Tonic Motor Activation (TOMAC) for Restless Legs Syndrome

Effective: November 1, 2026

Next Review: June 2027
Last Review: October 2026

IMPORTANT REMINDER

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

DESCRIPTION

Tonic motor activation (TOMAC) is a peroneal nerve stimulation device that uses electrodes worn on the lower legs to deliver bilateral high-frequency electrical stimulation to the common peroneal nerves, producing sustained muscle contractions that mimic voluntary leg movements known to relieve restless legs syndrome symptoms.

MEDICAL POLICY CRITERIA

Tonic motor activation as a treatment for restless legs syndrome is considered **investigational**.

NOTE: A summary of the supporting rationale for the policy criteria is at the end of the policy.

CROSS REFERENCES

1. Functional Neuromuscular Electrical Stimulation, Durable Medical Equipment, Policy No. 83.04
2. Interferential Current Stimulation, Durable Medical Equipment, Policy No. 83.07

BACKGROUND

RESTLESS LEGS SYNDROME

Restless legs syndrome (RLS) is a neurological condition characterized by an uncontrollable urge to move the legs, often accompanied by uncomfortable sensations. These symptoms typically worsen during periods of rest or inactivity, especially in the evening or at night, and are temporarily relieved by movement. RLS is frequently associated with sleep disturbances and periodic limb movements during sleep (PLMS), which can further impair rest and daytime functioning. When PLMS occurs without RLS or other related disorders, it is classified as periodic limb movement disorder (PLMD). Treatment for RLS generally involves pharmacologic therapy which is tailored based on symptom severity, patient age, comorbidities, and individual preferences, aiming to improve sleep quality and overall life functioning. Dopaminergic therapies have a known risk of augmentation.

For individuals with refractory RLS, where symptoms persist despite first-line treatments like gabapentinoids, alternative strategies are considered. These include combination pharmacotherapy using different drug classes, low-dose opioids, and a thorough review of iron levels, potential exacerbating substances, behavioral interventions, and bilateral peroneal nerve stimulation.

TONIC MOTOR ACTIVATION

Tonic motor activation (TOMAC), also known as bilateral peroneal nerve stimulation, is a form of external lower extremity nerve stimulation. TOMAC is proposed to work by delivering bilateral high-frequency electrical stimulation to the common peroneal nerves located near the fibula in the lower legs. This stimulation activates the tibialis anterior muscle, producing sustained, low-level muscle contractions that mimic the effects of voluntary leg movements like walking or stretching, which are activities known to relieve RLS symptoms.

The proposed biological mechanism involves afferent feedback.[1] The stimulation sends signals back to the central nervous system, which may help suppress the abnormal sensory signals that drive the urge to move the legs. By activating the same circuits used during natural movement, TOMAC may modulate spinal and supraspinal pathways involved in RLS pathophysiology.

TOMAC differs from transcutaneous electrical nerve stimulation (TENS) devices. TOMAC targets the common peroneal nerve with a goal of tonic activation of motor pathways to mimic movement with high-frequency, sustained, bilateral stimulation. TENS targets superficial sensory nerves often with the goal of pain relief by administering pulsed, often intermittent, stimulation.

CLINICAL PATHWAY

TOMAC is not a first-line therapy for RLS. It is indicated for moderate-to-severe primary RLS that is refractory to pharmacologic treatment. First-line therapies include, iron supplementation, gabapentinoids, lifestyle modifications (eg, regular moderate exercise, sleep habits, etc.).

REGULATORY STATUS

The NTX100 Tonic Motor Activation (TOMAC) System (Noctrix Health, Inc; Pleasanton, CA) received De Novo classification (DEN220059; Product Code: QWD) from the FDA for its

intended use "to reduce symptoms of primary moderate-severe Restless Legs Syndrome (RLS) and to improve sleep quality in adults refractory to medication."[2]

EVIDENCE SUMMARY

This evidence review examines tonic motor activation (TOMAC), also known as bilateral peroneal nerve stimulation, as a treatment option for individuals with restless legs syndrome (RLS) who are refractory to medication. TOMAC delivers bilateral high-frequency electrical stimulation to the common peroneal nerves, producing sustained muscle contractions that mimic voluntary leg movements known to relieve RLS symptoms. Current treatment comparators include iron supplementation, gabapentinoids, and lifestyle modifications. Key outcomes of interest include symptom relief, functional outcomes, quality of life, and medication use, measured primarily through the International Restless Legs Syndrome Score (IRLS), Patient/Clinician Global Impression of Improvement, and the Medical Outcomes Study Sleep Scale, with a minimum follow-up of six months recommended. Evidence was selected with preference for systematic reviews, comparative controlled prospective trials and randomized controlled trials.

