MTF Formulary Management for OTC Doxylamine

Defense Health Agency Pharmacy Operations Division

Bottom Line

- **Doxylamine was designated as an over-the-counter (OTC) Basic Core Formulary (BCF) agent with a prescription requirement and is limited to patients who are under 65 years old.**
- **The P&T Committee found doxylamine was a clinically and cost-effective option in the treatment of nausea and vomiting in pregnancy.**
- **The prescription product Diclegis (doxylamine/pyridoxine) remains nonformulary, with manual prior authorization required. (See May 2015 DoD P&T Committee meeting minutes.)**

Uniform Formulary Decision: The Director, DHA, approved the recommendations from the February 2016 DoD P&T Committee meeting on May 5, 2016, with an implementation date of July 6, 2016.

OTC Uniform Formulary (UF) Agents*
BCF drugs – MTFs must have on formulary
• Doxylamine 25 mg generic
* Note that other OTC drugs on the Uniform Formulary (UF) include the following (see the August 2015 P&T Committee meeting minutes): • Antihistamines: loratadine +/- PSE; cetirizine +/- PSE; co-pay and prescription required at the Retail Network and in Mail Order • Emergency contraceptives: levonorgestrel (Plan B, generic); no co-pay or prescription required at MTF, Retail, or Mail Order • Proton pump inhibitors: omeprazole generic; co-pay and prescription required at Retail Network and Mail Order

Nausea and Vomiting of Pregnancy (NVP)

- NVP is a diagnosis of exclusion, affecting 70% to 85% of pregnant women. Typically patients are worse in the morning, with symptoms starting early in pregnancy and peaking at 8 weeks to 12 weeks. While the etiology and pathogenesis is not fully understood, theories include evolutionary adaptation, beta HCG levels, estrogen, and psychologic predisposition as possible contributors. NVP can affect occupation, social, and domestic function.
- OTC doxylamine (Unisom, generics) has been utilized in the United States since the discontinuation of Bendectin from the U.S. market in 1983. The FDA and meta-analyses have supported that the removal of Bendectin was due to litigation concerns, and not due to any safety risk that can be directly attributed to the components of Bendectin (doxylamine/pyridoxine and originally, dicycolmine).
- Doxylamine was examined as an individual agent in the treatment of NVP as part of an FDA-required Drug Efficacy Study when Bendectin was required to be studied at the component level. Bendectin was reformulated, and dicyclomine, which was identified as an ineffective component, was removed from the formulation that remained on the market until 1983.
- In the FDA-required study above, doxylamine as a sole ingredient was as effective in some endpoints as the doxylamine/pyridoxine component.
- In 2014, Diclegis which contains doxylamine and pyridoxine, similar to Bendectin, was approved by the FDA. At the May 2015 DoD P&T Committee meeting, Diclegis was designated nonformulary and the manual prior authorization criteria originally approved in August 2013 was continued.
- There are many agents that have been used in the treatment of NVP but few have been studied as extensively as doxylamine. Doxylamine has a Category A pregnancy risk rating.
- A 2015 American College of Obstetrics and Gynecology (ACOG) practice bulletin found doxylamine in combination with pyridoxine to be a safe and effective treatment option and recommended it as first line treatment of NVP, consistent with prior guidance. They also commented that the individual components are commonly taken together for NVP. (Obstet Gynecol 2015;126:e12–24.)

Date of Original: Feb 2016

- As a result of the common practice of using this product, the efficacy data available, and ACOG recommendations, the P&T Committee found doxylamine a clinically effective and safe drug to add to the UF for treating NVP.
- The P&T Committee recommended BCF status for doxylamine 25 mg to encourage use of this agent over more costly products and agents that might have safety concerns.
- As part of this recommendation, a prescription will be required for OTC doxylamine 25 mg. Additionally, an age limit of patients less than 65 years was recommended, to ensure appropriate use in accordance with Beers Criteria. No co-pay will be required at the Retail Network or Mail Order.

OTC Program Permanent Authority

- Section 703 of the Fiscal Year 2013 National Defense Authorization Act provides legislative authority for the OTC Drug Program. The Final Rule was published in the Federal Register on July 27, 2015, and established the process for identifying OTC products for coverage under the TRICARE pharmacy benefit and the rules for making these products available to eligible DoD beneficiaries.
- The Final Rule can be found at https://www.federalregister.gov/articles/2015/07/27/2015-18290/civilian-health-and-medical-program-of-the-uniformed-services-champustricare-tricare-pharmacy.

References

- DoD P&T Committee minutes: http://www.health.mil/PandT
- Current/future drug classes under review by the DoD P&T Committee: http://www.health.mil/About-MHS/Other-MHS-Organizations/DoD-Pharmacy-and-Therapeutics-Committee
- TRICARE Formulary Search Tool: http://www.health.mil/formulary
- Prior Authorization/Medical Necessity forms: See Formulary Search Tool above.
- Formulary Management Documents (including this one) available at: http://www.health.mil/DoDPTResources
- Point of contact for additional information: dha.jbsa.pharmacy.list.poduf@mail.mil

Doxylamine Price Comparison at MTF	
Drug	**MTF Cost (Feb 2016)**
Basic Core Formulary	
Doxylamine 25 mg (Unisom; generic)	$ **Most Cost-Effective**
Nonformulary	
Doxylamine/Pyridoxine (Diclegis)	$$$$ **Least Cost-Effective**

Legend:
- $ = "Most Cost-Effective" represents Rxs with the lowest cost and best clinical efficacy
- $$ = "Less Cost-Effective" represents higher cost Rxs with similar clinical efficacy
- $$$ = "Less Cost-Effective" represents next higher cost Rxs with similar clinical efficacy
- $$$$ = "Least Cost-Effective" represents Rxs with the highest cost with similar clinical efficacy