Tedizolid phosphate (TR-701 FA) is a novel oxazolidinone prodrug whose active moiety, tedizolid, has improved potency against Gram-positive pathogens and pharmacokinetics, allowing once-daily administration. Given linezolid warnings for drug-drug and drug-food interactions mediated by monoamine oxidase (MAO) inhibition, including sporadic serotonergic toxicity, these studies evaluated tedizolid for potential MAO interactions. In vitro, tedizolid and linezolid were reversible inhibitors of human MAO-A and MAO-B; the 50% inhibitory concentration (IC₅₀) for tedizolid was 8.7 µM for MAO-A and 5.7 µM for MAO-B and 46.0 and 2.1 µM, respectively, with linezolid. Tedizolid phosphate was negative in the mouse head twitch model of serotonergic activity. Two randomized placebo-controlled crossover clinical studies assessed the potential of 200 mg/day tedizolid phosphate (at steady state) to enhance pressor responses to coadministered oral tyramine or pseudoephedrine. Sensitivity to tyramine was determined by comparing the concentration of tyramine required to elicit a ≥30-mmHg increase in systolic blood pressure (TYR₃₀) when administered with placebo versus tedizolid phosphate. The geometric mean tyramine sensitivity ratio (placebo TYR₃₀/tedizolid phosphate TYR₃₀) was 1.33; a ratio of ≥2 is considered clinically relevant. In the pseudoephedrine study, mean maximum systolic blood pressure was not significantly different when pseudoephedrine was coadministered with tedizolid phosphate versus placebo. In summary, tedizolid is a weak, reversible inhibitor of MAO-A and MAO-B in vitro. Provocative testing in humans and animal models failed to uncover significant signals that would suggest potential for hypertensive or serotonergic adverse consequences at the therapeutic dose of tedizolid phosphate. Clinical studies are registered at www.clinicaltrials.gov as NCT01539473 (tyramine interaction study conducted at Covance Clinical Research Center, Evansville, IN) and NCT01577459 (pseudoephedrine interaction study conducted at Vince and Associates Clinical Research, Overland Park, KS).
Tedizolid and Monoamine Oxidase Activity

R.N.; therefore, it is less reliant on residues associated with linezolid resistance mutations (21).

All doses studied in a phase 2 dose-ranging study in patients with complicated skin and skin structure infections provided similar efficacy (94 to 98% response rates) (22). The lowest effective dose of 200 mg was selected for phase 3 studies in subjects with acute bacterial skin and skin structure infections (ABSSSI); in ESTABLISH-1, 200 mg once-daily (QD) tedizolid phosphate for 6 days was found to be noninferior to 600 mg linezolid every 12 h for 10 days (23).

During nonclinical testing, tedizolid was screened for interactions across 177 biochemical, 30 enzyme, and 147 binding assays. Initial screens used 20 μM tedizolid, which is 20- to 40-fold greater than the estimated maximal plasma concentration (Cmax) for steady-state free drug when 200 mg per day tedizolid phosphate is administered to patients. Among all interactions tested, >50% binding or activity inhibition was detected only for MAO-A and MAO-B, prompting evaluation of in vitro MAO inhibitor activity and potential relevant consequences in vivo. Established methods (10, 12, 16, 17, 24, 25) were used to assess MAO inhibitor activity of tedizolid in vitro and evaluate the impact of tedizolid phosphate on MAO-related effects in human and animal models.

MATERIALS AND METHODS

Animal studies were conducted in accordance with the Guidance for the Care and Use of Laboratory Animals manual and approved by the local Institutional Animal Care and Use Committee. Human studies were conducted in accordance with current FDA regulations, International Conference on Harmonisation Good Clinical Practice guidelines, and the Basic Principles of the Declaration of Helsinki. Clinical studies are registered at www.clinicaltrials.gov as NCT01539473 (tyramine interaction study conducted at Covance Clinical Research Center, Evansville, IN) and NCT01577459 (pseudoephedrine interaction study conducted at Vince and Associates Clinical Research, Overland Park, KS).