SYSTEMATIC REVIEWS

Three systematic reviews and meta-analyses have been published evaluating the efficacy and safety of TOMAC for RLS.[3-5] Winkleman (2025) only included two of the available Randomized Controlled Trials (RCT) and will not be further discussed in this review.[4]

Karroum (2026) conducted an individual participant data systematic review and meta-analysis evaluating TOMAC as monotherapy and adjunctive therapy for moderate-to-severe RLS.[5] Five U.S. studies were included, with efficacy analyses pooling 252 participants from three RCTs. Compared with sham, TOMAC improved RLS severity (IRLS mean difference [MD], 3.50 points; p<.001), sleep problems (MOS-II MD, 8.50 points; p < 0.001), and PGI-I response (risk difference, 36%; p < 0.001); improvements were also noted in the monotherapy and adjunctive-therapy subgroups. Mild application-site discomfort was more common with TOMAC, but moderate, severe, and serious adverse event rates did not differ from sham. Limitations include the small number of industry-sponsored studies, short and variable follow-up, design differences across trials, lack of independent replication, and reliance on subgroup analyses, including a relatively small monotherapy subgroup.

Mohamed (2025) conducted a systematic review and meta-analysis evaluating the efficacy and safety of TOMAC for moderate-to-severe RLS.[3] Three RCTs and an open-label extension study (N=320) were included, with primary outcomes being changes in International IRLS scores, PGI-I responder rates, and sleep quality indices (MOS-I, MOS-II). TOMAC significantly reduced IRLS scores compared to sham (mean difference [MD]: -3.66; 95% CI: -5.07 to -2.25; p<.00001), improved PGI-I response (risk ratio [RR]: 3.16; 95% CI: 1.35 to 7.37; p=.008), and enhanced sleep quality (MOS-I MD: -9.28; p <.00001; MOS-II MD: -10.06; p <.00001). Adverse events were more frequent with TOMAC (RR: 1.68; p=.004) but were mild and self-limiting, with no severe or device-related discontinuations. Limitations include the small number of RCTs with underpowered samples sizes, inclusion of medication-naive individuals in the overall analysis, short follow-up durations, and limited data on long-term safety.

RANDOMIZED CONTROLLED TRIALS

Singh (2024) conducted a multicenter, randomized, participant-blinded, sham-controlled clinical trial evaluating the efficacy and safety of TOMAC for treating moderate-to-severe RLS in both medication-naïve and medication-refractory adults (n = 45).[6] Participants were randomized 1:1 to receive either TOMAC or sham treatment over two weeks, with self-administered 30-minute sessions during symptomatic periods. The primary outcome was the change in IRLS score, and secondary outcomes included the Patient Global Impression of Improvement (PGI-I) and sleep quality indices (MOS-I and MOS-II). TOMAC significantly reduced IRLS scores compared to sham (-6.59 vs. -2.17; p=.004) (mean difference = 4.42; 95% CI: 1.57 to 7.26; p=.0040), with similar effect sizes in both medication-naïve and refractory subgroups. PGI-I responder rates were notably higher in the TOMAC group (36% vs. 4%; p = 0.0073). The device was well tolerated, with no serious adverse events; mild discomfort and site irritation were the most common issues. Limitations included the short treatment duration and underpowered sample.

Bogan (2023), published a pivotal multicenter, randomized, double-blind, sham-controlled clinical trial (RESTFUL Study) evaluating the efficacy and safety of TOMAC for treating medication-refractory RLS (n =133).[7] Adults with moderate-to-severe primary RLS unresponsive to standard medications were randomized 1:1 to receive either active TOMAC or sham treatment for 4 weeks (stage 1), followed by 4 weeks of open-label active TOMAC for all participants (stage 2). The primary endpoint, the Clinical Global Impression of Improvement (CGI-I) responder rate, was significantly higher in the TOMAC group compared to the sham group (45% vs. 16%; difference: 28%; 95% CI: 14% to 43%; p = 0.00011). Secondary endpoints showed greater reductions in International RLS Study Group Rating Scale (IRLS) scores in the TOMAC group compared to the sham group (-7.2 vs. -3.8; p= 0.00093). No serious device-related adverse events occurred. Mild discomfort and site irritation were the most common side effects, both resolving quickly and decreasing over time. Limitations included some loss of blinding due to perceived treatment, short study duration, and lack of medication washout.

