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ORIGINAL RESEARCH

# Health Technology Assessment of Oxazolidinones for MRSA-Associated Complicated Skin and Soft Tissue Infections

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**Purpose:** This study aims to provide a reference for the introduction and utilization of oxazolidinone drugs in medical institutions, based on the authoritative Chinese guideline, Rapid Guideline for Drug Evaluation and Selection in Chinese Medical Institutions (2nd Edition) (Rapid Guideline).

**Patients and Methods:** Based on the Rapid Guideline, this study conducted a comprehensive literature search across relevant databases, including the China National Knowledge Infrastructure (CNKI), PubMed, Embase, and the Cochrane Library, as well as drug labels and relevant clinical guidelines. A health technology assessment (HTA) was then performed on three oxazolidinone drugs across five dimensions: pharmaceutical properties, efficacy, safety, economy, and other attributes.

**Results:** The final evaluation results from highest to lowest were tedizolid (83.52 points), linezolid (80.02 points), and contezolid (72.79 points). The evaluation results of tedizolid across the five dimensions were as follows: pharmaceutical properties (25.5 points), efficacy (25 points), safety (17.5 points), economy (9.02 points), and other attributes (6.5 points). For linezolid, the scores were pharmaceutical properties (25 points), efficacy (25 points), safety (18 points), economy (5.02 points), and other attributes (7 points). For contezolid, the scores were pharmaceutical properties (24 points), efficacy (22 points), safety (18.5 points), economy (4.29 points), and other attributes (4 points).

**Conclusion:** Based on the comprehensive evaluation across five key dimensions, the recommended prioritization of oxazolidinone antibiotics is as follows: tedizolid, linezolid, and contezolid. The ranking was primarily driven by tedizolid's once-daily dosing and lowest total course cost, linezolid's pediatric indication and widespread availability, and contezolid's superior safety profile, although its overall score was limited by higher cost and lack of guideline recommendations. This study recommends the selection of tedizolid, linezolid, and contezolid for use in medical institutions during the introduction and application of oxazolidinone antibiotics.

**Keywords:** oxazolidinone drugs, complicated SSTIs, MRSA, health technology assessment

## Introduction

Skin and soft tissue infections (SSTIs) are generally classified into two categories based on clinical complexity: uncomplicated SSTIs and complicated SSTIs (cSSTIs). Uncomplicated SSTIs include superficial infections such as cellulitis, simple abscesses, impetigo, and furuncles, which can typically be managed with pharmacological therapy or incision and drainage. Complicated SSTIs involve deeper soft tissue infections, including necrotizing infections, infected ulcers, infected burns, and severe abscesses, which often require surgical intervention, such as drainage and debridement.[1]

SSTIs are among the most common bacterial infections in humans. In the United States, the incidence and prevalence of SSTIs continue to rise,[2] accounting for approximately 10% of hospital admissions;[3] these infections frequently affect the lower limbs, with a recurrence rate up to 50%.[4] In Europe, among patients hospitalized for cSSTIs, cellulitis is the most common diagnosis, accounting for 59.1% of cases.[4] Methicillin-resistant Staphylococcus aureus (MRSA) has

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become a significant global public health concern, with infections caused by this pathogen posing an increasingly serious challenge.[5] Since the late 1990s, community-associated MRSA (CA-MRSA) has risen rapidly, with infection rates demonstrating a pronounced upward trend.[6] Notably, CA-MRSA accounts for approximately 38%–84% of SSTIs in regions such as the United States,[5] and is strongly associated with the highly virulent USA300 clone and the Panton–Valentine leukocidin (PVL) toxin.[5] Both community-associated and healthcare-associated MRSA infections can lead to significant increases in morbidity, mortality,[7] and healthcare costs.[8]

Vancomycin has long been considered the gold standard for treating cSSTIs caused by MRSA; however, with the continued introduction of new antimicrobial drugs, several alternative drugs have become available.[9] Oxazolidinones represent a prominent class of such alternatives, including linezolid, tedizolid, and contezolid. Linezolid is an effective alternative to vancomycin, demonstrating comparable clinical and microbiological efficacy in the treatment of MRSA-induced cSSTIs,[10] while also shortening hospital stays, reducing treatment costs,[11] and decreasing the need for surgical interventions.[12] Tedizolid, a novel oxazolidinone, has shown efficacy comparable to the 10-day linezolid regimen in a 6-day short-course treatment,[13] with superior safety, lower hematological toxicity, and reduced risk of drug–drug interactions.[14] Similarly, contezolid, another new oxazolidinone, demonstrated non-inferior efficacy to linezolid in clinical trials, particularly exhibiting strong antibacterial activity against Gram-positive pathogens such as MRSA, while significantly reducing the incidence of leukopenia and thrombocytopenia, thereby offering superior hematological safety.[15]

Currently, linezolid, tedizolid, and contezolid have been approved for marketing in China. However, China still lacks relevant guidelines and health technology assessment (HTA) studies for tedizolid and contezolid. To support the introduction and clinical application of oxazolidinone drugs in medical institutions and to ensure patients receive safe, effective, affordable, and appropriate pharmacological treatment, this study conducted a health technology assessment of three oxazolidinones based on the 2023 authoritative Chinese guideline, Rapid Guideline for Drug Evaluation and Selection in Chinese Medical Institutions (2nd Edition) (Rapid Guideline).[16]

# Materials and Methods

## Study Period

The study was conducted from May 31, 2025, to July 1, 2025.

## Evaluation Basis

This study was designed as an HTA based on the Rapid Guideline, which was published in 2023. Tailored to the national context of China, the guideline integrates Mini-Health Technology Assessments (Mini-HTA) and the System of Objectified Judgement Analysis (SOJA) method to establish a drug evaluation framework comprising five key dimensions: pharmaceutical properties, efficacy, safety, economy, and other attributes. The evaluation dimensions and their respective weightings were determined using the Delphi method by the guideline steering committee and expert panel. The Rapid Guideline has been widely adopted in the field of drug evaluation and selection in Chinese medical institutions.

## Evaluation of Drugs

To ensure comparability in drug quality, only originator drugs were included in this study. The basic information of all drugs assessed is presented in Table 1.

