and/or generic equivalent (if available) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met:

1. Individual is 18 years of age or older

2. Individual has a confirmed diagnosis of nausea and vomiting of pregnancy in a woman who has not responded to conservative measures

3. Requested agent will not be used in the treatment of hyperemesis gravidarum

4. Individual has documented failure, contraindication per FDA label, intolerance or is not a candidate for simultaneous use of over-the-counter generic **doxylamine** 12.5 mg and generic **pyridoxine** (Vitamin B6) 25 mg

5. **Additional criteria for Bonjesta (doxylamine-pyridoxine)**: Individual has failure, contraindication per FDA label, intolerance, or is not a candidate for Diclegis (doxylamine-pyridoxine) or generic doxylamine-pyridoxine delayed release product [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

6. Bonjesta (doxylamine-pyridoxine), Diclegis (doxylamine-pyridoxine), and generic doxylamine-pyridoxine will not be used concurrently with each other

7. There are **NO** FDA-label contraindications such as:
    a. Known hypersensitivity to doxylamine, other ethanolamine derivative antihistamines, pyridoxine or any inactive ingredient in the formulation
    b. Concurrent use with monoamine oxidase (MAO) inhibitors

Approval duration: 9 months

- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. **Off-Label Use of Non-Cancer Medications**

2. **Off-Label Use of Cancer Medications**

Description:

Bonjesta and Diclegis are fixed dose combination drug products of doxylamine succinate and pyridoxine hydrochloride, indicated for the treatment of nausea and vomiting of pregnancy (NVP) in women who do not respond to conservative management. These agents have not been studied in woman with hyperemesis gravidarum. The mechanism of action of Diclegis and Bonjesta are unknown, however, doxylamine is known to compete with histamine for H1-receptor sites and block the chemoreceptor trigger zone thereby decreasing nausea and vomiting.

Diclegis is formulated as a delayed release (enteric coated) tablet containing 10 mg of doxylamine and 10 mg of pyridoxine. Bonjesta is formulated as an extended-release tablet containing an enteric coated core of 10 mg doxylamine and 10 mg of pyridoxine and an immediate release coating containing 10 mg of doxycycline and 10 mg of pyridoxine.

PHARMACY COVERAGE GUIDELINE

BONJESTA® (doxylamine-pyridoxine) oral tablet extended release 20-20 mg
DICLEGIS® (doxylamine-pyridoxine) oral tablet delayed release 10-10 mg
Doxylamine-Pyridoxine oral tablet delayed release 10-10 mg
Generic Equivalent (if available)

Both Diclegis and Bonjesta are considered safe to use during pregnancy. However, women should not breastfeed while using doxylamine succinate/pyridoxine HCl.

The active ingredients of Bonjesta and Diclegis are available over-the-counter (OTC) as separate products. Some of the OTC products that contain doxylamine succinate are Unisom®, Nitetime Sleep-Aid, and Sleep Aid. Some OTC products that contain pyridoxine hydrochloride are pyridoxine and Vitamin B-6. One-half of a 25 mg OTC doxylamine tablet can be used off-label as an antiemetic. Use of OTC pyridoxine 25 mg can be taken along with the 12.5 mg of doxylamine. This is a reasonable substitute for combination extended-release and delayed-release tablets.

During pregnancy, 70-85% of women experience nausea and vomiting, commonly known as morning sickness. The most severe form, hyperemesis gravidarum, occurs in 0.5-2% of pregnancies, causes weight loss, and is the second most common cause of hospitalization during pregnancy. Early treatment of NVP may help prevent progression to hyperemesis gravidarum.

The 2015 clinical consensus guidelines for NVP from the American College of Obstetricians and Gynecologists (ACOG) recommends pyridoxine alone or in combination with doxylamine as first line pharmacologic therapy.

Definitions:

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting
MedWatch Forms for FDA Safety Reporting | FDA

Resources:

Bonjesta (doxylamine succinate 20 mg-pyridoxine hydrochloride 20 mg) extended-release product information, revised by Duchesnay USA, Inc. 10-2022. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed February 18, 2025.

Diclegis (doxylamine succinate 10 mg-pyridoxine hydrochloride 10 mg) delayed release product information, revised by Duchesnay USA, Inc. 06-2023. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed February 18, 2025.

Doxylamine succinate 10 mg-pyridoxine hydrochloride 10 mg delayed release product information, revised by Actavis Pharma, Inc. 10-2023. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed February 18, 2025.

Smith JA, Fox KA, Clark SM. Nausea and vomiting of pregnancy: Treatment and outcome. In: UpToDate, Lockwood CJ, Barss VA (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through January 2025. Topic last updated October 16, 2024. Accessed February 25, 2025.

ORIGINAL EFFECTIVE DATE: 11/16/2017 | ARCHIVE DATE: | LAST REVIEW DATE: 05/15/2025 | LAST CRITERIA REVISION DATE: 05/16/2024