# INSTRUCTIONS FOR USE
# VIBRANT SYSTEM

For oral use

**℞ ONLY**

This “Instructions for Use” contains information on how to use the Vibrant system.

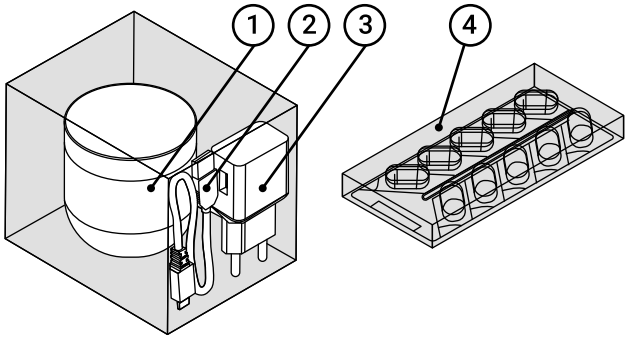
**Indications for Use**

The Vibrant System is an orally administered Capsule that is indicated for the treatment of adults with chronic idiopathic constipation who have not experienced relief of their bowel symptoms by using laxative therapies at the recommended dosage for at least one month.

## 1. Vibrant System Components

The Vibrant system is comprised of the following components:

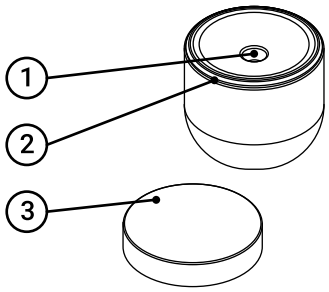
1. Pod
2. USB cable
3. AC/DC USB adapter
4. 2 blister packs of 10 Vibrant Capsules each, in 1 box




**The Pod**

The Pod is used to activate the Vibrant Capsule before swallowing the Capsule:

1. Designated Groove for Capsule
2. Light ring indicator
3. Pod lid




The Capsule should not cause any interference during travel activities such as flying and going through airport security.

## 2. Important Information for Patients

**Contraindications**

The Vibrant Capsules are contraindicated for use under the following conditions:

- History of complicated/obstructive diverticular disease
- History of intestinal or colonic obstruction or suspected intestinal obstruction
- Clinical evidence of current and significant gastroparesis
- History of significant gastrointestinal disorder, including any form of inflammatory bowel disease or gastrointestinal malignancy (celiac disease is accepted if the subject has been treated and is in remission), and/or anal fissures and fistulas
- History of Zenker’s diverticulum, dysphagia, esophageal stricture, eosinophilic esophagitis or achalasia
- Women who are pregnant or lactating

**Warnings**

- The Vibrant Capsule is MR (magnetic resonance) unsafe. The device has not been evaluated for safety and compatibility in the MR environment. It has not been tested for heating, migration, or image artifact in the MR environment. Undergoing an MRI (magnetic resonance imaging) while the Capsule is inside your body may result in patient injury, including serious damage to your intestinal tract or abdominal cavity.
    - If you require an MRI, instruct your physician to verify Capsule expulsion via abdominal X-ray before undergoing an MRI examination.
- After ingesting a Vibrant Capsule and until it is excreted, you should not be near any source of powerful electromagnetic fields such as one created near an MRI device.
- The Capsule should be kept away from implants such as pacemakers, defibrillators, nerve stimulators, and other devices that could be affected by proximity to a DC (direct current) magnetic field.
- If you have reasonable doubt concerning the integrity of a Vibrant Capsule, it should not be used and should be discarded.
- Under no circumstances should a Vibrant Capsule be swallowed without prior activation in the Pod.
- If after ingesting a Vibrant Capsule, you will experience one of the following symptoms, contact a physician immediately and stop taking additional Capsules until instructed by your physician
    - Black, bloody or tarry stools.
    - Abnormal abdominal pain, including new onset of abdominal pain, change in the character of a previously existing abdominal pain, or persistent abdominal pain.
    - Nausea or vomiting.
    - Believe a Capsule has not been expelled from the body, such as if no Capsule has been expelled from the body after 2 weeks from the time of ingestion.
- Vibrant Capsules must be stored in a safe place, out of the reach of children and/or infants.
    - If a child has accidentally swallowed an unused Vibrant Capsule, he/she should be brought immediately to a hospital.
- Use of Vibrant equipment adjacent to or stacked with other equipment should be avoided because it could result in improper operation. If such use is necessary, this equipment and the other equipment should be observed to verify that they are operating normally.
- Use of accessories, transducers and cables other than those specified or provided by the manufacturer of this equipment could result in increased electromagnetic emissions or decreased electromagnetic immunity of this equipment and result in improper operation.
- Portable RF (radio frequency) communications equipment (including peripherals such as antenna cables and external antennas) should be used no closer than 30 cm (12 inches) to any part of the Vibrant Pod, including cables specified by the manufacturer. Otherwise, degradation of the performance of this equipment could result.
- Users should inspect the Pod and Capsule blister pack for possible tampering. If you suspect someone tampered with the Pod, the device should not be used. If you suspect someone tampered with the blister cell for a Capsule, then that Capsule should not be used. Signs of possible tampering include, but are not limited to:
    - For the Pod - cracks or breaks in the Pod casing, scratches around the screw holes, and scratches/marks around the USB port that the user does not recognize.
    - For the Capsule – damage to the blister cell, or the Capsule is not in a sealed blister cell.
- Patients with pelvic floor dyssynergia may have impaired muscular ability to evacuate stool; therefore, they should be monitored for any signs of adverse response and to ensure ability to pass the Capsule.
- The use of this product has not been studied in patients who chronically use non-steroidal anti-inflammatory drugs (NSAIDs). Chronic use is defined as taking full dose NSAIDs more than three times a week for at least six months.