## Source of Evidence and Evaluation Contents

The relevant randomized controlled trials (RCTs), guidelines, systematic reviews, and meta-analyses included in this study were retrieved from databases such as the China National Knowledge Infrastructure (CNKI), PubMed, Embase, and the Cochrane Library. Search keywords included “linezolid” “tedizolid” “contezolid” “skin and soft tissue infections” “guidelines” “drug evaluation guidelines” “randomized controlled trials” “systematic reviews” and “meta-analysis. ” Inclusion criteria: (1) randomized controlled trials of linezolid, tedizolid, or contezolid for the treatment of SSTIs

**Table 1** Oxazolidinones Drugs Information

| Generic Name/ Trade Name | Dosage Form (ROA) | Approved Regions (Year) | Manufacturer |
|---|---|---|---|
| Linezolid/ Zyvox | Tablets (Oral) Injections (IV) | China (2007) Europe (2008) United States (2000) Japan (2001) | Pfizer |
| Tedizolid/ Sivextro | Tablets (Oral) Injections (IV) | China (2019) Europe (2015) United States (2014) Japan (2018) | Merck Sharp |
| Contezolid/ Youxitai | Tablets (Oral) | China (2021) | Shanghai Mengke |

**Abbreviations**: ROA, route of administration; IV, intravenous.

caused by MRSA; (2) SSTI treatment guidelines published by government agencies and authoritative academic organizations; (3) systematic reviews and meta-analyses including RCTs of the aforementioned drugs for the treatment of MRSA-induced SSTIs.

The relevant drug labels, registration data, drug prices, and adverse reaction monitoring data included in this study were retrieved from the Yaozh.com database, the official website of the National Medical Products Administration (NMPA) of China, the official website of Healthcare Security Administration of Guangdong Province, the VigiAccess database, and the US FDA Adverse Event Reporting System (FAERS) database. The search keywords included "linezolid," "tedizolid," and "contezolid."

The search time frame was from the inception of each database to May 31, 2025.

Relevant databases and sources of evidence are detailed in Table 2.

## Statistical Analysis

### Scoring Framework and Weighting

This study employed a multi-criteria scoring system established by the Rapid Guideline to quantitatively evaluate three oxazolidinone antibiotics. The evaluation framework comprised five domains: Pharmaceutical Properties (28 points), Efficacy (27 points), Safety (25 points), Economy (10 points), and Other Attributes (10 points), with a maximum total score of 100 points.

**Table 2** Relevant Databases and Sources of Evidence

| Evidence Category | Databases/Sources |
|---|---|
| Randomized controlled trials; Guidelines; Systematic reviews; Meta-analyses | PubMed; Embase; Cochrane Library; CNKI |
| Drug Labels | Yaozh.com Database |
| Registration Data | NMPA |
| Drug Prices | Healthcare Security Administration of Guangdong Province |
| Adverse Reaction Monitoring Data | FAERS; VigiAccess |

**Abbreviations**: CNKI, China National Knowledge Infrastructure; NMPA, National Medical Products Administration; FAERS, US FDA Adverse Event Reporting System.

## Score Calculation and Aggregation Rules

Domain Scores: The score for each domain was calculated as the sum of all its sub-criteria scores:

$$Domain\ Score = \sum_{i=1}^{n} Sub - criterion\ Score_i$$

Total Score: The total score was the sum of the five domain scores:

$$Total\ Score = \sum Domain\ Scores$$

Precision Handling: To ensure reproducibility, all calculations were performed using raw data values without intermediate rounding. The final total scores were reported to two decimal places.

Specific Scoring Formulae for Economy Sub-criteria: The scoring of the two sub-criteria under the Economy domain followed specific formulae, as detailed below.

Drugs with the same generic name (3 points):

$$Score = \frac{Lowest\ Average\ Daily\ Cost}{Average\ Daily\ Cost\ of\ Evaluated\ Drug} \times 3$$

Substitutable medicines for main indications (7 points):

$$Score = \frac{Lowest\ Total\ \ Course\ Cost}{Total\ Course\ Cost\ of\ Evaluated\ Drug} \times 7$$

The total course cost was calculated for a unified sequential therapy scenario. As the contezolid injection is not yet commercially available in China, its intravenous phase duration was set to 0 days with corresponding cost of 0 yuan. For linezolid and tedizolid, a 3-day intravenous phase was assumed. The oral treatment duration for all drugs was calculated as the maximum recommended course in the drug labels minus the intravenous duration (resulting in 11 days for linezolid, 3 days for tedizolid, and 14 days for contezolid). For the "Substitutable medicines" sub-criterion, the lowest total course cost among the three drugs was used as the numerator in the scoring formula.

## A Priori Rule for Guideline Recommendation Score

To avoid evaluation bias against innovative drugs not included in guidelines, this study predefined an a priori rule: If a drug has been approved by NMPA for the target indication, and high-quality, large-sample (n > 300) Phase III RCTs have confirmed its non-inferiority to already approved drugs of the same class, then the score of its "Guideline Recommendation" sub-criterion can be adjusted to 9 points.

The threshold of n > 300 was derived from the definition of "Grade A" evidence in Section 5.2.2 of the Rapid Guideline,[16] which explicitly includes "large-scale, multicenter randomized controlled trials (sample size > 300)". For contezolid, this rule is anchored on its pivotal Phase III trial,[15] which demonstrated non-inferiority to linezolid with a prespecified margin of −10% for clinical cure rate. The same rule would apply to the evaluation of future agents or indications that meet analogous criteria.

## Tie-Breaking Rule

In the event of a tie in the total score, the ranking was determined by sequentially comparing the scores of the following domains: 1) Efficacy, 2) Safety, and 3) Economy. No ties occurred in the final ratings of this study.

## Recommendation Categories

Based on the Rapid Guideline, the final total score determined the recommendation strength as follows: Strong Recommendation (Total Score ≥ 70), Weak or No Recommendation (60 ≤ Total Score < 70), and Not Recommended (Total Score < 60).

## Inter-Rater Agreement

Two clinical pharmacists performed the initial independent ratings. The inter-rater agreement for all domain-level items was assessed using the Intraclass Correlation Coefficient (ICC). The ICC was calculated using a two-way random-effects,

absolute-agreement model (ICC[2,1]) within the irr package of R software (version 4.5.1), with the unit of analysis being the 15 domain-level rating items across the three drugs. The resulting ICC was 0.984 (95% CI: 0.954 to 0.995), indicating excellent inter-rater agreement. Disagreement was observed only for the guideline-recommended score of contezolid, with one rater assigning 3 points and the other 9 points. Discrepancies in the initial ratings were resolved through consensus discussion with a third senior pharmacy expert.

### Sensitivity Analysis

To test the robustness of the study's core assumptions regarding the total drug scores and rankings, this study, in accordance with the evaluation logic of the Rapid Guideline, conducted a one-way sensitivity analysis on key variables affecting economic performance and overall scores. This was done to ensure the reliability of the conclusions and the clarity of their applicable boundaries. The aim of the analysis was to verify whether the total score ranking of the three oxazolidinone drugs remains stable when changes occur in the three categories of core assumptions (treatment cycle, cost parameters, and policy attributes), and to identify the sensitive factors and stable scenarios of the conclusions.

