Tedizolid Plasma Pharmacokinetics Are Comparable in Obese and Nonobese Patients and Healthy Subjects

INTRODUCTION

- Tedizolid phosphate is a novel oxazolidinone being investigated for the treatment of Gram-positive infections, including those caused by methicillin-resistant Staphylococcus aureus (MRSA).
- In 2 recent Phase 3 trials in patients with acute bacterial skin and skin structure infections (ABSSSI), tedizolid (200 mg once daily for 6 days) demonstrated noninferior efficacy to linezolid (600 mg twice daily for 10 days) and was generally well tolerated.1
- Obesity is a key patient characteristic shown to alter dose-exposure relationships with some drugs, resulting in the need for dose adjustments for this particular patient population.2,3
- Population Pharmacokinetics (PopPK) analysis used data from 647 patients with ABSSSI (obese = 193, nonobese = 454).

METHODS

- The analysis population consisted of 821 individuals who received either oral or IV tedizolid (200 mg once daily for 6 days) from 0 to 24 hours (AUCss(0-24)) and maximum plasma concentration at steady state curve from zero to infinity (AUC0-∞). Nonobese subjects were used as the reference population.
- The reason for this difference has not been determined, and it is not currently known whether linearized dose modification is warranted in obese patients.
- Previous studies have shown that, following oral or intravenous (IV) administration of tedizolid phosphate 200 mg, tedizolid exposure in elderly persons, adolescents, and subjects with severe hepatic or renal impairment (including those requiring hemodialysis) was similar to that of control groups.4,5,6
- In the current analysis, PopPK of body weight and body mass index (BMI) on tedizolid phosphate pharmacokinetics (PK) was evaluated to determine whether plasma exposure parameters of tedizolid are comparable in obese and nonobese individuals.

RESULTS

- NCA assessments showed that observed plasma exposure measures (AUC and Cmax) were similar for obese and nonobese healthy subjects who had received either oral or IV tedizolid phosphate (Table 1). AUC0-∞ was within the 80-125% noninferiority boundary.

<table>
<thead>
<tr>
<th>Classification</th>
<th>n</th>
<th>GM</th>
<th>90% CI</th>
<th>Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral obese</td>
<td>51</td>
<td>28.7</td>
<td>0.82-0.89</td>
<td>1.07</td>
</tr>
<tr>
<td>Oral nonobese</td>
<td>72</td>
<td>28.5</td>
<td>0.82-0.89</td>
<td>1.07</td>
</tr>
<tr>
<td>IV obese</td>
<td>26</td>
<td>29.4</td>
<td>0.88-0.93</td>
<td>1.07</td>
</tr>
<tr>
<td>IV nonobese</td>
<td>56</td>
<td>28.8</td>
<td>0.88-0.93</td>
<td>1.07</td>
</tr>
</tbody>
</table>

- PopPK analysis showed that only IBW had a statistically significant effect on tedizolid plasma PK.
- NCA population parameters for observed plasma exposure measures (AUCss(0-24)) and maximum plasma concentration (Cmax) were similar between obese and nonobese patients.
- IBW, as well as the lack of relationship between tedizolid exposure and baseline BMI, were used as covariates in the final model.
- These findings suggest that tedizolid phosphate could be administered to obese patients without dose adjustment.

CONCLUSIONS

- Observed tedizolid plasma levels were similar for obese and nonobese individuals who received tedizolid phosphate.
- PopPK analysis showed that baseline weight and BMI had a statistically significant effect on tedizolid plasma exposure and that the effect of BMI was not clinically meaningful.
- These findings suggest that tedizolid phosphate could be administered to obese patients without dose adjustment.

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REFERENCES

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