**Precautions**

- Do not use Pod or Capsules if packaging is damaged.
- Read this package insert in its entirety before using the Vibrant Capsule.
- Do not use the Pod if there are any changes or modifications made to it that are not expressly approved by Vibrant Ltd.
- A Vibrant Capsule should not be ingested after its expiration date.
- Avoid biting the Vibrant Capsule prior to swallowing.
- Long-Term Use: The safety and effectiveness of the Vibrant System for long-term use in the indicated population, i.e., for more than 8 weeks, has not been evaluated. Therefore, a physician who elects to use the Vibrant System for extended periods in adults with chronic idiopathic constipation, who have not experienced relief of their bowel symptoms by using laxative therapies, should re-evaluate the individual patient including for long-term usefulness of the device.

**Adverse Events / Side Effects**

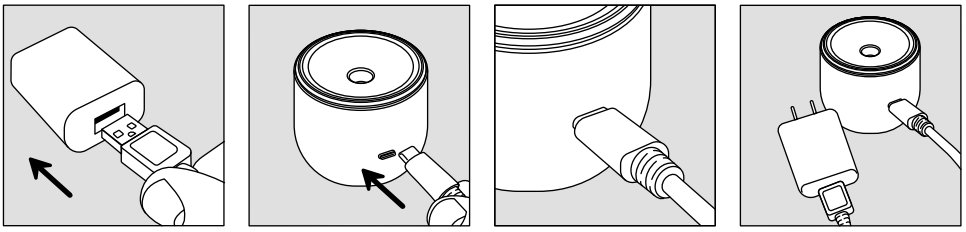
Potential adverse events associated with the use of this device may include abdominal pain, abdominal distension, abdominal discomfort, vomiting, nausea, blood in stool, diarrhea, flatulence, and proctalgia. In rare cases, obstruction may occur.

Note the safety and effectiveness of the Vibrant System for long-term use in the indicated population, i.e., for more than 8 weeks, has not been evaluated.

## 3. Preparation Instructions

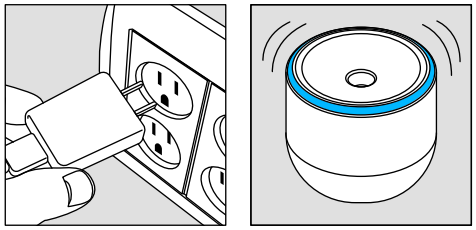
### 3.1. Setting Up the Pod

**3.1.1** Connect the USB cable to the AC/DC adaptor and to the Pod.



**3.1.2** Connect the AC/DC adaptor of the Pod to an electrical outlet.

**3.1.3** The blue light ring indicator on the Pod flashes for about 40 seconds and then turns ON and a short "beep" will be heard to indicate the unit is ready for use. The blue light ring indicator should stay ON at all times while the Pod is in use.



