Summaries of Safety Labeling Changes Approved By FDA—Boxed Warnings Highlights October–December 2014

As part of FDA’s MedWatch program, important changes to the safety labeling of drugs and therapeutic biologics, including boxed warnings, are posted on the agency’s website. Boxed warnings are ordinarily used to highlight (1) an adverse reaction so serious in proportion to the potential benefit from the drug that it is essential that the reaction be considered in assessing the risks and benefits of using the drug, (2) serious adverse reactions that can be prevented or reduced in frequency or severity by appropriate use of the drug, and (3) situations in which FDA approved a drug with restrictions to ensure safe use because FDA concluded that the drug can be safely used only if distribution or use is restricted. The following revisions to boxed warnings were implemented in the three months ending December 2014.

Cymbalta ( duloxetine delayed-release ) capsules for Oral Use

Edited Boxed Warning (updated as of October 2014)

The following statement was removed:

“Cymbalta is not approved for use in pediatric patients.”

Mircera ( methoxy polyethylene glycol-epoetin beta ) Solution for Injection

Edited Boxed Warning

<table>
<thead>
<tr>
<th>Chronic Kidney Disease</th>
<th>Mircera Previous Boxed Warning</th>
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<tbody>
<tr>
<td>• In controlled trials, patients experienced greater risks for death, serious adverse cardiovascular reactions, and stroke when administered erythropoiesis-stimulating agents (ESAs) to target a hemoglobin level of greater than 11 g/dL.</td>
<td>Renal failure: Patients experienced greater risks for death and serious cardiovascular events when administered erythropoiesis-stimulating agents (ESAs) to target higher versus lower hemoglobin levels (13.5 vs. 11.3 g/dL; 14 vs. 10 g/dL) in two clinical studies. Individualize dosing to achieve and maintain hemoglobin levels within the range of 10 to 12 g/dL.</td>
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<tr>
<td>• No trial has identified a hemoglobin target level, ESA dose, or dosing strategy that does not increase these risks.</td>
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<td>• Use the lowest Mircera dose sufficient to reduce the need for red blood cell (RBC) transfusions.</td>
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Cancer

• Mircera is not indicated and is not recommended for the treatment of anemia due to cancer chemotherapy. A dose-ranging study of Mircera was terminated early because of more deaths among patients receiving Mircera than another ESA.
• ESAs have shown shortened overall survival and/or increased the risk of tumor progression or recurrence in clinical studies in patients with breast, non-small cell lung, head and neck, lymphoid, and cervical cancers.

Cancer

Mircera is not indicated for the treatment of anemia due to cancer chemotherapy. A dose-ranging study of Mircera was terminated early because of significantly more deaths among patients receiving Mircera than another ESA. In other studies of ESAs in patients with cancer:
• ESAs shortened overall survival and/or time-to-tumor progression in clinical studies in patients with advanced breast, head and neck, lymphoid and non-small cell lung malignancies when dose to a target hemoglobin of ≥12 g/dL.
• The risks of shortened survival and tumor promotion have not been excluded when ESAs are dosed to target a hemoglobin of <12 g/dL.


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