DE NOVO CLASSIFICATION REQUEST FOR
RESTIFFIC™ RESTLESS LEG RELAXER FOOT WRAP

REGULATORY INFORMATION

FDA identifies this generic type of device as:

> **Nonpowered lower extremity pressure wrap.** A nonpowered lower extremity pressure wrap is a prescription device that applies mechanical pressure by wrapping around the lower extremity, such as the leg or foot, and is intended for primary Restless Leg Syndrome (RLS).

NEW REGULATION NUMBER: 890.5760

CLASSIFICATION: CLASS I (EXEMPT, from premarket notification review, subject to limitations in 21 CFR 890.9)

PRODUCT CODE: OTX

BACKGROUND

DEVICE NAME: RESTIFFIC™ RESTLESS LEG RELAXER FOOT WRAP

SUBMISSION NUMBER: K102707

DATE OF DE NOVO: JANUARY 23, 2011

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REQUESTER'S RECOMMENDED CLASSIFICATION: CLASS I

INDICATIONS FOR USE

The RESTIFFIC™ Restless Leg Relaxer Foot Wrap is a prescription device intended to reduce symptoms of moderate to severe primary Restless Leg Syndrome (RLS) in adults and used during periods of rest or relaxation, when symptoms of RLS occur.

LIMITATIONS

For prescription use only.

Limitations on device use are also achieved through the following statements included in the Instructions for Use Manual:

Warnings:

- *If you have neuropathy (numbness or tingling in hands or feet), poor circulation, peripheral vascular disease, varicose veins, deep vein thrombosis or history of blood clots, foot and/or leg swelling, DO NOT use the RESTIFFIC™ device.*

- *Do NOT wear if you have breaks, sprains, bruises and bruising problems, wounds, sores, fragile or thin skin, burns, cuts, rash or abrasions involving your feet and /or legs.*

- *Do NOT wear when engaged in activities that put pressure on your feet: examples: standing, walking, running, exercising, or operating a vehicle or bicycle.*

PLEASE REFER TO THE LABELING FOR A MORE COMPLETE LIST OF WARNINGS, PRECAUTIONS AND CONTRAINDICATIONS.

RATIONALE FOR EXEMPTION

The technology of a nonpowered lower extremity foot wrap is relatively simple in that it achieves its effect through mechanical pressure and there are low risks associated with use of the device. Therefore, a nonpowered lower extremity foot wrap, when indicated as prescription use devices, are appropriate for exemption from premarket notification, subject to the limitations of exemptions identified in 21 CFR 890.9. Given the simplicity of the design, including the lack of any electrical components, general controls provide reasonable assurance of safety and effectiveness if device manufacturers comply with such requirements, which includes current good manufacturing practice requirements (21 CFR part 820), and general labeling (21 CFR part 801).

Examples exceeding the limitations of exemption could include indications for over-the-counter use or a significant change in the technological characteristics.

DEVICE DESCRIPTION

The RESTIFFIC™ Restless Leg Relaxer Foot Wrap device is a foot wrap designed to apply continuous, adjustable squeezing pressure on specific muscles in the feet. The device is to be applied before bedtime or while the person is seated or supine.

A more complete description of the device includes the following:

- An outer cloth wrap to support and hold the pressure pad in place. (The wrap has an open end so the pad can be removed and replaced, if needed. Only the cloth comes in contact with the skin);
- VELCRO straps and plastic buckles to hold the cloth wrap in place and allow for adjusting the pressure; and
- Pressure pads of high density foam to put pressure on the medial and bottom part of

the foot. The RESTIFFIC™ achieves its targeted pressure with a T- shaped pad that presses into the medial and bottom part of the foot.

SUMMARY OF NONCLINICAL/BENCH STUDIES

The device design is relatively simple as it does not contain any software, electronics, circuit boards, nor is it electrically powered; therefore EMC or electrical safety testing is not necessary. The only 'mechanical aspect' of the device is the use of Velcro straps to tighten the wrap about the foot to apply 'therapeutic pressure' to the foot to have an impact on relieving RLS symptoms in adults.

BIOCOMPATIBILITY/MATERIALS

The RESTIFFIC™ foot wrap is intended to only contact intact skin for a limited duration (< 24 hours at a time). The patient-contacting, outer cover of the device is made of fabric, typically used in clothing. In lieu of biocompatibility testing, the sponsor provided a justification that the identical material has a demonstrated long history of safe use.

SHELF LIFE/STERILITY

The RESTIFFIC™ foot wrap is a non-sterile, single-patient reusable device. It is intended only for external use and the user manual includes appropriate cleaning instructions for the removable outer cover. The device does not have a stated shelf life, which, based upon the nature of the device components, is acceptable.

SUMMARY OF CLINICAL INFORMATION

The sponsor has provided evidence from a single arm, historically-controlled, open label study (n=30 adult subjects with symptoms of moderate to severe RLS) utilizing the RESTIFFIC™ wrap lasting eight weeks (six weeks of treatment with the RESTIFFIC™ wrap).

