



NATIONAL PBM BULLETIN

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DEPARTMENT OF VETERANS AFFAIRS VETERANS HEALTH ADMINISTRATION (VHA)
PHARMACY BENEFITS MANAGEMENT SERVICES (PBM), MEDICAL ADVISORY PANEL (MAP),
AND CENTER FOR MEDICATION SAFETY (VA MEDSAFE)

FDA WARNS OF INCREASED RISK OF DEATH WITH IV ANTIBACTERIAL TIGECYCLINE (TYGACIL) AND APPROVES NEW BOXED WARNING

I. ISSUE

FDA approved a new Boxed Warning about the increased risk of death when intravenous (IV) tigecycline (Tygacil) is used for FDA-approved uses as well as for non-approved uses. Additionally, updates will be made to the *Warnings and Precautions* and the *Adverse Reactions* sections of the product information.¹

II. BACKGROUND

Tigecycline is an anti-infective agent with FDA-approval for the treatment of complicated skin and skin structure infections (cSSSI), complicated intra-abdominal infections (cIAI), and community-acquired bacterial pneumonia (CABP). Tigecycline is not indicated for treatment of diabetic foot infection or for hospital-acquired or ventilator-associated pneumonia. In 2010, FDA issued a [Drug Safety Communication](#)² addressing results of a meta-analysis of 13 Phase 3 and 4 trials that showed a higher risk of death in patients receiving tigecycline [4.0% (150/3788)] compared to other antibacterial drugs [3.0% (110/3646)], with a 0.6% adjusted risk difference for death and corresponding 95% confidence interval of (0.1, 1.2). Risk appeared greatest in patients treated with tigecycline for ventilator-associated pneumonia, an off-label use.

III. DISCUSSION

Since 2010, FDA analyzed data from 10 clinical trials conducted solely on FDA-approved uses (cSSSI, cIAI, and CABP). Results indicated greater risk of death in patients receiving tigecycline for approved uses [2.5% (66/2640)] compared to other antibacterial drugs [1.8% (48/2628)], with a 0.6% adjusted risk difference for death and corresponding 95% confidence interval of (0.0%, 1.2%). These deaths came about from infections (exacerbations and/or complications) or other underlying medical conditions.

IV. PROVIDER RECOMMENDATIONS

FDA recommends that health care professionals should reserve tigecycline for use in situations when alternative treatments are not suitable.

V. REFERENCES

1. FDA Drug Safety Communication: FDA warns of increased risk of death with IV antibacterial Tygacil (tigecycline) and approves new Boxed Warning. <http://www.fda.gov/Drugs/DrugSafety/ucm369580.htm> . Accessed 09/27/2013.
2. FDA Drug Safety Communication: Increased risk of death with Tygacil (tigecycline) compared to other antibiotics used to treat similar infections. <http://www.fda.gov/Drugs/DrugSafety/ucm224370.htm> . Accessed 09/27/2013.

ACTIONS

- **Facility Director** (or physician designee): Forward this document to the Facility Chief of Staff (COS).
- **Facility COS and Chief Nurse Executives**: Forward this document to all appropriate providers who prescribe these medications (e.g., **primary care providers, hospitalists, critical care clinicians, and infectious disease specialists, including contract providers, etc.**). In addition, forward to the Associate Chief of Staff (ACOS) for Research and Development (R&D). Forward to other VA employees as deemed appropriate.
- **ACOS for R&D**: Forward this document to Principal Investigators (PIs) who have authority to practice at the facility and to your respective Institutional Review Board (IRB).