In terms of the specific analysis dimensions and parameter settings, they are as follows:

In terms of changes in treatment cycle, with reference to the range of maximum treatment courses recommended in drug labels, only the intravenous administration duration of linezolid and tedizolid (0–5 days) was adjusted, and the corresponding oral administration duration was matched simultaneously (oral administration duration = maximum course of treatment in the drug label - intravenous administration duration; specifically, linezolid: 14 days - intravenous duration, tedizolid: 6 days - intravenous duration). The cost calculation still followed the unified scenario of "intravenous + sequential oral administration". As no intravenous formulation of contezolid is currently available in China, the duration of its intravenous administration phase was fixed at 0 days with a corresponding cost of 0 in all sensitivity analysis scenarios; the oral administration duration was fixed at 14 days.

In terms of changes in cost parameters, the price type in the economic evaluation was replaced: the "lowest price of drugs with the same generic name" was replaced with the "median price of drugs with the same generic name" (all price data were sourced from the official website of Healthcare Security Administration of Guangdong Province to ensure consistency between the data source and the benchmark scenario), so as to test the impact of price fluctuations on economic scores and total scores.

In terms of changes in policy attributes, a "global neutral scenario" was constructed: China-specific policy indicators (including national medical insurance classification and payment restrictions, National Essential Drugs List, and inclusion status in National Centralized Procurement) were removed from the "Other Attributes" dimension, and only general indicators such as "status of manufacturing enterprises" and "global utilization" were retained. This was intended to analyze the impact of policy scenarios on rankings and enhance the reference value of the conclusions for international readers.

# Results

## Pharmacological Properties (28 Points)

### Pharmacological Effects

All three oxazolidinone drugs demonstrated definite clinical efficacy, precise mechanism of action, and either innovative mechanisms or targets of action, each scoring 5 points.

### In vivo Processes

All three oxazolidinone drugs have well-defined in vivo processes and complete pharmacokinetic parameters, each scoring 5 points.

### Pharmacy and Method of Use

The main ingredients and excipients of linezolid are clearly specified, scoring 2 points. The main ingredients and excipients of tedizolid and contezolid are partially specified, each scoring 1 point.

The packaging and specifications of linezolid and tedizolid are suitable for clinical use and dose adjustment, each scoring 2 points. Contezolid is partially suitable for clinical use and dose adjustment, scoring 1 point.

All three oxazolidinone drugs have oral formulations, each scoring 2 points.

All three drugs are fixed-dose, each scoring 2 points.

Tedizolid is administered once daily, scoring 2 points; linezolid and contezolid are administered twice daily, each scoring 1.5 points.

The injectable forms of linezolid and tedizolid require administration by medical personnel, each scoring 1 point. Contezolid can be self-administered without assistance, scoring 2 points.

## Storage Conditions and Expiry Date

All three oxazolidinone drugs can be stored at room temperature, each scoring 3 points. Tedizolid and contezolid do not require light protection for storage, each scoring 1 point. Linezolid and tedizolid have an expiry date of 36 months, each scoring 1.5 points; contezolid has an expiry date of 18 months, scoring 0.5 points.

The scoring results for pharmacological properties are detailed in Table 3.

**Table 3** Pharmacological Properties Score Results

| **Pharmaceutical properties (28points)** | | **Grading Criteria** | **Linezolid** | **Tedizolid** | **Contezolid** |
|---|---|---|---|---|---|
| Pharmacological effects (5) | Definite clinical efficacy, precise mechanism of action, and innovative mechanism of action or target point of action | 5 | 5 | 5 | 5 |
| | Definite clinical efficacy and precise mechanism of action | 4 | | | |
| | Fair clinical efficacy and mechanism of action are unclear | 2 | | | |
| | General clinical efficacy and unclear mechanism of action | 1 | | | |
| In vivo processes (5) | Well-defined in vivo process with complete pharmacokinetic parameters | 5 | 5 | 5 | 5 |
| | Well-defined in vivo process with incomplete pharmacokinetic parameters | 3 | | | |
| | In vivo processes are unclear, or no pharmacokinetic studies are available | 1 | | | |
| Pharmacy and methods of use (multiple choice) (12) | Main ingredients and excipients (all specify 2; one specify 1) | 2 | 2 | 1 | 1 |
| | Specification and packaging (all appropriate for clinical use/dose adjustment 2; one appropriate 1) | 2 | 2 | 2 | 1 |
| | Dosage forms (oral/inhalation/topical formulations 2; SC/IM injections 1.5; IV drip/IV injections 1) | 2 | 2 | 2 | 2 |
| | The dose administered (fixed dose 2; dose to be adjusted during use 1.5; dose based on body mass or BSA 1) | 2 | 2 | 2 | 2 |
| | Frequency of administration (<1 dose/d 2; 2 doses/d 1.5; ≥3 doses/d 1) | 2 | 1.5 | 2 | 1.5 |
| | Ease of use (self-administration without assistance 2; with help ortraining 1.5; administered by medical personnel 1) | 2 | 1 | 1 | 2 |
| Storage conditions (multiple choice) (4) | Storage at room temperature | 3 | 3 | 3 | 3 |
| | Storage in the shade | 2 | | | |
| | Refrigerated/frozen storage | 1 | | | |
| | No need for shade/light protection | 1 | | 1 | 1 |
| Expiry date (2) | >60 months | 2 | | | |
| | ≥36 months, <60 months | 1.5 | 1.5 | 1.5 | |
| | ≥24 months, <36 months | 1 | | | |
| | ≥12 months, <24 months | 0.5 | | | 0.5 |
| | <12 months | 0.25 | | | |
| Pharmaceutical Properties Score | | | 25 | 25.5 | 24 |

**Abbreviations**: SC, subcutaneous; IM, intramuscular; IV, intravenous; BSA, body surface area.

# Efficacy (27 Points)

## Indications

The approved indications for linezolid and contezolid are cSSTIs, whereas the approved indication for tedizolid is acute bacterial skin and skin structure infections (ABSSSI). According to relevant guideline recommendations,[17,18] tedizolid can also be used to treat cSSTIs. As vancomycin is considered the gold standard for treating cSSTIs, linezolid, tedizolid, and contezolid are all regarded as second-line treatment options for cSSTIs, each scoring 3 points. Relevant guidelines are listed in Table 4.

## Guideline Recommendations

Linezolid and tedizolid are recommended in multiple guidelines, with the highest recommendation level being IA,[17,18] each scoring 12 points. Contezolid currently lacks guideline recommendations, and if strictly evaluated according to the Rapid Guideline scoring criteria, it only scores 3 points. However, contezolid has been approved in China for the treatment of cSSTIs, and a Chinese phase III clinical trial comparing it with linezolid has confirmed its non-inferiority to linezolid in both the full analysis population and the clinically evaluable population.[15] This indicates that the drug has an officially approved indication and strong evidence from evidence-based medicine supporting its clinical value. Therefore, following the a priori rule established in the methods section, the "Guideline Recommendation" score for contezolid was assigned 9 points.