MAO inhibition in vitro. Inhibition of human MAO-A (recombinant or isolated from placenta) or human MAO-B (recombinant or isolated from platelets) was evaluated in vitro using standard methods, and each reaction was performed in duplicate (27–29). To determine the concentration of drug inhibiting 50% of enzyme activity (IC50), MAO-A or MAO-B was preincubated for 15 min at 37°C with various concentrations of tedizolid (0.3, 1, 3, 10, and 30 μM), linezolid (1, 3, 10, 30, 100, and 300 μM), and a positive irreversible inhibitor control [1 μM clorgyline for MAO-A or 10 μM (R)-deprenyl for MAO-B]. MAO-A activity was determined spectrophotometrically by monitoring conversion of 50 to 150 μM kynuramine to 4-hydroxyquinolone. The activity of MAO-B was assessed by monitoring the conversion of 500 μM benzylamine to benzaldehyde. To assess the reversibility of MAO inhibition, tedizolid or linezolid was incubated with MAO-A or MAO-B and the appropriate substrate, and then the reaction mixture was dialyzed overnight at 4°C. The following day, enzyme activity was determined as described above.

Moclobemide and clorgyline were used as positive controls for reversible and irreversible activity against MAO-A, respectively. Lazabemide and deprenyl were the positive controls for reversible and irreversible inhibition of MAO-B.

Human studies. Potential tedizolid interaction with oral tyramine or pseudoephedrine was evaluated in 2 randomized, double-blind, placebo-controlled crossover studies. Healthy men and women aged 18 to 45 years were screened for general health; absence of cardiovascular, neurologic, or ophthalmologic conditions; and use of dietary or herbal preparations or medications that would interfere with blood pressure and cardiovascular assessment. For subjects in the tyramine dose-escalation trial, systolic blood pressure response to a 100-mg test dose of tyramine was evaluated during screening to exclude those with increases of ≥30 mmHg.

After signing informed consent, subjects were admitted to the clinical study center to control diet, activity, and external factors that can influence blood pressure.

The dose of tyramine required to elicit an increase in systolic blood pressure of ≥30 mmHg (TYR30) was used to evaluate potential MAO interactions (16, 30). In each of 2 sequential cohorts, subjects were randomized to receive oral placebo or 200 mg tedizolid phosphate per day during the first treatment period (up to 14 days), with a 2-day minimum washout, followed by treatment with the opposite intervention for up to 14 days. For the first 2 days of each period, placebo or tedizolid phosphate was administered. Starting on day 3, a single dose of tyramine was administered under fasting conditions 2 h after placebo or tedizolid phosphate administration. Baseline systolic blood pressure and heart rate were recorded prior to tyramine administration on day 3 and were monitored every 5 min until 2 h after tyramine administration on day 3 and each subsequent day of the treatment period. The initial tyramine dose on day 3 was 25 mg; 50 mg per day was added on subsequent days until TYR30 was reached or to a maximum of 575 mg tyramine on day 14. TYR30 was...
determined by a 30-mmHg rise in systolic blood pressure (over baseline on day 3) recorded in 3 consecutive measurements (5 min apart) after tyramine administration. Trough drug concentrations were measured in blood collected within 15 min before tedizolid phosphate administration. Continuous-recording electrocardiograms started 20 min before tyramine administration and continued through the 2-h observation period.

Treatment effects were assessed in the subset of subjects achieving TYR30 in both treatment periods; the tyramine sensitivity factor was calculated as the ratio of placebo TYR30 to tedizolid TYR30. A tyramine sensitivity factor of $\geq 2$ is considered a clinically relevant increase in tyramine sensitivity (16).

The pseudoephedrine study followed the basic crossover design used to assess linezolid interactions (17). In each study period, subjects received 200 mg oral tedizolid phosphate or placebo per day for 5 days to ensure a steady-state level of tedizolid, with a 2-day washout between treatment periods. On day 5, 60 mg pseudoephedrine was administered with tedizolid phosphate or placebo. Baseline systolic blood pressure and heart rate were recorded 15 min prior to study drug administration on day 5 and then hourly for 8 h and at 10, 12, and 24 h after administration. Electrocardiograms were recorded prior to and at 3 and 10 h after drug administration. Measurements of tedizolid and pseudoephedrine in plasma indicated no effects of pseudoephedrine on tedizolid pharmacokinetics or tedizolid on pseudoephedrine pharmacokinetics.

