Add the following:

**Piperacillin and Tazobactam for Injection**

Piperacillin and Tazobactam for Injection contains amounts of Piperacillin Sodium and Tazobactam Sodium equivalent to not less than 90.0 percent and not more than 110.0 percent of the labeled amounts of piperacillin (C_{23}H_{27}N_{4}O_{5}S) and tazobactam (C_{10}H_{12}N_{5}O_{5}S), the labeled amounts representing proportions of piperacillin to tazobactam of 8 : 1. It may contain small amounts of a suitable buffer and stabilizer.

**Packaging and storage**—Preserve in Containers for Sterile Solids as described in the Packaging section under Injections (1). Store at controlled room temperature.

**Labeling**—Label it to indicate its sodium content.

**USP Reference standards** (11)—USP Endotoxin RS, USP Piperacillin RS, USP Tazobactam RS, USP Tazobactam Related Compound A RS.

**Identification**—The retention times of the main peaks for piperacillin and tazobactam in the chromatogram of the Assay preparation correspond to those in the chromatogram of the Standard preparation, as obtained in the Assay.

**Bacterial endotoxins** (85)—It contains not more than 0.08 USP Endotoxin Unit in a portion equivalent to 1 mg of a mixture of piperacillin and tazobactam (0.89 and 0.11 mg, respectively).

**Sterility** (71): meets the requirements.

**Uniformity of dosage units** (905): meets the requirements.

**Change to read:**

**pH** (791): *between 5.0 and 7.0, in a solution containing the equivalent of 40 mg of piperacillin per mL.*

**Water, Method I** (921): not more than 2.5%.

**Change to read:**

**Particulate matter** (788): meets the requirements.*

**Related compounds**—[NOTE—Refrigerate the Standard preparation and the Assay preparation immediately after preparation and during analysis, using a refrigerated autosampler set at 5 ± 3°C. The solutions should be analyzed within 24 hours of preparation.]

*Mobile phase, Diluent, System suitability solution, and Chromatographic system—Prepare as directed in the Assay.

*Standard solution—Use the Standard preparation as directed for the Assay.

*Test solution—Use the Assay preparation.

*Procedure—Separately inject equal volumes (about 20 µL) of the Standard solution and the Test solution into the chromatograph, record the chromatograms, and measure all the peak areas. Identify the impurity peaks, using the relative retention times provided in Table 1.

**Other requirements**—It meets the requirements under Injections (1).

**Assay**—

*[NOTE—Refrigerate the Standard preparation and the Assay preparation immediately after preparation and during analysis, using a refrigerated autosampler set at 5 ± 3°C. The solutions should be analyzed within 24 hours of preparation.]*

*20% Phosphoric acid—Prepare a mixture of phosphoric acid and water (1:4).*

*Mobile phase—Dilute the contents of one vial of tetrabutylammonium hydrogen sulfate ion pairing reagent with water to 1 L, and mix well. Prepare a mixture of this solution and acetonitrile (75:25), and adjust with 20% Phosphoric acid to a pH of 3.8. Make adjustments if necessary (see System Suitability under Chromatography (621)).*

*Diluent—Prepare a mixture of water and acetonitrile (75:25).*

*Tazobactam related compound A stock solution—Dissolve an accurately weighed quantity of USP Tazobactam Related Compound

### Table 1

<table>
<thead>
<tr>
<th>Compound</th>
<th>Relative Retention Time</th>
<th>Relative Response Factor (F)</th>
<th>Limit (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tazobactam related compound A</td>
<td>0.12</td>
<td>0.75</td>
<td>1.0</td>
</tr>
<tr>
<td>Tazobactam</td>
<td>0.25</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Piperacillin impurity 4</td>
<td>0.31</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Piperacillin impurity 1-6</td>
<td>0.36</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Piperacillin related compound A</td>
<td>0.51</td>
<td>0.56</td>
<td>5.0</td>
</tr>
<tr>
<td>Piperacillin related compound C</td>
<td>0.55</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Piperacillin impurity 5</td>
<td>0.62</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Piperacillin impurity 6</td>
<td>0.67</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Piperacillin</td>
<td>1.0</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Any individual unspecified impurity</td>
<td></td>
<td>—</td>
<td>1.0</td>
</tr>
<tr>
<td>Total of impurities other than Piperacillin related compound A</td>
<td>1.0</td>
<td>—</td>
<td>5.0</td>
</tr>
</tbody>
</table>

*Calculated relative to the peak area of piperacillin.