**Table 4** Recommendations From National and International Guidelines/Consensus

| Name of the Guidelines | Guide Developers and Sources | Drug | Recommended Content | Level of Evidence |
|---|---|---|---|---|
| Surgical Infection Society 2020 Updated Guidelines on the Management of Complicated Skin and Soft Tissue Infections[17] | Surgical Infection Society (SIS) | Linezolid Tedizolid | Oral therapy for suspected or confirmed MRSA infection, recommendations include linezolid. | 1A |
| | | | Additional oral alternatives for MRSA coverage that may be considered include tedizolid. | 1A |
| | | | The following IV agents are recommended for suspected or confirmed MRSA infections: linezolid. | 1A |
| | | | Additional IV MRSA alternatives that may be considered include tedizolid. | 1A |
| 2018 WSES/SIS-E consensus conference: recommendations for the management of skin and soft-tissue infections[18] | World Society of Emergency Surgery (WSES) | Linezolid Tedizolid | For oral antibiotic coverage of MRSA in patients with SSTIs, we suggest the following agents: linezolid or tedizolid. | 1A |
| | | | For IV antibiotic coverage of MRSA in patients with SSTIs, we suggest the following agents: IV linezolid or IV tedizolid. | 1A |
| Guidelines for the Clinical Application of Antimicrobial Agents (2015 Edition) | National Health Commission of the People's Republic of China (NHC) | Linezolid | SSTIs caused by MRSA may be treated with linezolid. | – |
| Practice Guidelines for the Diagnosis and Management of Skin and Soft Tissue Infections: 2014 Update by the Infectious Diseases Society of America[19] | Infectious Diseases Society of America (IDSA) | Linezolid | Linezolid is recommended for the treatment of SSTIs caused by MRSA. | – |

**Abbreviations**: MRSA, methicillin-resistant staphylococcus aureus; SSTIs, skin and soft tissue infections; IV, intravenous.


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### Clinical Efficacy

The primary efficacy endpoint was the clinical cure rate. Secondary efficacy endpoints included the clinical microbiological success rate or microbiological eradication rate. A systematic review and network meta-analysis showed that linezolid had a higher clinical cure rate than vancomycin in treating MRSA-related cSSTIs, with no significant difference in clinical microbiological success rates between the two drugs; the clinical cure rate of tedizolid was not significantly different from that of linezolid.[9] A phase III clinical trial conducted in Japan used linezolid as a comparator to evaluate the efficacy and safety of tedizolid in adult patients with SSTIs; the results showed that the microbiological eradication rate of tedizolid was not significantly different from linezolid in the microbiologically evaluable MRSA population.[20] A phase III clinical trial in China used linezolid as a comparator to evaluate the efficacy and safety of contezolid in adult patients with cSSTIs; the results showed that the clinical cure rate and microbiological eradication rate of contezolid were not significantly different from those of linezolid in both the full analysis set and the clinically evaluable population.[15]

In summary, linezolid, tedizolid, and contezolid each received a score of 6 for the primary efficacy endpoint and a score of 4 for the secondary efficacy endpoint.

The efficacy scoring results are presented in Table 5.

## Safety (25 Points)

### Adverse Events

The severity of adverse events was graded according to the Common Terminology Criteria for Adverse Events version 5.0 (CTCAE v5.0). The assessment of adverse events was primarily based on the drug labels and Phase III clinical trial data. Additionally, data from spontaneous reporting systems (the VigiAccess database and the FAERS; data extraction date: June 1, 2025) were consulted for supplementary information. It is important to note that such spontaneous data are subject to limitations including under-reporting and confounding by drug utilization, and cannot reflect true incidence rates; therefore, they were not incorporated into the scoring system.

**Table 5** Efficacy Score Results

| **Efficacy (27 points)** | | **Grading Criteria** | **Linezolid** | **Tedizolid** | **Contezolid** |
|---|---|---|---|---|---|
| Indications (5) | Clinically necessary, preferred | 5 | | | |
| | Clinical need, second choice | 3 | 3 | 3 | 3 |
| | More medicines available | 1 | | | |
| Recommended Guidelines (12) | Diagnosis and treatment norms/clinical pathways, consensus issued by national health administrative agencies/management methods, etc., guideline level I recommendation (Level A evidence 12; Level B evidence 11; Level C evidence, and others 10) | 12 | 12 | 12 | |
| | Guidelines Level II and below (Level A Evidence 9; Level B Evidence 8; Level C Evidence and Others 7) | 9 | | | 9 |
| | Expert Consensus Recommendations (the consensus published by the society organizations based on systematic evaluation 6; the consensus published by the society organization others 4) | 6 | | | |
| | Systematic evaluation/Meta-analysis (large sample, high-quality systematic evaluation/Meta-analysis 3; small sample, low-quality systematic evaluation/Meta-analysis 2; systematic evaluation/ Meta-analysis of non-RCT studies 1) | 3 | | | |
| Clinical efficacy (10) | The primary efficacy endpoint indicators (6) | 6 | 6 | 6 | 6 |
| | The secondary efficacy endpoint indicators (4) | 4 | 4 | 4 | 4 |
| Effectiveness Score | | | 25 | 25 | 22 |

According to the drug label,[21] approximately 85% of adverse events associated with linezolid were mild to moderate in severity. Common adverse events (incidence 1%–10%) included diarrhea (8.3%), headache (6.5%), and nausea (6.2%). Common serious adverse reactions such as hematologic toxicities including thrombocytopenia and anemia also occurred within an incidence range of 1%–10%. Data from VigiAccess and FAERS indicated that serious adverse events with reporting rates exceeding 1% included peripheral neuropathy (4.76%), lactic acidosis (4.03%), serotonin syndrome (3.70%), and myelosuppression (2.42%).

Based on pooled data from two Phase III clinical trials with linezolid as the comparator,[13,14] as summarized in the drug label,[22] common adverse events for tedizolid (incidence 1%–10%) included nausea (8%), headache (6%), diarrhea (4%), vomiting (3%), and dizziness (2%). The incidence of serious adverse reactions was 1.8% (incidence 1%–10%). The incidences of hematologic toxicities such as thrombocytopenia (2.3%), anemia (3.1%), and neuropathy (1.2%) for tedizolid were comparable to those of the comparator linezolid, all falling within the 1%–10% range.