Buchfuhrer (2021) conducted a randomized, participant-blinded, crossover trial investigating the efficacy and safety of TOMAC as a treatment for moderate-to-severe RLS (n = 43).[8] Participants self-administered both TOMAC and sham treatments nightly for 14 days each, in randomized order. The TOMAC device delivered 30-minute electrical stimulation sessions to the common peroneal nerve via wearable units. The primary outcome was change in the IRLS, with secondary outcomes including the CGI-I scale and numerical rating scales (NRS) for symptom severity. TOMAC significantly reduced IRLS scores by 6.81 points versus 3.38 for sham (p<.01), and yielded a 66% CGI-I responder rate compared to 17% for sham (p<.01). No moderate or serious device-related adverse events were reported; mild events included transient discomfort and skin irritation. Limitations included potential unblinding due to paresthesia, short treatment duration, and underpowered sample.

NONRANDOMIZED STUDIES

Roy (2023) reported results of the 24-week open-label extension of the RESTFUL study evaluating the long-term efficacy and safety of TOMAC in adults with medication-refractory moderate-to-severe primary RLS.[9] Among 44 participants receiving TOMAC, 72.7% were CGI-I responders and 75.0% were PGI-I responders at week 24, with a mean IRLS score reduction of -11.3 points (95% CI: -8.8 to -13.9; p<.0001) compared to baseline. Sleep quality improved significantly (MOS-II: -17.2; MOS-I: -15.8; both p<.0001), and symptom frequency decreased by 46%, from 5.9 to 3.2 days/week. Compared to 59 control participants receiving

standard care, TOMAC produced significantly greater improvements across all endpoints (CGI-I: 72.7% vs. 13.6%, p<.0001; IRLS: -11.3 vs. -5.4, p=.0001). Benefits partially persisted after 8 weeks of treatment cessation without rebound above baseline. Safety showed no grade ≥2 device-related adverse events and only mild, transient discomfort in 6.8% of participants. Limitations included non-randomized control assignment, open-label design, and use of patient-reported outcomes.

Buchfuhrer (2023) conducted a prospective, open-label, single-arm clinical trial evaluating whether TOMAC could enable opioid dose reduction in patients with refractory RLS.[10] Twenty adults on ≤60 morphine milligram equivalents (MME)/day were enrolled, having failed an average of 3.2 prior RLS medications and maintained stable opioid therapy for an average of 5.3 years. Participants self-administered 30-minute TOMAC sessions bilaterally over the peroneal nerve during symptom onset. Opioid doses were tapered every 2–3 weeks until the CGI-I score exceeded 5. The primary endpoint, ≥20% opioid dose reduction with CGI-I ≤5, was achieved by 70% of participants (14/20), exceeding the prespecified 50% success criterion. The mean opioid dose reduction was 29.9% (SD 23.7%), from 39.0 to 26.8 MME/day. Of 15 participants who had any successful opioid dose reduction the average CGI-I score at the reduced dose was 4.0 (95% CI: 3.3 to 4.7) and the average change in IRLS score from baseline at the reduced dose was 3.4 (95% CI: 0.4 to 6.4). Adherence to TOMAC was 85%, and all adverse events were mild and non-serious. Limitations included the underpowered sample, lack of a control group, short study duration, and open-label design, which may introduce bias.

SECTION SUMMARY

The evidence includes randomized controlled trials, nonrandomized studies, and systematic reviews. Across trials and meta-analyses, including the Karroum individual participant data systematic review, TOMAC improved RLS symptoms, patient-reported response, and sleep outcomes compared with sham, with generally mild adverse events. However, the evidence is limited by small and underpowered samples, short follow-up, potential unblinding, reliance on subgroup and patient-reported analyses, and a lack of long-term randomized data. Larger RCTs with longer follow-up are needed to establish safety, durability, and net health benefit; therefore, the evidence is insufficient to determine that TOMAC improves net health outcomes.