Serotonergic activity in murine model. Head twitch response was measured in adult male mice using validated protocols (24–26, 31). Head twitch response is a short burst of rapid left-right head shaking that is distinct from grooming behavior; the frequency of head shakes is a surrogate measure of in vivo serotonin receptor 2A activation (26). Study animals were randomized to 1 of 8 treatment groups and pretreated with intraperitoneal injection of the priming agent carbidopa (10 mg/kg) at time zero, followed by intraperitoneal injection of test agent at 15 min later. Test agents were vehicle (phosphate-buffered saline), 50 mg/kg of body weight linezolid (human therapeutic equivalent dose), 20 mg/kg fluoxetine HCl, 10 mg/kg moclobemide (all from AK Scientific Inc., Union City, CA), or 10, 30, 100, or 300 mg/kg tedizolid phosphate (TR-701 FA; to provide 1×, 3×, 10×, or 30× the human equivalent therapeutic exposure; Trius Therapeutics). Fifteen minutes later, each animal received an intraperitoneal injection of 50 mg/kg 5-hydroxy-5-tryptophan (Spectrum Chemical Manufacturing Corporation, Gardena, CA), a serotonin precursor. Head twitches were counted for 30 min after 5-hydroxy-5-tryptophan injection by technicians blinded to treatment assignment.

After the observation period, animals were anesthetized and blood collected by cardiac puncture for measurement of tedizolid and linezolid drug concentrations. Cerebellar concentrations of neurotransmitters and metabolites generated by MAO activity were determined from brains stored at $-80^\circ$C. Concentrations of norepinephrine, dopamine, metabolites homovanillic acid and 3,4-dihydroxyphenylacetic acid, and serotonin and its metabolite, 5-hydroxyindoleacetic acid, were determined in brain tissue homogenates in 0.2 N perchloric acid using C18 reverse-phase high-performance liquid chromatography with electrochemical detection (CoulArray detector; Thermo Fisher, Chelmsford, MA) and 3,4-dihydroxybenzylamine as an internal standard. The mobile phase was a mixture of 90 mM sodium acetate, 35 mM citric acid, 130 $\mu$M EDTA, 230 $\mu$M 1-octanesulfonic acid, and 10% (vol/vol) methanol. The flow rate was set at 1 ml/min, and all analytes were identified according to the retention times of the appropriate standards and quantified by calculations using peak areas.

Statistical analyses. Continuous data were summarized using descriptive statistics, and categorical data were expressed as counts and percentages.

<table>
<thead>
<tr>
<th>Subject</th>
<th>Placebo</th>
<th>Tedizolid phosphate</th>
<th>Tyramine sensitivity factor$^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>275</td>
<td>275</td>
<td>1.00</td>
</tr>
<tr>
<td>2</td>
<td>325</td>
<td>425</td>
<td>0.76</td>
</tr>
<tr>
<td>3</td>
<td>425</td>
<td>425</td>
<td>1.00</td>
</tr>
<tr>
<td>4</td>
<td>575</td>
<td>275</td>
<td>2.09</td>
</tr>
<tr>
<td>5</td>
<td>375</td>
<td>275</td>
<td>1.36</td>
</tr>
<tr>
<td>6</td>
<td>475</td>
<td>325</td>
<td>1.46</td>
</tr>
<tr>
<td>7</td>
<td>475</td>
<td>375</td>
<td>1.27</td>
</tr>
<tr>
<td>Median (range)</td>
<td>425.0 (275, 575)</td>
<td>325.0 (275, 425)</td>
<td>1.270 (0.76, 2.09)</td>
</tr>
<tr>
<td>Geometric mean</td>
<td>439</td>
<td>330</td>
<td>1.33 (1.05, 1.69)</td>
</tr>
</tbody>
</table>

$^a$ TYR30 is the dose of tyramine required to elicit a $\geq 30$-mmHg increase in systolic blood pressure.

RESULTS

MAO enzyme activity. Tedizolid demonstrated weak, reversible inhibition of MAO activity in vitro, with mean IC50s of 8.7 and 5.7 $\mu$M for MAO-A and MAO-B, respectively. Mean IC50 for linezolid was 46.0 and 2.1 $\mu$M, respectively. For reference, the mean IC50 for clorgyline inhibition of MAO-A was 2.1 nM, and the mean IC50 for deprenyl inhibition of MAO-B was 12 nM. Tedizolid and linezolid are 3 orders of magnitude less potent than clorgyline and 2 orders less potent than deprenyl. Incubation with 10 $\mu$M tedizolid inhibited MAO-A by 64% and MAO-B by 62%, while the prodrug tedizolid phosphate had minimal effects (7 and 6% inhibition, respectively). Reversibility studies confirmed that, like linezolid, tedizolid is a reversible inhibitor of MAO-A and MAO-B in vitro after overnight incubation (data not shown).