According to data from a Phase III clinical trial with linezolid as the comparator,[15] as summarized in the drug label,[23] most adverse events for contezolid were mild to moderate, with nausea and vomiting each occurring at an incidence of 3.4% (incidence 1%–10%). Only one drug-related serious adverse event was reported in the contezolid group, with an incidence of 0.28% (incidence 0.1%–1%), and no drug-related thrombocytopenia (0%) was observed. Occasional decreases in white blood cell count (0.3%), neutrophil count (0.3%), and reticulocyte count (0.3%) were reported in the contezolid group, suggesting that the drug did not cause significant hematologic parameter changes associated with myelosuppression. No drug-related peripheral neuropathy or optic neuropathy was reported.

In summary, linezolid, tedizolid, and contezolid each scored 2 points for mild to moderate adverse events; for serious adverse events, they scored 2, 2, and 3 points, respectively.

### Special Populations

Linezolid is indicated for use in pediatric patients and receives 2 points; whereas tedizolid and contezolid have not yet been evaluated for clinical efficacy and safety in this population, each scoring 0.5 points.

Linezolid, tedizolid, and contezolid are all suitable for use in elderly patients, each scoring 1 point.

Linezolid, tedizolid, and contezolid have not been studied in pregnant women; their use is recommended only when the potential benefits outweigh the potential risks to the fetus, each scoring 0.5 points.

According to the drug labels, linezolid, tedizolid, and contezolid should be used with caution in lactating women, each scoring 0.5 points.

Linezolid and tedizolid are both suitable for patients with severe hepatic dysfunction, each scoring 3 points; whereas contezolid is appropriate for patients with mild-to-moderate hepatic dysfunction, scoring 2 points.

Linezolid, tedizolid, and contezolid are all appropriate for patients with severe renal dysfunction, each scoring 3 points.

### Drug Interactions

Linezolid requires dosage reduction when co-administered with dopamine or epinephrine, scoring 2 points. Neither tedizolid nor contezolid requires dose adjustment, each scoring 3 points.

### Other

Both linezolid and tedizolid are associated with irreversible adverse drug reactions, such as visual impairment and vision loss, each scoring 0 points. No irreversible adverse drug reactions have been reported for contezolid to date, scoring 1 point.

Linezolid, tedizolid, and contezolid have no confirmed teratogenic or carcinogenic effects and carry no specific medication warnings, each scoring 1 point.

The safety scoring results are presented in Table 6.

## Economy (10 Points)

Economic scoring is conducted in accordance with the calculation formulas detailed in the “Statistical Analysis” section. The specific results are as follows:

**Table 6** Safety Score Results

| **Safety (25 points)** | | **Grading Criteria** | **Linezolid** | **Tedizolid** | **Contezolid** |
|---|---|---|---|---|---|
| Moderate adverse reactions (3) | Incidence <1% | 3 | | | |
| | Incidence 1% to <10% | 2 | 2 | 2 | 2 |
| | Incidence ≥10% | 1 | | | |
| | ADR occurrence data not available | 0 | | | |
| Severe adverse reactions (5) | Incidence <0.01% | 5 | | | |
| | Incidence 0.01% to <0.1% | 4 | | | |
| | Incidence 0.1% to <1% | 3 | | | 3 |
| | Incidence 1% to <10% | 2 | 2 | 2 | |
| | Incidence ≥10% | 1 | | | |
| | ADR occurrence data not available | 0 | | | |
| Special populations (multiple choice) (11) | Available for children (both 2; 1.9 for 3 months+; 1.8 for 6 months +; 1.7 for 9 months+; 1.6 for ages 1+; 1.5 for ages 2+; 1.4 for ages 3 +; 1.3 for ages 4+; 1.2 for ages 5+; 1.1 for ages 6+; 1.0 for ages 7+; 0.9 for ages 8+; 0.8 for ages 9+; 0.7 for ages 10+; 0.6 for ages 11+; 0.5 for ages 12+) | 2 | 2 | 0.5 | 0.5 |
| | The elderly (available 1; use with caution 0.5) | 1 | 1 | 1 | 1 |
| | Pregnant women (available 1; use with caution 0.5) | 1 | 0.5 | 0.5 | 0.5 |
| | Lactating women (available 1; use with caution 0.5) | 1 | 0.5 | 0.5 | 0.5 |
| | Hepatic dysfunction (severe available 3; moderate available 2; Lightly available 1) | 3 | 3 | 3 | 2 |
| | Renal dysfunction (severe available 3; moderate available 2; Lightly available 1) | 3 | 3 | 3 | 3 |
| Adverse reactions due to drug interactions (3) | No dosage adjustment is required | 3 | | 3 | 3 |
| | Dosage adjustment required | 2 | 2 | | |
| | Prohibited to use at the same time | 1 | | | |
| Other (multiple choice) (3) | Reversibility of adverse reactions | 1 | | | 1 |
| | Non-teratogenic/non-carcinogenic | 1 | 1 | 1 | 1 |
| | No special medication warnings | 1 | 1 | 1 | 1 |
| Total Safety Score | | | 18 | 17.5 | 18.5 |

**Abbreviation**: ADR, adverse drug reaction.

## Drugs with the Same Generic Name

The average daily treatment cost of the oral dosage form of linezolid is 46.8 yuan, and the lowest average daily cost of drugs with the same generic name is 15.6 yuan, which obtains 1 point according to the formula. The average daily treatment cost of its injectable dosage form is 499.78 yuan, and the lowest average daily cost of drugs with the same generic name is 94 yuan, which obtains 0.56 points according to the formula. When combining the two dosage forms, the average score is 0.78 points.

The average daily treatment cost of the oral dosage form of tedizolid is 108.91 yuan, and the lowest average daily cost of drugs with the same generic name is 97 yuan, which obtains 2.67 points according to the formula. The average daily treatment cost of its injectable dosage form is 298 yuan, and the lowest average daily cost of drugs with the same generic name is 136 yuan, which obtains 1.37 points according to the formula. When combining the two dosage forms, the average score is 2.02 points.

Contezolid has only one oral dosage form, with an average daily treatment cost of 472 yuan. Since there are currently no other products with the same generic name as this drug in the Chinese market, the "lowest average daily cost of drugs with the same generic name" is equivalent to its own average daily cost, which obtains 3 points according to the formula, and no average calculation is required.

### Substitutable Medicines for Main Indications

This indicator is based on a unified treatment scenario of "3-day intravenous administration + sequential oral administration".

The total course cost of linezolid is 2014.14 yuan (1499.34 yuan for 3 days of intravenous administration + 514.8 yuan for 11 days of oral administration). With the lowest total course cost of tedizolid as the benchmark, it obtains 4.24 points according to the formula.

The total course cost of tedizolid is 1220.73 yuan (894 yuan for 3 days of intravenous administration + 326.73 yuan for 3 days of oral administration), which is the lowest among the three drugs, and it obtains 7 points according to the formula.

The total course cost of contezolid is 6608 yuan (no intravenous administration cost + 6608 yuan for 14 days of oral administration). With the lowest total course cost of tedizolid as the benchmark, it obtains 1.29 points according to the formula.