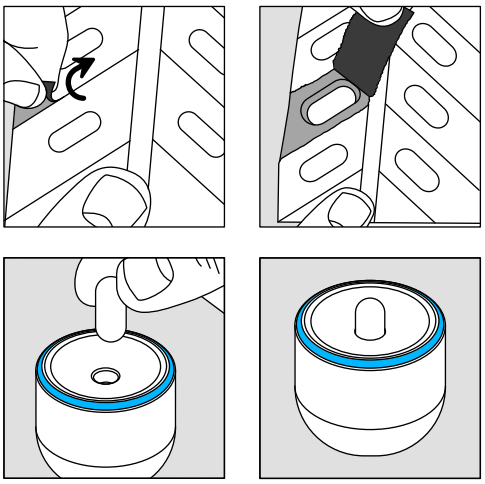
## 4. Administration Instructions

### 4.1 Activating the Capsule

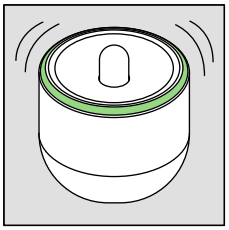
**4.1.1** Remove one Capsule from the blister package.

**4.1.2** Remove the Pod cover.

**4.1.3** Verify the blue light ring indicator is “ON”.



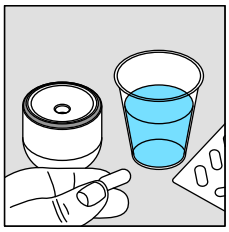
**4.1.4** Check to ensure the absence of foreign matter in the Capsule groove prior to use. Place the Capsule in the designated groove in the center of the Pod. Remove your hand and wait.



**4.1.5** After a few seconds, the "Ready" green light indicator will turn on, and a "beep" will be heard. The Capsule is then ready to be removed from the Pod.

**Now the Capsule is ready to be swallowed.**

**4.1.6** Immediately swallow the Capsule with one glass (~8 ounce) of water. After removing the Capsule from the Pod, the light ring indicator turns blue.



**4.1.7** Replace the Pod cover.

**4.1.8** The Capsules are intended to be orally ingested up to 5 times per week, as directed by a physician. The Capsule should be taken shortly before going to sleep on 5 out of 7 days of the week according to the following schedule: 3 days on, 1 day off, 2 days on, 1 day off.

**Caution:** Do not connect the USB cable to any other device (such as a computer) as this may potentially harm the Pod.

## 5. Storage and Maintenance Instructions

**Pod**

• Keep the Pod in a dry place away from direct sunlight (not in the kitchen or in the bathroom.)
• Thoroughly clean the Pod prior to first use and after each use. The Pod should be cleaned using a clean cloth and 70% isopropyl alcohol and the lid should be closed after cleaning and between uses.
• In the case of electromagnetic disturbance (refer to Section 7, Table 10: Impact of Electromagnetic (EM) Disturbances on Device Function/Performance), reset the Pod by unplugging the AC/DC adaptor from the wall power outlet and plugging it back in after a few seconds.

**Capsules**

• The Vibrant Capsules should be stored in a dry, cool place (below 25˚C/77˚F), away from magnetic sources and away from direct sunlight (not in the kitchen or in the bathroom).
• Keep the Vibrant Capsules in the sealed blister pack until use.
• Even if stored in their original containers and according to recommendations, the Vibrant Capsules can be kept for a limited period only. Please note the expiration date of the Capsules.

## 6. Summary of Clinical Information

A pivotal study (V270) was conducted to evaluate the safety and effectiveness of the Vibrant Capsules. The study was conducted in compliance with 21 CFR parts 50, 56, and 812. V270 was a prospective, randomized, multi-center, double-blinded, placebo-controlled pivotal study. The study included 2 active treatment arms that used different vibration patterns (i.e., Active Mode 1 and Active Mode 2) and a placebo control arm. For the first part of the study, subjects were randomized equally to each arm in a 1:1:1 ratio, for a treatment period of 8 weeks. A “drop the loser” design was pre-specified, whereby the lower performing active treatment was dropped from the study following an interim analysis. After the lower performing active arm was dropped, future subjects were randomized to each of the remaining arms on a 1:1 ratio. The alpha value was adjusted to two-sided 0.025 to account for this design.

Vibrant Capsules were administered 5 times per week, and the treatment arm was compared to a placebo which consisted of a biodegradable soft-gel Capsule filled with soybean oil, beeswax and calcium carbonate. The study population was comprised of subjects with chronic idiopathic constipation (CIC) who were refractory to existing OTC or Rx treatments or could not tolerate the side effects. Patient eligibility was assessed during the initial screening visit and was re-assessed and confirmed during the Baseline visit following a 2 to 3 week run-in period. Randomization occurred following the 2 to 3-week run-in period and verification that the patient satisfied all inclusion criteria and did not meet any exclusion criteria.

**Endpoints**

**Primary Effectiveness Endpoints**

• Complete Spontaneous Bowel Movements (CSBM1) success rate, defined as an increase from the run-in period of at least one weekly CSBM during at least 6 of the 8 weeks of treatment.