Subject demographics. The tyramine sensitivity study enrolled 30 subjects; 50% were men. The mean (standard deviation [SD]) age was 32.7 (6.9) years, and mean (SD) body mass index was 26.1 (2.6) kg/m². The pseudoephedrine study enrolled 18 subjects; the majority (83%) were men. The mean (SD) age was 34.4 (7.5) years, and mean body mass index was 26.7 (2.5) kg/m².

Tyramine pressor sensitivity. Trough levels of tedizolid were relatively unchanged after day 2 of tedizolid phosphate administration, indicating the steady state was achieved prior to the beginning of tyramine administration on day 3. Seven subjects experienced a systolic blood pressure increase of $\geq 30$ mmHg following tyramine administration during both placebo and tedizolid phosphate treatment phases, with median TYR30 values of 425 and 325 mg, respectively (Table 1). The geometric mean ratio (placebo to tedizolid phosphate) was 1.33 (90% confidence interval [CI], 1.05 to 1.69). Individual tyramine sensitivity factor values were $>2$ in only 1 of the 7 subjects, for whom the value was 2.1.

Tedizolid phosphate was generally well tolerated, with no serious treatment-emergent adverse events. Almost all subjects (29/30) experienced at least 1 adverse event during one or both treat-
ment periods. Most subjects (25/30) experienced palpitations, a recognized side effect of tyramine challenge studies (16, 30, 32). All 7 subjects who achieved a TYR30 with both tedizolid phosphate and placebo treatments reported palpitations. These events were balanced between the treatments with 3 subjects having palpitations during tedizolid phosphate treatment only, 2 during placebo treatment only, and 2 during both treatment periods. Three subjects were withdrawn due to mild palpitations concomitant with tyramine administration during the tedizolid phosphate treatment period. Other common adverse events included gastrointestinal disorders, headache, and dizziness.

**Pseudoephedrine challenge.** Blood pressure responses to pseudoephedrine were recorded for 24 h on day 5 (Fig. 2). Mean maximum increases in blood pressure and heart rate were not significantly different between placebo and tedizolid phosphate treatments (Table 2). When exposed to concomitant pseudoephedrine and tedizolid phosphate, only 4 (22%) subjects experienced a systolic blood pressure rise of ≥15 mmHg. Similarly, 5 (28%) subjects experienced a systolic blood pressure elevation of ≥15 mmHg when pseudoephedrine was administered with placebo.

There were no serious adverse events or adverse events leading to study drug discontinuation. All treatment-emergent adverse events were mild, occurred only after pseudoephedrine administration on day 5 of either treatment period, and were reported by 5 (22%) and 4 (16%) subjects during placebo and tedizolid phosphate treatments, respectively. The only adverse events experienced by more than 1 subject were headache (1 with placebo, 1 with tedizolid phosphate) and a blood bilirubin increase (1 during both treatment periods, 1 during tedizolid phosphate treatment only). No meaningful electrocardiogram changes were noted.

**Murine serotoninergic model.** Compared to that of vehicle-treated animals, the number of head twitches was statistically significantly elevated in animals treated with 10 mg/kg moclobemide (a potent, reversible MAO-A inhibitor), with 20 mg/kg fluoxetine (a potent serotonin reuptake inhibitor) (5), or with 50 mg/kg linezolid (Fig. 3). In contrast to 50 mg/kg linezolid, tedizolid phosphate did not increase head twitch response over the vehicle level at any dose examined. The plasma linezolid concentration in mouse at 45 to 60 min after intraperitoneal administration was similar to the $C_{max}$ in humans administered 600 mg twice daily (BID) (18), whereas tedizolid concentrations in mice exceeded the tedizolid $C_{max}$ in humans administered 200 mg/day tedizolid phosphate by up to ~25-fold (33) (Table 3). Protein binding is similar in mice and humans for both tedizolid (~80%) and linezolid (~30%) (33–36). Only moclobemide caused significant decreases in MAO-dependent metabolites of serotonin (5-hydroxyindoleacetic acid) and dopamine (homovanillic acid and 3,4-dihydroxyphenylacetic acid) and an increase in mean (SD) brain serotonin from 3,716 (305) to 7,265 (637) ng/g tissue ($P < 0.05$), explaining the markedly greater head twitch rate with moclobemide than with linezolid or fluoxetine.

