IMPORTANT RISK INFORMATION

General Information
As with any medical procedure, there are risks and complications associated with treatment using the PneumRx RePneu™ Endobronchial Coil System. There are also risks associated with the associated bronchoscopy procedure.

Patients should contact their doctor immediately if they experience any unusual respiratory symptoms after RePneu™ Coil treatment.

Contraindications
The RePneu™ Endobronchial Coil System is contraindicated for use in:

- Patients with a known sensitivity to drugs required for performing bronchoscopy or in whom bronchoscopic procedures are contraindicated
- Patients with evidence of active infection in the lungs
- Patients with hypersensitivity or allergy to nitinol (nickel-titanium) or its constituent metals
- Patients with clinically significant bleeding disorders
- Patients with clinically significant pulmonary fibrosis
- Patients with giant bullae >1/3 of the lung volume
- Patients with clinically significant, generalized bronchiectasis
- Patients with severe pulmonary hypertension defined by right ventricular systolic pressure >50mmHg (preferably measured by right heart catheterization)
- Patients with vessels that visually exceed the adjacent airway size (potential for severe pulmonary hypertension)
- Patients taking immunosuppressive drugs for the treatment of cancer, rheumatoid arthritis, autoimmune disease, or prevention of tissue or organ rejection
- Patients taking >20 mg prednisone (or equivalent dose of a similar steroid) daily
Warnings

Clinician Use Warnings

- The RePneu™ System should only be used by those physicians skilled in the use of therapeutic bronchoscopes and who have appropriate training. Users should be familiar with the principles, clinical applications, complications, side effects, and hazards commonly associated with interventional pulmonology procedures and the RePneu™ Endobronchial Coil Procedure.

General Warnings

- Hemoptysis is a known complication of Coil treatment and of diagnostic and interventional bronchoscopic procedures in general. In infrequent cases, fatal hemoptysis has occurred in patients who have undergone Coil treatment. As such, the use of anticoagulant drugs in patients undergoing Coil treatment should be carefully considered, as it may be associated with an increased bleeding risk.
  - To decrease the risk of serious pulmonary bleeding events, use of antiplatelet (e.g., aspirin, clopidogrel) or anticoagulant therapy (e.g., warfarin, NOAC’s) should be stopped for seven (7) days prior to and seven (7) days following the Coil implantation procedure, or as recommended by the pharmaceutical manufacturer.
  - The benefits and risks of initiation or continuing use of antiplatelet or anticoagulant medications in patients who have undergone Coil treatment should be carefully assessed.

- Do not implant RePneu™ Coils in any area of the lung exhibiting bronchiectasis or significant atelectasis. To decrease the risk of serious pulmonary bleeding events, Coil implantation should be performed in patients with bronchiectasis only after careful consideration, avoiding any suspect areas of the lung.

- Exercise additional caution when considering implanting RePneu™ Coils in patients with DLCO <20% of predicted value since the safety and effectiveness of RePneu™ System therapy has not been evaluated in these patient populations.

- Exercise additional caution when considering treatment of patients with suspicious or confirmed cancerous lung nodules or evidence of other severe disease or lung conditions.
that may compromise survival of the patient post procedure, or the patient’s likelihood of benefiting from RePneu™ Coil therapy.

**General Precautions**

- Carefully read all labels and instructions prior to using the RePneu™ System. Observe all contraindications, warnings, and precautions noted throughout these instructions. Failure to follow the Instructions for Use may result in increased risk of patient harm, procedural difficulties, complications, or device damage.

- The RePneu™ Endobronchial Coil procedure is a bilateral treatment that should be performed in separate sessions.

**Individualization of Treatment**

The risks and benefits should be considered for each patient before use of the RePneu™ System. Patient selection factors should be assessed, such as patient comorbidities and important risk factors, including antiplatelet or anticoagulant therapy.

