Montana
EXPERIMENTAL TREATMENT REVIEW BOARD

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montanaetrb.org

RDL-2026-002

WST-057 (Topical Pirenzepine 4%)

APPROVED WITH CONDITIONS

Review Decision Letter · Decided October 26, 2026

Legal basis: SB 535 (69th Leg., Ch. 621) · ARM 37.106.3301-3325

APPLICANT	WinSanTor, Inc. (San Diego, CA).
TREATMENT	WST-057: pirenzepine free base monohydrate 4% topical solution (formulation WinFB61.1), 4 pumps (approximately 4 mL) applied once daily to both lower legs and feet, with any excess applied to the hands; ongoing treatment with formal assessment at 24 weeks.
INDICATION	Peripheral neuropathy in adults, including diabetic, chemotherapy-induced, HIV-associated, and idiopathic neuropathy.
SUBMISSION	First submission: October 4, 2026; final submission: October 14, 2026.
REVIEW MEETING	October 26, 2026, 12:00-3:00 pm MT. Quorum confirmed; conflict-of-interest declarations (none) confirmed on the record; Applicant session and Q&A minuted; deliberation and vote in closed session.
DECISION	**APPROVED WITH CONDITIONS. Vote: 5 for, 0 against.**
EFFECTIVENESS	This RDL was approved by the Board. The approval is effective upon (a) written confirmation of concordance with the Conditions by the Chair, under the process approved by the Board in this RDL, and (b) becomes effective for use at a given ETC upon that ETC's valid designation of this ETRB (Submission Agreement 4.9).

1. Treatment summary

A once-daily, patient-administered topical solution of pirenzepine, a selective M1 muscarinic receptor antagonist, applied to the lower legs and feet and intended to promote regeneration of peripheral sensory nerve fibers.

Pirenzepine has not been approved by the FDA but has been marketed outside the United States as an oral treatment for peptic ulcer.

The topical product completed Phase 1 in WST-PZP-001 (Adelaide, Australia, 2018; 24 healthy volunteers; 4% pirenzepine at 2.5 to 5.0 mL daily for 14 days) and remains in clinical development under FDA IND 144,090, including the Phase 2a studies WST-PZP-002 (NCT04005287) and WST-PZP-003 (NCT04786340) in diabetic peripheral neuropathy.

The proposed formulation, WinFB61.1, is the Applicant's Phase 3 formulation; it differs from the Phase 2 formulation (WinFB61) by a 0.05% increase in hydroxypropyl cellulose.

Delivery contemplates prescription by the treating physician with self-administration outside the ETC under ARM 37.106.3325.

2. Conditions of approval (binding; Submission Agreement 4.7)

Condition 1 - Informed consent revisions
The Applicant shall revise the Informed Consent Form and the Patient Summary / Consent Script to:

- **a.** state application-site skin irritation rates accurately, consistent with the Phase 2a data, making clear that irritation is common even with daily moisturizer use and that moisturizer chiefly reduces discontinuation, and remove the statement that only 3% of patients experienced irritation with moisturizer;
- **b.** inform patients that they may experience itching or tingling at the application site;
- **c.** disclose that no patient has used WST-057 for longer than 24 weeks;
- **d.** limit statements of potential benefit to the clinical evidence, including revising or removing statements of improved nerve conduction and quality of life, restored nerve-cell energy production, and first-ever nerve regeneration, and state that benefit has not been studied in neuropathies other than diabetic peripheral neuropathy;
- **e.** remove the baseline-video comparison presented to patients as a means of seeing their improvement; and
- **f.** align the provisions on patients who lack capacity to consent, including the legally authorized representative signature block, with the protocol.

Condition 2 - Adverse-event classification
The Applicant shall remove from the protocol and related documents the provision that expected application-site itching is not an adverse event. Itching shall be recorded and reported as an adverse event, graded and classified by expectedness and relationship to treatment under NCI Common Terminology Criteria for Adverse Events (CTCAE).

Condition 3 - Consistent eligibility criteria
The Applicant shall state identical inclusion and exclusion criteria, with clarity, across the dossier, the ETC Delivery Protocol, the Informed Consent Form, the consent script, and the Provider Assessment Form. In particular:

- **a.** the renal-impairment and hepatic-impairment exclusions shall be retained until the Applicant obtains the corresponding FDA waivers, and stated consistently;
- **b.** the treatment of patients who lack capacity to consent shall be stated consistently (see Condition 1(f)); and
- **c.** the symptom survey shall state its rating scale correctly (0 to 3).

The Applicant and the ETC shall address the Conditions in writing. The Chair confirms concordance in writing without reconvening the Board; upon confirmation, the approval takes effect subject to ETC designation.