**DISCUSSION**

Tedizolid and linezolid both show weak and reversible MAO inhibitory activity in vitro, but for tedizolid the greater antimicrobial potency, longer half-life (allowing once-daily dosing), greater plasma protein binding (resulting in lower free-drug concentrations), minimal accumulation after several days of administration, and shorter duration of therapy may result in reduced potential for MAO interactions than linezolid. Using a worst-case scenario for $C_{max}$ and the inhibitory effects of tedizolid and linezolid on MAO-A and MAO-B activity from this study, the relationship between the anticipated peak concentration of tedizolid or lin-

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**FIG 2** Blood pressure response to 60 mg pseudoephedrine in placebo- and tedizolid phosphate-pretreated study populations. Patients ($n=18$) were randomized to oral placebo or oral tedizolid phosphate doses of 200 mg per day for 4 days; on the fifth day, 60 mg pseudoephedrine was administered with the morning dose of placebo or tedizolid phosphate, and blood pressure was recorded over the subsequent 24 h. Blood pressure was measured within 15 min prior to drug administration (Pre), every hour for 8 h after study drug administration, and at 10, 12, and 24 h.

**TABLE 2** Maximum changes in blood pressure and heart rate following pseudoephedrine coadministration with placebo and tedizolid phosphate

<table>
<thead>
<tr>
<th>Parameter $^a$</th>
<th>Tedizolid phosphate ($n=18$)</th>
<th>Placebo ($n=18$)</th>
<th>Difference (95% CI)</th>
<th>$P$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic BP (mmHg)</td>
<td>11.6</td>
<td>12.1</td>
<td>-0.5 (-3.8, 2.7)</td>
<td>0.7309</td>
</tr>
<tr>
<td>Diastolic BP (mmHg)</td>
<td>6.7</td>
<td>6.8</td>
<td>-0.1 (-2.0, 0.7)</td>
<td>0.8966</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>13.6</td>
<td>15.2</td>
<td>-1.6 (-3.8, 0.7)</td>
<td>0.1689</td>
</tr>
</tbody>
</table>

$^a$ Least-square (LS) means from analysis of variance model.

$^b$ BP, blood pressure.
ezolid can be compared to the concentration required to inhibit 50% of MAO activity (Table 4). The tedizolid estimated free-drug concentration at C\(_{\text{max}}\) (fC\(_{\text{max}}\)) is severalfold lower than the IC\(_{50}\) of MAO-A and MAO-B activity, while the linezolid free-drug concentration is similar to and greater than IC\(_{50}\)s for MAO-A and MAO-B, respectively.

Negative results in the clinical studies assessing the potential for tedizolid phosphate to interact with tyramine or pseudoephedrine support results of nonclinical studies which failed to detect a meaningful increase in tyramine sensitivity in rats with tedizolid at greater than 30-fold the exposure of a human therapeutic dose (37). Although using linezolid as a direct positive control in the clinical studies might have strengthened the results, demonstrating similarity to placebo was deemed to be a more stringent and meaningful endpoint. Adding an additional linezolid arm to the preferred crossover design of the clinical studies was not feasible due to increased complexity and subject burden. The linezolid package insert cautions patients to avoid high-tyramine diets and use of preparations containing pseudoephedrine or phenylpropanolamine to minimize the risk of blood pressure elevation (18).

Results of these clinical studies, showing no meaningful interaction with pseudoephedrine or tyramine, contrast with evidence of MAO inhibition reported for linezolid (16, 17). Individual tyramine sensitivity values in the tyramine study only slightly exceeded 2.0 in 1 of 7 subjects (maximum of 2.1), compared to 8 of 10 linezolid-treated subjects with tyramine sensitivity factor values of 2.0 (maximum of 5.0) (16). The tedizolid phosphate geometric mean tyramine sensitivity ratio of 1.33 is lower than reported values of 3.48 for linezolid and 4.97 for moclobemide (16) and similar to a value of 1.5 for placebo (38).