Exercise additional caution when considering treatment of patients with homogeneous emphysema in combination with less severe air trapping. A post-hoc analysis of this subgroup in the RENEW study showed a deterioration in the median 6-Minute Walk Test, although the change was not statistically significant. ¹

The RePneu™ System should be used with caution and only after careful consideration, especially in patients with:

- History of frequent recurrent clinically significant respiratory infections
- Hypercapnia
- Uncontrolled or severe congestive heart failure or recent myocardial infarction
- Low FEV₁

¹ Sciruba FC et al. JAMA 2016; 315:2178-2189
Use in Special Populations

The safety and effectiveness of REPNEU System therapy has not been evaluated in the following patient populations:

- Pregnant or lactating women
- Patients who have not quit smoking
- Patients with FEV$\text{1}_1$ $>$ 45% of predicted value
- Patients who have had Lung Volume Reduction Surgery or lobectomy
- Patients with alpha-1 antitrypsin deficiency
- Patients with Residual Volume (RV) $<$ 175% predicted
- Patients with low levels of visible parenchymal structure on CT
- Patients with severe gas exchange abnormalities as defined as PaCO$_2$ $>$ 55 mm Hg, or PaO$_2$ $<$ 45 mm Hg on room air (high altitude criterion: PaO$_2$ $<$ 30 mm Hg)

Potential Adverse Events

Adverse events that may be observed with endobronchial devices, systems for placement of these devices, and related procedures (including diagnostics and bronchoscopy procedures) and use of the RePneu™ System include, but are not limited to, the events shown below. These events may vary in frequency and severity.

- Allergic Reaction
- Aspiration
- Bleeding or Hemorrhage
- Bronchial Blood Clot
- Bronchial Ulceration
- Bronchospasm
- Cardiac Arrhythmias
- COPD Exacerbation
- Cough
- Death
- Device Dislocation
- Dyspnea
- Emphysema, Subcutaneous
- Hemoptysis, including severe hemoptysis
- Hoarseness
- Hypertension
- Hypotension
- Infection
- Inflammation
- Pain
- Painful Respiration
- Pleural Effusion
- Pleural Fistula
- Pneumonia*
- Pneumothorax
- Procedure-Related Complications (e.g., fever, spasm)
- Pulmonary Embolism
- Respiratory Distress
- Respiratory Failure
- Respiratory Tract Infection
- Sedation-Related Complications (e.g., nausea, vomiting, headache)
- Sepsis
- Tissue Reaction, Localized (a.k.a. Coil Associated Opacity*)
- Tissue Trauma, Procedural (e.g., tissue perforation, dissection)

**Note:** Additional interventional procedures may be necessary if patients experience some of these potential adverse event(s) following RePneu™ Coil treatment.

* There have been reports of non-infectious localized tissue reaction, also termed Coil Associated Opacity (CAO), in the area of implanted RePneu™ Coils. This is believed to be an inflammatory reaction that presents with pneumonia-like symptoms, including chest or pleuritic pain/discomfort, increased dyspnea, fatigue, and/or haze or infiltrates on chest X-ray, and may be difficult to
distinguish from pneumonia. Therefore, patients should be instructed at discharge to contact their implanting physician if they experience symptoms that may be indicative of pneumonia or CAO.

**Peri-procedural Care**

A chest X-ray should be done post-procedure to verify Coil placement and to ensure no pneumothorax is present. A second chest X-ray should be done at least 4 hours following the first chest X-ray.

Provide detailed instructions to the patient on expected side-effects of the Coil procedure, including the potential adverse events listed above, and instruct the patient to contact the treating physician immediately should any of the potential adverse events be experienced.

It is particularly important that patients be instructed at discharge to contact their implanting physician if they experience symptoms that may be indicative of pneumonia or CAO, to ensure that appropriate treatment is delivered.

**Coil Removal**

Although RePneu™ Coils are designed to be permanently implanted in the lungs, removal can be performed if the patient experiences persistent pain and removal is medically necessary.

**Patient Brochure**

PneumRx has developed a Patient Brochure that includes information specifically designed for patients regarding how the RePneu™ Coils work and procedural information including potential risks and benefits. Copies of the brochure can be obtained by emailing PneumRx at **CS@btgplc.com** or by calling (+49) (0) 211 54 22 75 0. Instruct all patients to obtain and read the Patient Brochure prior to treatment.