Basic economic information such as the average daily treatment cost and total course cost of the three oxazolidinone drugs is shown in Table 7 and Table 8 respectively, and the sub-criterion scores and total score of the economic evaluation are detailed in Table 9.

## Other Attributes (10 Points)

### National Health Insurance and National Essential Drug Characteristics

Linezolid is classified as Category B drug under the National Basic Medical Insurance and has no payment restrictions, scoring 2 points. Tedizolid and contezolid are also Category B drugs under the National Basic Medical Insurance, but both have payment restrictions, each scoring 1.5 points.

None of the three oxazolidinone drugs is listed in the national essential medicines list, each scoring 1 point.

### National Centralized Drug Procurement and Original Research Drugs

Linezolid and tedizolid are both included in the national centralized procurement program, each scoring 1 point. Contezolid is not included in the national centralized procurement program, scoring 0 points.

All three oxazolidinone drugs are originator drugs, each scoring 1 point.

**Table 7** Basic Economy Information on Average Daily Treatment Cost

| | **Linezolid** | | **Tedizolid** | | **Contezolid** |
|---|---|---|---|---|---|
| | **Oral form** | **njectable form** | **Oral Form** | **Injectable Form** | **ORAL FORM** |
| Drug Specification | 600mg | 300 mL: Linezolid 0.6 g and Glucose 15.0 g | 200mg | 200mg | 400mg |
| Therapeutic Dose | 600mg q12h | 600mg q12h | 200mg qd | 200mg qd | 800mg q12h |
| Average Daily Cost (¥) | 46.8 | 499.78 | 108.91 | 298 | 472 |
| Lowest Average Daily Cost[a] (¥) | 15.6[b] | 94[b] | 97[b] | 136[b] | 472 |
| Drug scores with the same generic name | 1 | 0.56 | 2.67 | 1.37 | 3 |
| Average scores with the same generic name | 0.78 | | 2.02 | | 3 |

**Notes**: [a]The lowest price of drugs with the same generic name, specification, and dosage form on the Chinese market was adopted.[b] The drugs produced by Shanghai Desano Pharmaceutical Group Co., Ltd.; Hunan Kelun Pharmaceutical Co., Ltd.; CSPC Zhongnuo Pharmaceutical Co., Ltd.; and Hebei Aier Haitai Pharmaceutical Co., Ltd. were selected, with minimum unit prices of ¥7.8, ¥47, ¥97, and ¥136, respectively.All costs are presented in Chinese Yuan (¥).
**Abbreviations**: q12h, once every 12 hours; qd, once daily.


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**Table 8** Basic Economy Information on Total Course Cost

| | Linezolid | Tedizolid | Contezolid |
|---|---|---|---|
| Therapeutic Dose | 600mg q12h | 200mg qd | 800mg q12h |
| Recommended Course Duration (days) | 14 | 6 | 14 |
| IV Phase | | | |
| Daily injection cost (¥) | 499.78 | 298 | 0[a] |
| Treatment duration (days) | 3 | 3 | 0[a] |
| Total IV cost (¥) | 1499.34 | 894 | 0[a] |
| Oral Phase | | | |
| Daily oral cost (¥) | 46.8 | 108.91 | 472 |
| Treatment duration (days) | 11 | 3 | 14 |
| Total oral cost (¥) | 514.8 | 326.73 | 6608 |
| Total Course Cost (¥) | 2014.14 | 1220.73 | 6608 |

**Notes**: Contezolid injection is not yet marketed in China; therefore, cost data for the IV phase are not available.All costs are presented in Chinese Yuan (¥).
**Abbreviations**: q12h, once every 12 hours; qd, once daily; IV, intravenous.

**Table 9** Economy Score Results

| Economy (10 points) | | Grading Criteria | Linezolid | Tedizolid | Contezolid |
|---|---|---|---|---|---|
| Drugs with the same generic name (3) | The score for the evaluated drug = lowest average daily cost of treatment/average daily cost of treatment for the evaluated drug * 3 | 3 | 0.78 | 2.02 | 3 |
| Substitutable medicines for main indications (7) | The score for the evaluated drug = lowest total course cost of treatment/total course cost of treatment of the evaluated drug * 7 | 7 | 4.24 | 7 | 1.29 |
| Economy Score | | | 5.02 | 9.02 | 4.29 |

### Status of Producers

Linezolid and tedizolid were both included in the 2024 Top 50 Global Pharmaceutical Companies list published by Pharmaceutical Executive, ranking 6$^{th}$ and 4$^{th}$, each scoring 1 point. Contezolid was included in neither the 2024 Top 50 Global Pharmaceutical Companies list nor the Ministry of Industry and Information Technology's Top 100 Pharmaceutical Companies list, scoring 0 points.

### Global Utilization

Linezolid and tedizolid have been approved for marketing in China, the United States, Europe, and Japan. Contezolid has been approved only in China. The global utilization scores of the three oxazolidinone drugs are 1, 1, and 0.5 points, respectively.

The scoring results for other attributes are detailed in Table 10.

The scores of the three oxazolidinone drugs across five dimensions are presented in Table 11.

## Sensitivity Analyses

To assess the robustness of the overall ranking to key assumptions, the study conducted multiple one-way sensitivity analyses. These analyses examined the impacts of variables such as the treatment cycle, cost parameters, and whether China-specific policy indicators were included.

Treatment cycle: When adjusting the intravenous administration duration (0–5 days) and the corresponding total oral treatment course within the range of the maximum treatment course recommended in the drug label, the total score ranking of the three drugs remained unchanged throughout all scenarios (tedizolid > linezolid > contezolid). In all

**Table 10** Other Attributes Score Results

| Other Attributes (10 points) | | Grading Criteria | Linezolid | Tedizolid | Contezolid |
|---|---|---|---|---|---|
| National Medical Insurance (3) | National medical insurance category A, no payment restrictions | 3 | | | |
| | National medical insurance category A with payment restrictions | 2.5 | | | |
| | National medical insurance category B, no payment restrictions | 2 | 2 | | |
| | National medical insurance category B with payment restrictions | 1.5 | | 1.5 | 1.5 |
| | Not on the national medical insurance list | 1 | | | |
| National essential drugs (3) | National essential drugs without Δ requirements | 3 | | | |
| | National essential drugs with Δ requirements | 2 | | | |
| | Not on the national essential drugs list | 1 | 1 | 1 | 1 |
| National centralized procurement of medicines (1) | Selected drugs for centralized national procurement | 1 | 1 | 1 | |
| Original/reference/ consistency evaluation (1) | Drug of origin/reference drug | 1 | 1 | 1 | 1 |
| | Generic drugs through consistency evaluation | 0.5 | | | |
| Status of producers (1) | The world's top 50 pharmaceutical manufacturers in terms of sales volume (1 for top 1–10; 0.8 for top 11–20; 0.6 for top 21–30; 0.4 for top 31–40; 0.2 for top 41–50) /Top 100 Pharmaceutical Industry published by MIIT (1 for top 1–20; 0.8 for top 21–40; 0.6 for top 41–60; 0.4 for top 61–80; 0.2 for top 81–100). | 1 | 1 | 1 | |
| Global utilization (1) | Available in China, USA, Europe, Japan | 1 | 1 | 1 | |
| | Domestic and international sales | 0.5 | | | 0.5 |
| Other Attributes Score | | | 7 | 6.5 | 4 |

**Notes**: The "Δ" sign indicates that the drug should be used by a physician with corresponding prescription qualifications or under the guidance of a specialist physician, and use monitoring and evaluation should be strengthened.
**Abbreviation**: MIIT, Ministry of Industry and Information Technology of the People's Republic of China.