The primary outcome measure for assessment of effectiveness for the RESTIFFIC™ wrap was the International Restless Legs Scale (IRLS) score, a patient-reported outcome measure. The IRLS score is the best validated and most widely used measure of effectiveness of a RLS treatment, though it is prone to significant placebo effects. The placebo response of the IRLS is unknown in a single-arm study, although it has been reported as greater than 40% in randomized, controlled trials. As the supporting data were derived from a single arm, historically controlled trial, there is some uncertainty regarding the benefits.

Secondary outcome measures included Clinical Global Impression-Improvement (CGI-I), Clinical Global Impression-Severity (CGI-S) and Clinical Global Impressions-Efficacy Index (CGI-EI), all of which are the investigators' assessed measures of the subject's illness.

Subjects in the study demonstrated a statistically significant decrease in symptoms from severe or moderate to mild RLS, overall as measured by the IRLS rating scale (mean 17.22 reduction in IRLS score overall). CGI-I results demonstrated that all subjects improved; none became worse after wearing the device. Ninety (90%) percent (27/30) of subjects were "much improved" or "very much improved" by study end. CGI-S results revealed that 97% (29/30) of subjects experienced a decrease in severity. 83% (25/30) of subjects decreased at least two levels in

severity. CGI-EI revealed 86% (26/30) of subjects showed moderate to marked improvement with no side effects.

Safety was assessed by recording adverse events and analyzing them for severity and relation to the study device. There were 11 non-serious device-related adverse events (AEs) in 10 subjects due to use of the RESTIFFIC™ wrap. These included transient numbness, pain, or burning that resolved when the device was loosened. No serious AEs were noted in the study population. It was also reported that no subjects stopped using the device due to AEs.

The results of the RESTIFFIC™ clinical study were compared with historical drug studies using meta-analyses. Comparison of the results of the RESTIFFIC™ subjects to those of the historical control appeared to show a substantial treatment effect. However, this treatment effect is uncertain due to the unknown placebo response in the study (IRLS is prone to placebo effects) and identified differences between the historical control and RESTIFFIC™ groups (in length of treatment and underlying disease severity).

The RESTIFFIC™ wrap has been studied for 6 weeks. It is unknown if the effect of the device will extend beyond 6 weeks, which is a limitation in the data given that RLS is a chronic condition.

LABELING

The RESTIFFIC™ User Manual is consistent with the clinical data and covers all the hazards and other clinically relevant information that may impact use of the device. The labeling is sufficient and satisfies the requirements of 21 CFR § 801.109 Prescription devices.

CONTROLS

Given the design aspects of the nonpowered lower extremity pressure foot wraps, compliance with the general controls of the FD&C Act, including compliance with the labeling requirements in 21 CFR 801 and the Quality System Regulation (21 CFR 820), are sufficient to reasonably assure safety and effectiveness for the RESTIFFIC™ foot wrap.

In addition, this is a prescription device and must comply with 21 CFR 801.109.

BENEFIT/RISK DETERMINATION

The risks of the device are based on data collected in the clinical experience described above. There were no serious device-related adverse events reported in the clinical performance data with use of the device. There were 11 non-serious device-related adverse events (AEs) in 10 subjects due to use of the RESTIFFIC™ wrap, which resolved with adjustment of the device. Based on this information, the risk associated with the RESTIFFIC™ foot wrap is considered low.

The probable benefits of the device are also based on data collected in the clinical experience described above. The study used the IRLS score, a well-validated, widely used patient-reported outcome which is prone to placebo effects. Subjects treated with the RESTIFFIC™ foot wrap reported a mean reduction in the IRLS score (i.e., a mean improvement) of 17 points. This compares favorably with the mean improvement of IRLS score seen in studies of one drug

approved for the treatment of RLS (mean change 12 points for the treatment arm and 8 points for the control arm), though there were differences between the RESTIFFIC™ and historical control study designs and populations. Improvement was also noted for the RESTIFFIC™ treated subjects based on the Clinician's Global Impression (CGI) assessment. For CGI-S, 83% decreased at least two levels in severity. For CGI-I, all subjects improved at least minimally and 90% were "much" or "very much" improved.

Additional factors to be considered in determining probable risks and benefits for the RESTIFFIC™ foot wrap include: (1) there are no legally marketed devices available for patients with RLS. There are approved drug treatments, but these have known adverse events that are more common and more severe than those seen in the clinical experience for the RESTIFFIC™ foot wrap. (2) Although RLS is a chronic disease, long-term safety and effectiveness data are not available. The clinical data is limited to 6 weeks in duration.

Although there is some uncertainty regarding the benefits due to the potential placebo effects, given the available information, the data support that for reducing symptoms of moderate to severe primary Restless Leg Syndrome (RLS) in adults, the probable benefits outweigh the probable risks for the RESTIFFIC™ foot wrap. The device risks can be mitigated by the use of general controls, including prescription use.

CONCLUSION

The *de novo* for the RESTIFFIC™ foot wrap is granted and the device is classified under the following:

Product Code: OTX
Device Type: Nonpowered lower extremity pressure wrap
Class: Class I (Exempt from premarket notification, subject to limitations in 21 CFR 890.9)
Regulation: 21 CFR 890.5760