Bioelectronic Medicine Comes to Rheumatology

A CME Activity Development Package: Vagus Nerve Stimulation for Difficult-to-Treat Rheumatoid Arthritis

Prepared as a medical-education development sample *Contents: (I) Needs Assessment Summary · (II) CME Activity Proposal · (III) Outcomes Assessment Instrument*

All content derived from public sources. Data verified against the RESET-RA primary publication (Tesser et al., Nature Medicine, 2025) and the FDA PMA record (P240039).

Part I — Needs Assessment Summary

Statement of the Problem

Rheumatoid arthritis (RA) affects a substantial population in whom current pharmacologic therapy is inadequate. Despite conventional synthetic DMARDs, biologics, and JAK inhibitors, a meaningful subset develops difficult-to-treat RA — persistent disease activity or intolerance after multiple advanced therapies. Under the EULAR definition, this population represents a well-recognized and growing clinical challenge.

On July 30, 2025, the FDA granted premarket approval (PMA P240039) to the SetPoint System, the first implantable vagus nerve stimulation (VNS) device indicated for difficult-to-treat RA. This is the first bioelectronic therapy to enter a treatment paradigm that has been, until now, exclusively pharmacologic.

Current State of Practice

Rheumatology is a pharmacology-driven specialty. Disease management is built around drug selection, sequencing, and monitoring. The specialty has no established framework for evaluating, referring for, or co-managing an implantable device therapy. VNS implantation is procedural — involving a proceduralist — while disease management remains rheumatology-led, creating an inherently interdisciplinary care model that does not currently exist in most practices.

Evidence of Practice and Knowledge Gaps

Four gaps are documented:

1. **Mechanism unfamiliarity.** The rationale for VNS rests on the inflammatory reflex and cholinergic anti-inflammatory pathway — neuroscience largely outside standard rheumatology training.
2. **No patient-selection framework.** Clinicians lack criteria for identifying appropriate candidates within the difficult-to-treat population.
3. **Absent care pathway.** No established referral, implantation, and co-management workflow between rheumatology and proceduralists.
4. **Reimbursement uncertainty.** Coverage and prior-authorization pathways for a newly approved device therapy are unfamiliar in rheumatology practice.

Expert commentary has characterized the arrival of bioelectronic medicine in rheumatology as a paradigm shift, underscoring that clinician readiness has not kept pace with the science.

Educational Need and Target Audience

Primary audience: Rheumatologists. **Secondary audience:** Pain/neuromodulation specialists, neurosurgeons/proceduralists, and advanced practice providers in rheumatology.

An accredited educational activity is needed to close the mechanism, selection, pathway, and reimbursement gaps so that eligible patients can be appropriately identified, referred, and co-managed.

Part II — CME Activity Proposal

Title: Bioelectronic Medicine Comes to Rheumatology: Integrating Vagus Nerve Stimulation into the Management of Difficult-to-Treat Rheumatoid Arthritis

Format: Enduring material (on-demand monograph with interactive cases) **Estimated credit:** 1.0 *AMA PRA Category 1 Credit™* **Provider model:** Jointly provided / commercially supported via independent educational grant

Gap-to-Objective Mapping

#	Documented gap	Learning objective (measurable)
1	Mechanistic rationale unfamiliar	**Explain** the inflammatory reflex and cholinergic anti-inflammatory pathway as the scientific basis for VNS in RA
2	No candidate-selection framework	**Identify** appropriate VNS candidates using RESET-RA enrollment criteria and difficult-to-treat RA definitions
3	No interdisciplinary care pathway	**Describe** the referral, implantation, and co-management pathway across rheumatology and procedural teams
4	Reimbursement navigation unclear	**Apply** current coverage and reimbursement considerations when integrating VNS into an RA treatment plan

Objectives use measurable Bloom's verbs (explain, identify, describe, apply).

Content Outline (faculty-ready)

Section 1 — The Inflammatory Reflex *(Objective 1)* Cholinergic anti-inflammatory pathway; vagal modulation of TNF-α and pro-inflammatory cytokines; bioelectronic medicine as an emerging field.

Section 2 — The Evidence Base *(Objectives 1–2)* RESET-RA design, population, and endpoints;

primary ACR20 result and its effect size over sham; 12-week blinded data; Nature Medicine publication; honest framing of a modest primary effect alongside longer-term signal.

Section 3 — Patient Selection *(Objective 2)* Difficult-to-treat RA definitions; the inadequate-response population; where VNS fits in the algorithm; setting realistic expectations.

Section 4 — The Care Pathway *(Objective 3)* Referral triggers; implantation overview; rheumatology–proceduralist co-management; monitoring and follow-up cadence.

Section 5 — Access & Reimbursement *(Objective 4)* Coverage landscape for a newly approved device; documentation; prior authorization; practical integration.