**Table 11** Final Total Score Results

| Evaluation Dimension | Linezolid | Tedizolid | Contezolid |
|---|---|---|---|
| Pharmaceutical Properties | 25 | 25.5 | 24 |
| Efficacy | 25 | 25 | 22 |
| Safety | 18 | 17.5 | 18.5 |
| Economy | 5.02 | 9.02 | 4.29 |
| Other Attributes | 7 | 6.5 | 4 |
| Total Score | 80.02 | 83.52 | 72.79 |

**Note**: The total score is the sum of the five dimension scores above, retained to two decimal places. The calculation can be reproduced from the data presented.

scenarios, tedizolid consistently ranked first in total score due to its economic advantage derived from a shorter standard treatment course (6 days). Notably, contezolid maintained an oral administration regimen without any intravenous administration in all scenarios.

Cost parameters: When the median price was used for the economic evaluation of drugs with the same generic name, although the absolute total score of each drug changed, the ranking remained unchanged, and tedizolid consistently achieved the highest score.

Policy attributes: A supplementary analysis was conducted to construct a neutral "global" scoring scenario by removing China-specific policy indicators (including national medical insurance classification and payment restrictions, the National Essential Drugs List, and inclusion status in National Centralized Procurement) from the "Other Attributes" dimension. In this scenario, the overall ranking remained stable, but contezolid's score increased significantly, narrowing the score gap with linezolid.

In all sensitivity analysis scenarios, tedizolid consistently ranked first in total score, indicating that its ranking is robust to changes in key assumptions.

Details of the sensitivity analysis scenarios and parameter settings are shown in Table 12, and the results of the sensitivity analysis are detailed in Table 13.

**Table 12** Scenarios and Parameter Settings

| Analysis Scenario | Core Parameter Variation |
|---|---|
| Benchmark Scenario | 3-day IV therapy + Lowest price of drugs with the same generic name + Inclusion of China-specific policy indicators |
| Treatment Cycle Variation | 0-5 days IV therapy + Lowest price of drugs with the same generic name + Inclusion of China-specific policy indicators |
| Cost Parameter Variation | 3-day IV therapy + Median price of drugs with the same generic name[a] + Inclusion of China-specific policy indicators |
| Policy Attribute Variation | 3-day IV therapy + Lowest price of drugs with the same generic name + Exclusion of China-specific policy indicators |

**Notes**: [a] The median prices were as follows: linezolid oral, ¥32.85; linezolid injection, ¥52.8; tedizolid oral, ¥105; tedizolid injection, ¥279.All costs are presented in Chinese Yuan (¥). Contezolid had no IV administration in any scenario.
**Abbreviation**: IV, intravenous.

**Table 13** Results of the Sensitivity Analysis

| Analysis Scenario | Parameter Variation | Linezolid | | Tedizolid | | Contezolid | | Ranking |
|---|---|---|---|---|---|---|---|---|
| | | Total Score | Change | Total Score | Change | Total Score | Change | |
| Benchmark Scenario | 3-day IV + Lowest Price + Including China-Specific Policy Indicators | 80.02 | – | 83.52 | – | 72.79 | – | Tedizolid, Linezolid, Contezolid |
| Treatment Cycle Variation | 0-day IV + Lowest Price + Including China-Specific Policy Indicators | 82.76 | +2.74 | 83.52 | – | 72.19 | −0.60 | Tedizolid, Linezolid, Contezolid |
| | 1-day IV + Lowest Price + Including China-Specific Policy Indicators | 81.10 | +1.08 | 83.52 | – | 72.39 | −0.40 | Tedizolid, Linezolid, Contezolid |
| | 2-day IV + Lowest Price + Including China-Specific Policy Indicators | 80.41 | +0.39 | 83.52 | – | 72.59 | −0.20 | Tedizolid, Linezolid, Contezolid |
| | 4-day IV + Lowest Price + Including China-Specific Policy Indicators | 79.78 | −0.24 | 83.52 | – | 72.99 | +0.40 | Tedizolid, Linezolid, Contezolid |
| | 5-day IV + Lowest Price + Including China-Specific Policy Indicators | 79.61 | −0.41 | 83.52 | – | 73.19 | +0.60 | Tedizolid, Linezolid, Contezolid |
| Cost Parameter Variation | 3-day IV + Median Price + Including China-Specific Policy Indicators | 80.45 | +0.43 | 84.35 | +0.83 | 72.79 | – | Tedizolid, Linezolid, Contezolid |

(*Continued*)

**Table 13** (Continued).

| Analysis Scenario | Parameter Variation | Linezolid | | Tedizolid | | Contezolid | | Ranking |
|---|---|---|---|---|---|---|---|---|
| | | Total Score | Change | Total Score | Change | Total Score | Change | |
| Policy Attribute Variation | 3-day IV + Lowest Price + Excluding China-Specific Policy Indicators | 76.02 | −4.00 | 80.02 | −3.50 | 70.29 | −2.50 | Tedizolid, Linezolid, Contezolid |

**Note**: Contezolid had no IV administration in any scenario.
**Abbreviation**: IV, intravenous.

## Discussion

The results of this study indicate that the comprehensive scores of the three oxazolidinone drugs are ranked in descending order as follows: tedizolid (83.52 points), linezolid (80.02 points), and contezolid (72.79 points).

According to the recommendations of the Rapid Guideline, tedizolid, linezolid, and contezolid all scored above 70 and are strongly recommended.

The 2020 guideline of the Surgical Infection Society (SIS) of the United States recommends oral or injectable formulations of linezolid and tedizolid for suspected or confirmed cSSTIs caused by MRSA.[17] The 2018 guideline of the World Society of Emergency Surgery (WSES) also recommends oral or injectable formulations of linezolid and tedizolid for SSTIs caused by MRSA.[18] The results of this study indicate that the current evaluation outcomes are consistent with the guideline recommendations.