1([2R,3S])-2-Amino-3-methyl-3-sulfino-4-(1H-1,2,3-triazol-4-yl)butyric acid.

*Specified unidentified impurities.

1([4S]-2-[(2-(4-Ethyl-2,3-dioxopiperazine-1-carboxamido)-2-phenylacetamido)methyl]-5,5-dimethylthiazolidine-4-carboxylic acid.

This compound has two epimers that usually co-elute but that may be separated as a result of minor changes in the chromatographic conditions.

1([2R,4S])-3-(Acetyl-2-[(1R)-Carboxyl-2-(4-ethyl-2,3-dioxopiperazine-1-carboxamido)-2-phenylacetamido]methyl)-5,5-dimethylthiazolidine-4-carboxylic acid.

Calculated the percentage of each impurity in the portion of Piperacillin and Tazobactam for Injection taken by the formula:

\[
P(1 / F)(C_3 / W_3)(D(\text{r}_1 / \text{r}_3))(100)
\]

in which \( P \) is the potency in mg of piperacillin per mg of USP Piperacillin RS; \( F \) is the relative response factor as listed in Table 1; \( C_3 \) is the concentration, in mg per mL of piperacillin in the Standard solution; \( W_3 \) is the weight, in mg, of the product used to prepare the Test solution; \( D \) is the dilution factor used to prepare the Test solution; \( r_1 \) is the response for each impurity peak in the Test solution; and \( r_3 \) is the response for the piperacillin peak in the Standard solution: the specified and unspecified impurities meet the limits in Table 1.
2 Piperacillin

A RS in Diluent to obtain a solution having a known concentration of about 0.06 mg per mL.

Tazobactam stock preparation—Dissolve an accurately weighed quantity of USP Tazobactam RS in Diluent to obtain a solution having a known concentration of about 0.5 mg per mL.

Piperacillin stock preparation—Dissolve an accurately weighed quantity of USP Piperacillin RS in acetonitrile, using about 4% of the final volume, and dilute quantitatively with Diluent to obtain a solution having a known concentration of about 1.0 mg per mL.

System suitability solution—Transfer accurately measured volumes of Tazobactam related compound A stock solution and Tazobactam stock preparation to a suitable volumetric flask, and dilute quantitatively, and stepwise if necessary, with Diluent to obtain a solution having known concentrations of about 0.006 mg of tazobactam related compound A and 0.025 mg of tazobactam per mL.

Standard preparation—Transfer accurately measured volumes of Tazobactam stock preparation and Piperacillin stock preparation to a suitable volumetric flask, and dilute quantitatively, and stepwise if necessary, with Mobile phase to obtain a solution having known concentrations of about 0.025 mg of tazobactam and 0.2 mg of piperacillin per mL.

Assay preparation—Dissolve an accurately weighed quantity from a vial of Piperacillin and Tazobactam for Injection in Mobile phase, and dilute quantitatively to obtain a solution having a nominal concentration of about 0.025 mg of tazobactam and 0.2 mg of piperacillin per mL, based on the label claim.

Chromatographic system—The liquid chromatograph is equipped with a 210-nm detector and a 4.6-mm × 15-cm column that contains 3-µm packing L11. The flow rate is about 1.0 mL per minute. The autosampler temperature is maintained at 5 ± 3°C. Chromatograph the System suitability solution, and record the peak areas as directed for Procedure: the resolution, R, between peaks for tazobactam related compound A and tazobactam is not less than 3. Chromatograph the Standard preparation, and record the peak areas as directed for Procedure: the tailing factor for the tazobactam and piperacillin peaks is not more than 1.8; and the relative standard deviation for replicate injections is not more than 2%.

Procedure—Separately inject equal volumes (about 20 µL) of the Standard preparation and the Assay preparation into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the percentage of the label claim of tazobactam (C₁₀H₁₂N₄O₅S) and piperacillin (C₂₃H₂₇N₅O₇S) in the portion of Piperacillin and Tazobactam for Injection taken by the formula:

\[
(P) = \left( \frac{C_S}{C_U} \right) \left( \frac{r_U}{r_S} \right) (100)
\]

in which P is the potency of tazobactam or piperacillin, in mg per mg, in USP Tazobactam RS and USP Piperacillin RS, respectively; C_S is the concentration, in mg per mL, of tazobactam or piperacillin in the Standard preparation; C_U is the nominal concentration, in mg per mL, of tazobactam or piperacillin in the Assay preparation; and r_U and r_S are the tazobactam or piperacillin peak area responses obtained from the Assay preparation and the Standard preparation, respectively.

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