Uptake Medical®

12 July 2019

IMPORTANT
CUSTOMER SAFETY ADVISORY NOTICE

Attention: Physicians Using InterVapor System

Device Details

Uptake Medical is providing you with updated safety information for your consideration when using the InterVapor System, Model # UM-GEN-100. Uptake Medical Technology began its commercial operations in 2017 and is the manufacturer of the current CE marked InterVapor® System (CE 661757).

The InterVapor System is intended for treatment of patients with heterogeneous upper lobe emphysema to achieve bronchoscopic lung volume reduction.

Description of the Events

Patients with bleeding disorders, those on anticoagulation therapy, and unstable cardiovascular conditions or other concomitant illnesses are at a significant increased risk for complications following InterVapor treatment.

In a review of safety data collected during commercial experience using the InterVapor System, (01 May 2017 through June 30 2019), almost 300 successful bronchoscopic thermal vapor ablation (BTVA) procedures have been performed with patients undergoing sequential treatments, with some patients having bilateral treatments. In this population, a total of 42 procedure-related serious adverse event (SAE) complaints have been reported through the Uptake Medical Technology complaint handling process, including the BTVA data registry. No device malfunctions have been associated with these adverse events.

During this time period, three (3) serious events of hemoptysis have been reported, resulting in the death of two (2) patients. In particular, one patient was taking anticoagulation medication therapy (Eliquis 5mg (Apixaban)). The patient presented on day 30 post-treatment with signs of severe COPD exacerbation, and a chest CT verified findings of pulmonary infiltrates (pneumonia). Six (6) days later, the patient developed severe hemoptysis and resuscitation efforts were unsuccessful. The patient died of hemoptysis due to severe COPD exacerbation and pneumonia.

Uptake Medical Technology convened a Medical Advisory Board consisting of key opinion leaders with significant experience with the InterVapor System to review and discuss the safety data for the InterVapor System. Based on the recommendations from the advisory board, Uptake Medical is advising you to take the following actions.

Requested Actions

To reduce the risk of similar incidents, Uptake Medical Technology recommends you take the following actions:

1. Review and consider available medical and therapeutic options for the patients, including other treatments for LVR;

2. Treat patients with InterVapor System only if there is **no increased risk of bleeding** (incl. drug-induced, e.g. oral anticoagulation or platelet aggregation inhibitors) and for which this type of medication can be discontinued for at least 6 weeks post-procedure;
3. Review and understand the contraindications listed in the User Manual;

Uptake Medical Technology will clarify the language in the Instructions For Use (IFU - User Manual). In the meantime, ensure a thorough medical history is taken, and become familiar with the patient's medical condition and medication therapy prior to InterVapor treatment. Advise the patients that 2-4 weeks post procedure, they may experience symptoms of varying severity including, cough, sputum, hemoptysis, dyspnea, fever, fatigue and chest discomfort. The discharge x-ray or CT scan should be reviewed for signs of infiltrates, pneumonia, and other abnormalities. These patients require increased vigilance. Post-treatment monitoring of the patient will ensure the continued safety and favorable outcomes for your patients.

As stated in the InterVapor IFU, the safety and efficacy of the InterVapor procedure has not been established in patients with known coagulopathy or current use of anticoagulants. Additionally, patients with bleeding disorders and unstable cardiovascular conditions or other concomitant illnesses that could pose a significant increased risk for complications should not be treated with the InterVapor System.

Supporting Information

Results from the commercial experience for InterVapor System show an event rate of 1.2% for serious hemoptysis, 0.75% for serious hemoptysis leading to death, and 2.3% death rate overall. These rates align with that reported during the STEP-UP Randomized Clinical Trial (RCT) evaluating the InterVapor System, as referenced in Table 1.

Table 1. **Serious Adverse Event Rate**

Serious Adverse Event Category	STEP-UP RCT (n = 85 procedures)	Post-Market InterVapor (n=266 procedures)
Total Respiratory SAE's	47% (40)	*NA*
Total SAEs possibly related to procedure	29.4% (25)	15.8% (42)
Hemoptysis	1.2% (1)	1.1% (3)
Mortality • Possibly related to procedure • Related to patient's medical condition	1.2% (1)	2.3% (6) 0.75% (2) 1.5% (4)

The post-market rates in Table 1 are also consistent with literature from other lung volume reduction technologies and with the published literature and expected rates for COPD patients suffering from severe emphysema. In this patient population, there are few treatment options. Hemoptysis is well documented and a known risk in Lung Volume Reduction (LVR) therapies. Hemoptysis events reported from clinical trials and clinically similar treatment options (lung volume reduction) are reported in the literature and yield similar rates and frequency, as summarized in Table 2.

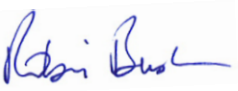
Table 2: **Hemoptysis Events Reported From Similar Treatment Options (Lung Volume Reduction)**

Trial (Product)	Results related to rate and frequency of hemoptysis or death
STEP-UP (InterVapor)[5]	• 1.2% serious hemoptysis in treatment group • 1.2% death rate in treatment group, not related to hemoptysis
Liberate Trial (Valves)[1]	• 3% death rate in 45 days, no serious hemoptysis reported
Vent Trial (Valves)[2]	• 0.5% serious hemoptysis, led to death • 0.9% death rate in 6 months (related to procedure/device) • Hemoptysis (defined as bleeding requiring bronchoscopic inspection) during both the early and late windows was significantly increased in the EBV group (5.6% of patients in the early window and 6.1% in the late window), as compared with no patients in the control group (P=0.02 for both comparisons)
Post-Market Registry (Coils)[3]	• 0.9% serious hemoptysis
Renew Trial (Coils)[4]	• 4.0% serious hemoptysis (SAEs) through 12 months, 1% Hemoptysis Major complication requiring surgery • 4.5% death possibly related to procedure/device in treatment group • 3% death possibly related to procedure/device in crossover treatment group • 2% death rate in crossover group due to massive hemoptysis

Uptake Medical is committed to providing a product that delivers a favorable benefit to risk profile with a low rate of events.

Please acknowledge receipt of this communication and share this safety notice to those within your hospital or staff who should be made aware. Should you have any questions regarding this notice, please contact your local representative or the Clinical team at Uptake Medical (clinical@uptakemedical.com).

Sincerely,



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