PRACTICE GUIDELINE SUMMARY

AMERICAN ACADEMY OF SLEEP MEDICINE

In 2025, the American Academy of Sleep Medicine (AASM) published clinical practice guidelines on the treatment of RLS and periodic limb movement disorder.[11] The AASM gave a conditional recommendation with moderate certainty of evidence for the use of bilateral high-frequency peroneal nerve stimulation over no peroneal nerve stimulation in adults with RLS. This conditional recommendation was founded on the graded evidence of two RCTs of 2-4 weeks of randomized data which showed a very modest effect on one subjective outcome. There is no analysis of the durability of the benefit, the benefit of TOMAC compared to existing treatments, or the applicability of the evidence or efficacy to different age groups, particularly those who are older and/or have comorbidities. The guideline's framing is narrower than its wording as the evidence is derived mostly from medication-refractory adults however the recommendation states "adults with RLS".

Additionally, the chair and first author disclosed consulting for the device manufacturer and is a co-author of the RESTFUL trial as a consultant and independent medical monitor. The guideline policy requires recusal for level 2 conflicts but does not address how this relationship was classified or whether recusal occurred or not.

SUMMARY

There is not enough research to show that tonic motor activation (TOMAC) or bilateral peroneal nerve stimulation improves health outcomes for individuals with restless legs syndrome. Based on the available published evidence, additional randomized controlled trials comparing this combined therapy to standard treatment are needed. Therefore, tonic motor activation (TOMAC) or bilateral peroneal nerve stimulation is considered investigational for restless legs syndrome.

REFERENCES

1. Charlesworth JD, Adlou B, Singh H, et al. Bilateral high-frequency noninvasive peroneal nerve stimulation evokes tonic leg muscle activation for sleep-compatible reduction of restless legs syndrome symptoms. *J Clin Sleep Med.* 2023;19(7):1199-209. PMID: 36856064
2. Food & Drug Administration. 2023. De Novo Classification Request For NTX100 Tonic Motor Activation (NTX100 TOMAC) System. Decision Summary. [cited 09/24/2025]. 'Available from:' https://www.accessdata.fda.gov/cdrh_docs/reviews/DEN220059.pdf.
3. Mohamed RG, Sarhan K, Hegazi A, et al. Efficacy and safety of tonic motor activation for the treatment of restless legs syndrome: A meta-analysis of randomized controlled trials. *Sleep Med.* 2025;132:106580. PMID: 40381601
4. Winkelman JW, Berkowski JA, DelRosso LM, et al. Treatment of restless legs syndrome and periodic limb movement disorder: an American Academy of Sleep Medicine systematic review, meta-analysis, and GRADE assessment. *J Clin Sleep Med.* 2025;21(1):153-99. PMID: 39324664
5. Karroum EG, Bachmann CG, Bronstone A, et al. Efficacy and safety of tonic motor activation (TOMAC) for restless legs syndrome as adjunctive and monotherapy: An individual participant data systematic review and meta-analysis. *Sleep Med.* 2026;140:108810. PMID: 41581285
6. Singh H, Baker FC, Ojile J, et al. Efficacy and safety of TOMAC for treatment of medication-naive and medication-refractory restless legs syndrome: A randomized clinical trial and meta-analysis. *Sleep Med.* 2024;122:141-48. PMID: 39173210
7. Bogan RK, Roy A, Kram J, et al. Efficacy and safety of tonic motor activation (TOMAC) for medication-refractory restless legs syndrome: a randomized clinical trial. *Sleep.* 2023;46(10). PMID: 37458698
8. Buchfuhrer MJ, Baker FC, Singh H, et al. Noninvasive neuromodulation reduces symptoms of restless legs syndrome. *J Clin Sleep Med.* 2021;17(8):1685-94. PMID: 33949942
9. Roy A, Ojile J, Kram J, et al. Long-term efficacy and safety of tonic motor activation for treatment of medication-refractory restless legs syndrome: A 24-Week Open-Label Extension Study. *Sleep.* 2023;46(10). PMID: 37439365

10. Buchfuhrer MJ, Roy A, Rodriguez S, et al. Adjunctive tonic motor activation enables opioid reduction for refractory restless legs syndrome: a prospective, open-label, single-arm clinical trial. *BMC Neurol.* 2023;23(1):415. PMID: 37990163
11. Winkelman JW, Berkowski JA, DelRosso LM, et al. Treatment of restless legs syndrome and periodic limb movement disorder: an American Academy of Sleep Medicine clinical practice guideline. *J Clin Sleep Med.* 2025;21(1):137-52. PMID: 39324694

CODES

Codes	Number	Description
CPT	None	
HCPCS	A4544	Electrode for external lower extremity nerve stimulator for restless legs syndrome
	E0743	External lower extremity nerve stimulator for restless legs syndrome, each

Date of Origin: *June 2026*