Outcomes Measurement Plan

Moore's level	Measurement	Tied to
Level 2 (satisfaction)	Post-activity evaluation	Whole activity
Level 3 (knowledge)	Paired pre/post items, one per objective	Objectives 1–4
Level 4 (competence)	Case-vignette decision items	Objectives 2–3
Level 5 (performance, optional)	Commitment-to-change + 60-day follow-up	Objectives 2–4

Faculty & Independence

Faculty: a rheumatology KOL (RA clinical trialist), a bioelectronic-medicine/mechanism expert, and a proceduralist for the pathway section. All disclosures collected and mitigated per ACCME Standards for Integrity and Independence. Commercial supporter has no control over content, faculty, or objectives.

Traceability Grid

Gap	Objective	Content section	Outcome item
Mechanism unfamiliarity	Obj 1	§1–2	L3 Q1
No selection framework	Obj 2	§2–3	L3 Q2 + L4 case
No care pathway	Obj 3	§4	L3 Q3 + L4 case
Reimbursement unclear	Obj 4	§5	L3 Q4 + L5 CTC

Part III — Outcomes Assessment Instrument

Single-best-answer items. The same items run pre- and post-activity so knowledge change is measurable per objective. Correct answers marked ✓.

Knowledge Item 1 — Objective 1 (mechanism)

The scientific rationale for vagus nerve stimulation in rheumatoid arthritis is based primarily on which of the following?

A. Direct vagal innervation of synovial joints reducing local nociception B. Stimulation of the cholinergic anti-inflammatory pathway, reducing pro-inflammatory cytokine release including

TNF-α ✓ C. Vagal upregulation of regulatory T-cell production in lymph nodes D. Parasympathetic suppression of cartilage-degrading matrix metalloproteinases

Rationale: VNS activates the inflammatory reflex / cholinergic anti-inflammatory pathway, attenuating TNF-α and other cytokines. It is not a local joint or nociceptive mechanism.

Knowledge Item 2 — Objective 2 (patient selection / evidence)

In the RESET-RA pivotal trial, the SetPoint System was studied in patients who had which of the following?

A. Newly diagnosed RA, DMARD-naïve B. RA with inadequate response or intolerance to biologic and/or targeted synthetic DMARDs ✓ C. RA in sustained remission seeking to taper therapy D. Seronegative inflammatory arthritis of any duration

Rationale: The trial and approved population target difficult-to-treat RA with inadequate response/intolerance to prior advanced therapies — not early or DMARD-naïve disease.

Knowledge Item 3 — Objective 3 (care pathway)

Which statement best describes the care model required to deliver VNS therapy for RA?

A. The rheumatologist implants the device during a standard clinic visit B. It is a pharmacologic add-on requiring no procedural referral C. It requires interdisciplinary coordination between rheumatology and a proceduralist for implantation, with ongoing rheumatology-led disease management ✓ D. Management transfers entirely to the implanting surgeon after placement

Rationale: Implantation is procedural; disease management remains rheumatology-led. The novel practice element is building the referral and co-management pathway.

Knowledge Item 4 — Objective 4 (reimbursement/integration)

When integrating a newly FDA-approved implantable device therapy such as VNS for RA, which is the most appropriate first step for a rheumatology practice?

A. Assume coverage parity with biologic infusions and proceed B. Verify payer coverage policy and prior-authorization requirements for the specific device and indication before referral ✓ C. Bill under an existing DMARD administration code D. Defer all reimbursement questions to the device manufacturer

Rationale: A newly approved device requires verifying specific coverage/PA pathways; parity with pharmacologic therapy cannot be assumed.

Case Vignette 1 — Objectives 2 + 3 (competence: selection + referral)

A 54-year-old woman with seropositive RA of 9 years has active disease despite sequential trials of methotrexate, two TNF inhibitors, and a JAK inhibitor, with intolerance to a third biologic. She is otherwise stable and interested in non-pharmacologic options.

What is the most appropriate next step?

A. Rechallenge with a previously failed TNF inhibitor B. Evaluate her as a candidate for VNS given difficult-to-treat RA, and initiate referral to the interdisciplinary pathway for implantation assessment ✓ C. Refer to pain management for symptom control only D. Defer any change and repeat disease-activity assessment in 6 months

Rationale: She meets a difficult-to-treat profile consistent with the studied population. The competence step is recognizing candidacy and knowing the referral pathway exists.

Case Vignette 2 — Objectives 1 + 4 (competence: counseling + expectations)

Your patient, a candidate for VNS, asks how the device works and what response she should expect.

Which counseling approach is best supported by the public evidence?

A. “It blocks pain signals from your joints directly and works within days.” B. “It stimulates a nerve pathway that lowers inflammatory signaling; in the trial the primary response over the sham group was modest, and we’ll monitor your disease activity closely to judge your benefit.” ✓ C. “It replaces your DMARDs entirely, so you can stop other therapy.” D. “Results are guaranteed given FDA approval.”

Rationale: Accurate mechanism plus honest framing of the modest primary effect size — the ethically and clinically correct counseling for a novel therapy.

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