A typical tyramine-rich meal is expected to contain no more than 40 mg tyramine (4). The lowest TYR\(_{30}\) dose for any subject in this study was 275 mg (for both placebo- and tedizolid phosphate-treated groups) of tyramine under fasted conditions. Sensitivity to tyramine as part of a meal is expected to be decreased approximately 2-fold due to reduced tyramine bioavailability with food (39). Extrapolating results of our study, a 30-mmHg increase in systolic blood pressure might be expected with a meal containing 550 mg of tyramine. Therefore, it is not anticipated that tedizolid at steady state after repeated 200-mg tedizolid phosphate administrations would produce a clinically meaningful pressor response to a tyramine-rich meal.

### TABLE 4 Relationship between free-drug concentrations in plasma and IC\(_{50}\) for MAO inhibition

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Tedizolid phosphate (200 mg QD)</th>
<th>Linezolid (600 mg BID)</th>
</tr>
</thead>
<tbody>
<tr>
<td>C(_{\text{max}}) μM</td>
<td>6.5(^*)</td>
<td>62.8(^*)</td>
</tr>
<tr>
<td>Protein binding, %</td>
<td>80</td>
<td>31</td>
</tr>
<tr>
<td>fC(_{\text{max}}) μM</td>
<td>1.3</td>
<td>43.4</td>
</tr>
<tr>
<td>MAO-A IC(_{50}) μM</td>
<td>8.7</td>
<td>46.0</td>
</tr>
<tr>
<td>fC(<em>{\text{max}})/IC(</em>{50})</td>
<td>0.15</td>
<td>0.94</td>
</tr>
<tr>
<td>MAO-B IC(_{50}) μM</td>
<td>5.7</td>
<td>2.1</td>
</tr>
<tr>
<td>fC(<em>{\text{max}})/IC(</em>{50})</td>
<td>0.23</td>
<td>21.0</td>
</tr>
</tbody>
</table>

\(^*\) Adjusted for molecular weight of 370.34 (31).

\(^*\) Adjusted for molecular weight of 337.35 (18).

#### FIG 3 Mouse head twitch rate following tedizolid phosphate, linezolid, fluoxetine, or moclobemide treatment. Twitch frequency is shown as means ± SD (n = 8 mice/group). Tedizolid refers to tedizolid phosphate. *, P < 0.05 versus the control group.
Rare cases of serotonin syndrome associated with concomitant linezolid and serotonergic medication have been reported. A retrospective review of 20 comparator-controlled linezolid clinical trials involving >10,000 participants identified approximately 2.8-fold higher, but not significantly different, incidence of serotonin toxicity for linezolid-treated versus comparator-treated patients (40). A number of drugs with potential (alone or in combination) for linezolid interaction leading to serotonin syndrome, including certain tricyclic antidepressants, serotonin reuptake inhibitors, serotonin-norepinephrine reuptake inhibitors, and opioids, have been identified (13, 41–43).

Serotonergic effects cannot ethically be investigated prospectively in humans due to low frequency of events and severe and potentially lethal consequences. Simple and predictable murine behavioral models, reflecting central serotonergic overstimulation, have been used in antidepressant drug development for decades. In our study, mouse head twitch response results showed no propensity for MAO-related serotonergic adverse effects of tedizolid, unlike the possible controls fluoxetine, moclobemide, and linezolid, which demonstrated serotonergic overstimulation via serotonin reuptake inhibition (fluoxetine) or MAO inhibition (moclobemide and linezolid).

The consistent lack of evidence for linezolid peripheral MAO inhibitor activity in two clinical studies and central MAO inhibitor activity in a mouse model of serotonergic response, even at a 25-fold multiple of the anticipated therapeutic exposure, suggest that physiologically relevant MAO interactions can be avoided with linezolid phosphate therapy.

Summary. While tedizolid has weak MAO inhibitory activity in vitro, its antibacterial potency (allowing lower doses) and favorable pharmacokinetic profile suggest low probability for MAO-related adverse consequences at doses currently being investigated for clinical use in ABSSSI. Provocative testing in both humans and animal models failed to uncover clinically significant signals for potential MAO interactions observed with clinical use of linezolid.

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