3. Required determinations (ARM 37.106.3316(6))

Determination	Finding	Board position	Basis (summary)
Statutory qualification (50-12-102(1), MCA)	Met (reasonable grounds)	Unanimous	Based on the Applicant's submission and supporting record. Phase 1 predicate WST-PZP-001 tested the same active ingredient at the same 4% concentration; the proposed 4 mL daily dose falls within the 2.5 to 5.0 mL Phase 1 range.
Safety standards equivalent to or higher than recognized regulatory authorities (16(6)(a)(i))	Met subject to satisfactory resolution of Conditions 2 and 3	Unanimous	ETC protocol modeled on the Phase 2a protocol WST-PZP-002 under Health Canada and IND 144,090 oversight; extension to other neuropathy etiologies accepted given the product's risk profile; renal and hepatic exclusions retained pending FDA waivers.
Informed consent comprehensive and understandable (16(6)(a)(ii))	Met subject to satisfactory resolution of Condition 1	Unanimous	The corrections in Condition 1 to skin-irritation disclosure, benefit statements, treatment duration, and capacity provisions are required before consent materials are final.
Risk-benefit demonstrates a reasonable safety profile (16(6)(a)(iii))	Met	Unanimous	Principal risk is reversible application-site skin reaction, mitigated by prophylactic moisturizer; minimal systemic exposure; no drug-related deaths or serious adverse events in completed studies. Treatment beyond 24 weeks is disclosed through Condition 1.
Alternative treatments appropriately evaluated (16(6)(a)(iv))	Met	Unanimous	Protocol establishes adequate per-patient procedures: documented alternatives evaluation in the consent and eligibility process per 50-12-104, MCA.
Risk level and outside-ETC administration (16(6)(f))	Risk level: Low. Safe for administration outside an ETC, subject to the approved protocol and applicable conditions.	Unanimous	Topical take-home product, patient- or caregiver-administered; risk profile consistent with self-administration under the protocol's monitoring, skin-care regimen, and AE-reporting pathways.

4. Principal matters deliberated

(1) Formulation and dose identity: the Phase 1 study tested earlier formulations (WinFB34, WinFB90, WinFB100) and the ETC product is WinFB61.1; the Applicant explained that each change was to excipients only, with pirenzepine held at 4%, the concentration established in Phase 1 and carried forward into Phase 3 clinical development. The Board based the statutory determination on the active ingredient, concentration, and dose, and found the proposed 4 mL dose within the Phase 1 range.

(2) Expansion beyond diabetic peripheral neuropathy: accepted. Although the underlying pathology differs between neuropathies, the product's principal risk is a local, reversible skin reaction with minimal systemic exposure, which is not expected to vary with the cause of the neuropathy, and the extension is between conditions of comparable severity; the Applicant has also studied the product in HIV-associated and chemotherapy-induced neuropathy (WST-PZP-004, WST-PZP-005). The Board noted that extensions of indication will be considered case by case and this determination is not a precedent.

(3) Treatment duration beyond the 24-week Phase 2 experience: addressed through disclosure in Condition 1 rather than a time-limited approval.

(4) Classification of expected skin effects: itching is to be recorded as an adverse event (Condition 2); the Applicant explained that tingling may accompany nerve regeneration.

(5) Upper age limit of 75: the Applicant stated the limit originated from early efficacy and anticholinergic-burden considerations rather than an observed safety signal, and that its Phase 2 studies enrolled patients over 80; the Board would permit its removal.

(6) Renal and hepatic exclusions: retained at the Applicant's proposal pending FDA waivers.

Not all deliberations are recorded here, only the most substantial; per-member vote rationales are preserved in the Review Record.

5. Continuing obligations

The Applicant shall report Serious Adverse Events to the Board within 24 hours and other Adverse Events within 3 business days (Submission Agreement 9.2.2); the ETC reports SAEs to the department within five days, with adverse-event data reported to this Board simultaneously (ARM 37.106.3317(1), (4)). Material amendments require prior Board review (9.3). Annual continuing review applies (9.4). Outcome data are collected and shared per the approved protocol's outcome dataset. Records of this review are preserved for at least five years (16(6)(d)).

6. Disclaimers and reliance

This approval reflects the Board's professional judgment on the record submitted. It is not FDA approval or clearance, is not a determination of efficacy or therapeutic benefit, is not medical advice or a recommendation to any patient, and is not a warranty that the treatment is safe (Submission Agreement 8.2-8.4). Responsibility for development, manufacture, supply, and clinical delivery rests with the Applicant, the ETC, and treating providers.

MONTANA EXPERIMENTAL TREATMENT REVIEW BOARD ETRB

Matt Kaeberlein

Matt Kaeberlein, PhD - Chair, for the Board.

Signed on November 2, 2026. Docusign Envelope ID: 57A90CE1-9ADE-8A06-837E-53C01C6CE41F