PHARMACY COVERAGE GUIDELINES
SECTION: DRUGS

ORIGINAL EFFECTIVE DATE: 11/16/2017
LAST REVIEW DATE: 5/19/2022
LAST CRITERIA REVISION DATE: 5/20/2021
ARCHIVE DATE:

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

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)

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864-3126 or emailed to Pharmacyprecert@azblue.com. **Incomplete forms or forms without the chart notes will be returned.**

Criteria:

- **Criteria for therapy:** Bonjesta (doxylamine-pyridoxine) extended release, Diclegis (doxylamine-pyridoxine) delayed release, or generic doxylamine-pyridoxine delayed release are 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 nausea and vomiting of pregnancy in a woman who has not responded to conservative measures
  3. Will not be used in the treatment of hyperemesis gravidarum
  4. Documented failure, contraindication per FDA label or intolerance to simultaneous use of over-the-counter of generic **doxylamine** 12.5 mg and generic **pyridoxine** (Vitamin B6) 25 mg
  5. **Additional criteria for Bonjesta (doxylamine-pyridoxine) only**: Individual has failure, contraindication per FDA label or intolerance to Diclegis (doxylamine-pyridoxine) or generic doxylamine-pyridoxine delayed release product
  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**

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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.

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

Resources:

Bonjesta (doxylamine succinate-pyridoxine hydrochloride) extended release product information, revised by Duchesnay USA, Inc. 06-2018. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed April 29, 2022.

Diclegis (doxylamine succinate-pyridoxine hydrochloride) delayed release product information, revised by Duchesnay USA, Inc. 06-2018. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed April 29, 2022.

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Doxylamine succinate-pyridoxine hydrochloride delayed release product information, revised by Mylan Pharmaceuticals, Inc. 01-2019. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed April 29, 2022.

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. Last updated February 23, 2022. Accessed April 29, 2022.