Dear Ms. Koukoutsis:

Please refer to your Supplemental New Drug Application (sNDA) dated and received July 25, 2016 submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Digoxin 0.05mg/mL Oral Solution.

We also refer to our December 1, 2016 Approval letter for Supplement 9 (S-009). The labeling appended to the December 1st Approval letter contained a formatting error in Table 7.3, making some of the content unreadable. This letter corrects the error and supersedes the December 1, 2016 Approval letter. The date of the action remains December 1, 2016.

This supplemental new drug application provides for revisions to the approved label as follows (additions are shown as underlined text and deletions are shown as strikethrough text):

1. Under **DRUG INTERACTIONS**, the following text was added/deleted to/from the table in 7.3:

<table>
<thead>
<tr>
<th>Antiarrhythmics</th>
<th>Dofetilide</th>
<th>Concomitant administration with digoxin was associated with a higher rate of torsades de pointes.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antiarrhythmics</td>
<td>Moricizine</td>
<td>Reported to increase PR interval and QRS duration. There are reports of first degree atrioventricular block, or bundle branch block developing with digitalis administration. The known effects of moricizine on calcium conductance may explain the effects on atrioventricular node conduction.</td>
</tr>
<tr>
<td>Antiarrhythmics</td>
<td>Sotalol</td>
<td>Proarrhythmic events were more common in patients receiving sotalol and digoxin than on either alone; it is not clear whether this represents an interaction or is related to the presence of CHF, a known risk factor for proarhythmia, in patients receiving digoxin.</td>
</tr>
<tr>
<td>Parathyroid Hormone Analog</td>
<td>Teriparatide</td>
<td>Sporadic case reports have suggested that hypercalcemia may predispose patients to digitalis toxicity. Teriparatide transiently increases serum calcium.</td>
</tr>
<tr>
<td>Thyroid Supplement</td>
<td>Thyroid</td>
<td>Treatment of hypothyroidism in patients taking digoxin may increase the dose requirements of digoxin.</td>
</tr>
<tr>
<td>Sympathomimetics</td>
<td>Epinephrine</td>
<td>Can increase the risk of cardiac arrhythmias.</td>
</tr>
<tr>
<td>Sympathomimetics</td>
<td>Norepinephrine</td>
<td></td>
</tr>
<tr>
<td>Sympathomimetics</td>
<td>Dopamine</td>
<td></td>
</tr>
</tbody>
</table>

Reference ID: 4026802
Neuromuscular Blocking Agents

<table>
<thead>
<tr>
<th></th>
<th>Succinylcholine</th>
<th>May cause sudden extrusion of potassium from muscle cells causing arrhythmias in patients taking digoxin.</th>
</tr>
</thead>
</table>

Supplements

<table>
<thead>
<tr>
<th></th>
<th>Calcium</th>
<th>If administered rapidly by intravenous route, can produce serious arrhythmias in digitalized patients.</th>
</tr>
</thead>
</table>

Beta-adrenergic blockers and calcium channel blockers

<table>
<thead>
<tr>
<th></th>
<th>Additive effects on AV node conduction can result in complete heart block.</th>
</tr>
</thead>
</table>

Hyperpolarization-Activated Cyclic Nucleotide-Gated Channel Blocker

<table>
<thead>
<tr>
<th></th>
<th>Ivabradine can increase the risk of bradycardia.</th>
</tr>
</thead>
</table>

2. Several editorial revisions were noted (removal of the term “USP” from HIGHLIGHTS, route of administration added).

3. The product contact information was updated to reflect West-Ward Pharmaceuticals Corp.

4. The information regarding nitrendipine was deleted from Table 7.2.

5. The revision date was updated.

**APPROVAL & LABELING**

We have completed our review of this supplemental application and it is approved, effective on the date of this letter, for use as recommended in the enclosed, agreed-upon labeling text.

**CONTENT OF LABELING**

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at [http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm](http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm). Content of labeling must be identical to the enclosed labeling (text for the package insert, text for the patient package insert, Medication Guide), with the addition of any labeling changes in pending “Changes Being Effected” (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.


The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that include labeling changes for this NDA, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in MS Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes and annotate each change. To facilitate review of your submission, provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).
REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, please call:

Lori Anne Wachter, RN, BSN, RAC  
Regulatory Project Manager for Safety  
(301) 796-3975

Sincerely,

{See appended electronic signature page}

Mary Ross Southworth, PharmD.  
Deputy Director for Safety  
Division of Cardiovascular and Renal Products  
Office of Drug Evaluation I  
Center for Drug Evaluation and Research

ENCLOSURE(S):  
Content of Labeling
This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

MARY R SOUTHWORTH
12/01/2016