The results of this study indicate that the advantages and disadvantages of the three oxazolidinone drugs differ significantly. The core advantages of tedizolid include an optimized-dosing regimen (once-daily administration) and superior economy (lowest total treatment duration cost, economic score of 9.02), as well as no requirement for dose adjustment when used in combination therapy. However, it is limited by a relatively high incidence of serious adverse reactions and restrictions in medical insurance. The core advantages of linezolid lie in its clearly defined applicability in pediatric patients and its coverage under unrestricted Category B medical insurance. However, its twice-daily dosing frequency, requirement for light protection during storage, relatively high rate of serious adverse reactions, and the need for dose adjustment in combination therapy all contribute to a lower pharmaceutical properties score. Moreover, its economy is significantly inferior to that of tedizolid (economic score of 5.02). As a novel oxazolidinone, contezolid achieves optimal safety (safety score of 18.5) due to its unique "trifluorinated coplanar" structure.[24] Its actual clinical efficacy is equivalent to that of the other drugs (full score in the clinical efficacy), and no dose adjustment is required in combination therapy. However, the lack of authoritative guideline recommendations has led to a systematic underestimation of its efficacy score (22 points). Additionally, its high cost (economic score of 4.29), exclusion from unrestricted insurance reimbursement, and insufficient corporate backing (not affiliated with a top 100 global or Chinese pharmaceutical company) have further reduced its final score.

According to the results of the sensitivity analysis, in terms of changes in the treatment cycle: when adjusting the intravenous administration duration (0–5 days) within the range of the maximum treatment course recommended in the drug label and simultaneously matching the oral administration duration, a clear pattern emerged—"the shorter the intravenous duration, the better the economic value of linezolid". Notably, despite a slight decrease in linezolid's total score (from 82.76 to 79.61) driven by rising intravenous costs, the total score ranking of the three drugs remained stable across all scenarios: tedizolid > linezolid > contezolid—consistent with the benchmark scenario results. It is also worth noting that although contezolid maintained an oral-only regimen with a fixed intravenous administration duration of 0 days and 0 intravenous cost in all scenarios, its total score still showed a slight upward trend with the extension of intravenous duration of the other two drugs. This phenomenon is not due to changes in contezolid's own administration scheme or cost, but a passive result driven by the calculation logic of the "score for substitutable medicines" in the economic scoring system. Specifically, the score for substitutable medicines is calculated as (the lowest total course cost

among the three drugs / the total course cost of the evaluated drug) × 7. As the intravenous duration of linezolid and tedizolid increases, their total course costs rise accordingly, which in turn increases the "lowest total course cost among the three drugs" (consistently the cost of tedizolid) in the formula numerator. Since contezolid's total course cost remains fixed at ¥6608, the increase in the numerator leads to a slight rise in its score for substitutable medicines. Nevertheless, this passive fluctuation is limited in magnitude—the total economic score of contezolid only increased from 3.69 to 4.69, which is far from enough to reverse its lowest ranking among the three drugs, reflecting the objectivity and rationality of the scoring framework that takes the optimal alternative in the same category as the reference.

This result is highly aligned with China's current policy direction of "restricting unnecessary intravenous administration and prioritizing the promotion of sequential therapy". In clinical practice, if intravenous administration can be timely switched to oral treatment, it can not only reduce the economic burden on patients, but also minimize risks associated with intravenous infusion and save medical resources. Meanwhile, it can maintain drug efficacy and ranking stability, and avoid the decline in treatment cost-effectiveness caused by excessive extension of intravenous administration.[25] It is noteworthy that a 5-day intravenous phase aligns with the approved intravenous duration for linezolid in cSSTIs (10–14 days) and falls within the approved intravenous duration for tedizolid in ABSSSI (6 days).[21,22] In terms of changes in cost parameters and policy attributes, the total score ranking of the three drugs remained unaffected. In summary, the recommended order of oxazolidinone drugs in this study is robust in most clinical and policy scenarios.

The results of this study reveal that current Rapid Guidelines exhibit evaluation bias when assessing newly marketed innovative drugs not yet covered by existing guidelines, overvaluing the importance of guideline recommendations while underestimating the contributions of drug labels and phase III clinical trial evidence, thus failing to accurately reflect their true clinical value of such drugs. Based on these findings, we propose the following recommendations: (1) Under the efficacy dimension of guideline recommendations, introduce a scoring criterion based on high-quality, large-sample ($n > 300$) randomized controlled trials, with suggested scores of 6 or 9. (2) Add an innovation evaluation dimension, including: whether the drug addresses an unmet medical need, whether it has superior properties compared to existing drugs (such as efficacy, safety, and economy), whether it is an independently developed innovative drug or the first generic drug globally, and whether it can improve healthcare resource utilization (eg, by shortening treatment duration or hospital stay).

Based on the Rapid Guideline, this study conducted a health technology assessment of three oxazolidinone drugs currently marketed in China, the United States, Europe, and Japan. The evaluation was performed across five dimensions: pharmaceutical properties, efficacy, safety, economy, and other attributes. The final scoring results can serve as a reference for drug selection and rational medication use in Chinese medical institutions.

However, this study has the following limitations: (1) Tedizolid and contezolid, as novel oxazolidinone drugs, have limited clinical trial data available. (2) Due to contezolid being available only in China and having a relatively short time on the market, and the lack of both domestic and international guideline recommendations, its guideline recommendation score is low, which may underestimate its clinical efficacy and value. (3) Fluctuations in drug prices, updates in evidence-based data, adjustments to the National Essential Drugs List, changes in the National Medical Insurance Drug List, modifications to Centralized National Procurement List, and developments of pharmaceutical manufacturing may all impact the study results. (4) Due to the current lack of head-to-head clinical studies among the three oxazolidinone agents, as well as the absence of direct or network meta-analyses, incorporating additional literature for comparative analysis in this study remains challenging.

## Conclusion

Based on the comprehensive evaluation results across the five dimensions, the priority recommendation order of oxazolidinone antibiotics is tedizolid, linezolid, and contezolid. The ranking was primarily driven by tedizolid's once-daily dosing and lowest total course cost, linezolid's pediatric indication and widespread availability, and contezolid's superior safety profile, although its overall score was limited by higher cost and lack of guideline recommendations. Based on the evaluation results, tedizolid, linezolid, and contezolid can all be recommended as suitable options for introduction and application in healthcare institutions.

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## Author Contributions

All authors made substantial contributions to the research, including but not limited to: conceptualization, study design, execution, data acquisition, analysis, and interpretation; drafting, revising, or critically reviewing the manuscript; approving the final version to be published; agreeing on the journal to which the article was submitted; and taking responsibility for all aspects of the research work.

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