• Complete Spontaneous Bowel Movements (CSBM2) success rate, defined as an increase from the run-in period of at least 2 weekly CSBM during at least 6 of the 8 weeks of treatment.

Study success was defined as either the CSBM1 or the CSBM2 success rate being statistically significantly higher in the active arm that was continued after interim analysis, than in the control arm.

**Primary Safety Endpoint**

All adverse events (AEs) related and unrelated to the study treatment.

**Secondary Endpoints**

• Change from baseline in average straining.

• Change from baseline in average stool consistency, using the Bristol Stool Scale.

• Change from baseline in average bloating.

**Selected Additional Secondary Endpoints**

• Treatment satisfaction score using the Treatment Satisfaction Questionnaire for Medication (TSQM).

• Change from baseline in quality of life using the Patient Assessment of Constipation Quality of Life Questionnaire (PAC-QOL).

**Subject Accountability**

A total of 904 subjects were consented and screened. 555 subjects were not randomized: 89% (493/555) were considered screen failures, 5% (28/555) withdrew consent prior to randomization, 2% (10/555) were lost to follow up before randomization, and the other 4% (24/555) for other reasons. A total of 349 consenting subjects were enrolled in the study and randomized. It was subsequently determined that one (1) of the 349 randomized subjects did not meet the eligibility criteria, and 12/349 subjects had less than 2 weeks of diary entries with at least 5 days/week (requirement for randomization); these subjects were thus included in the Intention to Treat (ITT) analysis set, but excluded from the modified ITT (mITT) analysis set. Three (3) subjects in the mITT analysis set had major protocol deviations and were thus excluded from the Per Protocol (PP) analysis set. Subjects with less than 6 weeks of diary data were considered as failures for the CSBM1 and CSBM2 success rates.

The final treatment allocation and analysis sets are shown in Table 1.

**Table 1: Treatment Allocation**

| | Active Mode 1 | Active Mode 2 | Control | Total |
|---|---|---|---|---|
| ITT analysis set | 163 | 37 | 149 | 349 |
| mITT analysis set | 158 | 34 | 144 | 336 |
| PP analysis set | 155 | 34 | 144 | 333 |

Patient demographics are shown in Table 2.

**Table 2: Demographic Characteristics – ITT**

| | | | Active Mode 1 | Active Mode 2 | Control | Total | p-value (Active Mode 1 vs Control) |
|---|---|---|---|---|---|---|---|
| Age (years) | N | | 163 | 37 | 149 | 349 | 0.4391(*) |
| | Mean (SD) | | 47.1 (13.33) | 45.0 (12.25) | 45.9 (13.47) | 46.4 (13.26) | |
| | Median [Range] | % (n/N) | 47.4 [20.6;77.8] | 44.0 [22.2;76.0] | 44.8 [22.1;78.1] | 45.0 [20.6;78.1] | |
| Gender | Male | % (n/N) | 12.3% (20/163) | 24.3% (9/37) | 15.4% (23/149) | 14.9% (52/349) | 0.4177(#) |
| | Female | % (n/N) | 87.7% (143/163) | 75.7% (28/37) | 84.6% (126/149) | 85.1% (297/349) | |
| Race / Ethnicity | Caucasian | % (n/N) | 47.2% (77/163) | 59.5% (22/37) | 40.3% (60/149) | 45.6% (159/349) | 0.7624(#) |
| | Hispanic or Latino | % (n/N) | 19.0% (31/163) | 8.1% (3/37) | 22.8% (34/149) | 19.5% (68/349) | |
| | Black or African American | % (n/N) | 25.2% (41/163) | 29.7% (11/37) | 26.2% (39/149) | 26.1% (91/349) | |
| | Asian / Pacific Islander | % (n/N) | 6.1% (10/163) | 2.7% (1/37) | 8.1% (12/149) | 6.6% (23/349) | |
| | Other | % (n/N) | 2.5% (4/163) | - | 2.7% (4/149) | 2.3% (8/349) | |

(*) t-test
(#) $X^2$ test

**Effectiveness Results**

The pre-specified interim analysis was conducted on the results available from 116 subjects. At the interim analysis timepoint, the Active Mode 2 arm was dropped, and the study continued with only 2 arms: the most promising effectiveness treatment arm (Active Mode 1) and the placebo arm.

