CHLORHEXIDINE GLUCONATE SAFETY

I. ISSUE
FDA is requesting the manufacturers of over-the-counter (OTC) antiseptic products containing chlorhexidine gluconate to add a warning about the risk of serious allergic reactions to the Drug Facts labels. Although rare, serious allergic reactions, including fatal anaphylaxis, can develop within minutes of exposure, and can occur with topical or oral use of the drug.

II. BACKGROUND
Prescription chlorhexidine gluconate mouthwashes for gingivitis and oral chips used for periodontal disease already contain a warning about the possibility of serious allergic reactions in their labels. However, since the number of reports of serious allergic reactions to these products has increased over the last several years, FDA is extending the warning to the OTC products containing chlorhexidine gluconate as well, which includes topical solutions, washes, sponges, and swabs. They are marketed under brand names such as Avagard, Bioscrub, Brian Care, CHG Scrub, ChloraPrep, CIDA-Stat, Dyna-Hex, Exidine, Hibiclens, Hibistat, Pharmaseal Scrub Care, and Prevantics. They are also available as generic products and store brands. Some medical devices such as dressings and intravenous lines also contain chlorhexidine gluconate.

III. DISCUSSION
FDA identified 43 worldwide cases reported in the FDA Adverse Event Reporting System (FAERS) database from January 1, 1969, through June 4, 2015, of anaphylactic reaction with the use of chlorhexidine gluconate topical products.

- 24 were reported after 2010.
- All were serious:
  - 26 classified as life-threatening,
  - 12 required hospitalization, and
  - 2 deaths attributed to the anaphylactic reaction.
  - 39 involved hypotension in association with either skin, respiratory, or gastrointestinal symptoms.
  - 12 involved elevated histamine or tryptase levels.
- All reported that the reaction occurred the same day the product was used, and seven reported a positive allergy rechallenge.

IV. PROVIDER CONSIDERATIONS/RECOMMENDATIONS
FDA recommends that healthcare professionals:

- Inquire from patients if they have experienced any reaction to the ingredient chlorhexidine gluconate or to antiseptic products containing chlorhexidine gluconate prior to use, such as:
  - Wheezing or difficulty breathing
  - Swelling of the face
  - Hives that can quickly progress to other more serious symptoms
  - Severe rash
  - Shock

Page 1 of 2 (continued on page 2)
CHLORHEXIDINE GLUCONATE SAFETY (continued from page 1)

- If a patient exhibits an unexplained allergic reaction prior to or during an injection or surgical procedure:
  - check whether chlorhexidine gluconate was used,
  - monitor the reaction carefully,
  - provide immediate respiratory and/or cardiovascular support as needed, and
  - discontinue the use of the drug or medical device containing chlorhexidine gluconate immediately.
- Consider using alternative antiseptics such as povidone-iodine, alcohols, benzalkonium chloride, benzethonium chloride, or parachlorometaxylenol (PCMX) when any previous allergy to chlorhexidine gluconate is documented or suspected.

Providers should continue to report any adverse reactions with the use of chlorhexidine gluconate by entering the information into CPRS’ Allergies/Adverse Reactions field and/or via local reporting mechanisms. Adverse events should also be reported, as appropriate, to the VA ADERS program and FDA MedWatch (1-800-FDA-1088, fax 1-800-FDA-0178, online at https://www.accessdata.fda.gov/scripts/medwatch/medwatch-online.htm, or by mail).

V. REFERENCES