Table 3 presents the CSBM1 and CSBM2 success rates by study arm and analysis set. In the mITT set, the CSBM1 success rate was higher in the treatment arm than in the control arm by 17.6 percentage points (chi-square p-value = 0.0011); and the CSBM2 success rate was higher in the active arm than in the placebo arm by 10.0 percentage points (chi-square p-value = 0.0085). The primary effectiveness results met the study success criteria with both the CSBM1 and the CSBM2 success rates statistically significantly higher in the active arm compared to the control. These results were also found in the PP and ITT analysis sets.

**Table 3: CSBM1 and CSBM2 Success Rates in mITT, ITT, and PP Analysis Sets**

| | | Treatment | | Placebo | | p-value (chi-square) |
|---|---|---|---|---|---|---|
| | | % (n/N) | 97.5% CI (Wilson Score) | % (n/N) | 97.5% CI (Wilson Score) | |
| mITT | Imp. by ≥ 1 CSBM - 6 out of 8 weeks | 40.51% (64/158) | [32.18%;49.42%] | 22.92% (33/144) | [16.06%;31.60%] | 0.0011 |
| | Imp. by ≥ 2 CSBM - 6 out of 8 weeks | 23.42% (37/158) | [16.76%;31.72%] | 11.81% (17/144) | [7.03%;19.16%] | 0.0085 |
| PP | Imp. by ≥ 1 CSBM - 6 out of 8 weeks | 40.65% (63/155) | [32.23%;49.65%] | 22.92% (33/144) | [16.06%;31.60%] | 0.0010 |
| | Imp. by ≥ 2 CSBM - 6 out of 8 weeks | 23.23% (36/155) | [16.54%;31.60%] | 11.81% (17/144) | [7.03%;19.16%] | 0.0098 |
| ITT | Imp. by ≥ 1 CSBM - 6out of 8 weeks | 39.26% (64/163) | [31.13%;48.04%] | 22.15% (33/149) | [15.50%;30.61%] | 0.0011 |
| | Imp. by ≥ 2 CSBM - 6 out of 8 weeks | 22.70% (37/163) | [16.23%;30.80%] | 11.41% (17/149) | [6.79%;18.55%] | 0.0085 |

**Secondary Endpoints**

There was an observed reduction in straining in the active arm compared to the placebo arm.

**Table 4: Change from Baseline in Straining (Adjusted for Baseline)**

| | | Adj. Mean | SE | Two-sided 97.5% CI |
|---|---|---|---|---|
| mITT | Treatment | -1.78 | 0.15 | [-2.12;-1.44] |
| | Placebo | -1.32 | 0.16 | [-1.68;-0.97] |
| | Diff. (Treatment-Placebo) | -0.46 | 0.22 | [-0.95;0.03] |
| PP | Treatment | -1.80 | 0.15 | [-2.15;-1.46] |
| | Placebo | -1.33 | 0.16 | [-1.69;-0.98] |
| | Diff. (Treatment-Placebo) | -0.47 | 0.22 | [-0.96;0.02] |
| ITT | Treatment | -1.71 | 0.15 | [-2.04;-1.37] |
| | Placebo | -1.29 | 0.16 | [-1.65;-0.94] |
| | Diff. (Treatment-Placebo) | -0.41 | 0.22 | [-0.90;0.08] |

There was an observed improvement in stool consistency (rated using the Bristol Stool Scale) in the active arm compared to the placebo arm.

**Table 5: Change from Baseline in Stool Consistency (Adjusted for Baseline)**

| | | Adj. Mean | SE | Two-sided 97.5% CI |
|---|---|---|---|---|
| mITT | Treatment | 1.03 | 0.08 | [0.85;1.21] |
| | Placebo | 0.58 | 0.08 | [0.39;0.76] |
| | Diff. (Treatment-Placebo) | 0.45 | 0.11 | [0.19;0.71] |
| PP | Treatment | 1.02 | 0.08 | [0.84;1.20] |
| | Placebo | 0.58 | 0.08 | [0.40;0.77] |
| | Diff. (Treatment-Placebo) | 0.44 | 0.12 | [0.18;0.70] |
| ITT | Treatment | 0.99 | 0.08 | [0.81;1.16] |
| | Placebo | 0.57 | 0.08 | [0.38;0.75] |
| | Diff. (Treatment-Placebo) | 0.42 | 0.11 | [0.16;0.68] |

There was not an observed difference in bloating sensation between study arms.

**Table 6: Change from Baseline in Bloating Sensation (Adjusted for Baseline)**

| | | Adj. Mean | SE | Two-sided 97.5% CI |
|---|---|---|---|---|
| mITT | Treatment | -0.42 | 0.11 | [-0.67;-0.17] |
| | Placebo | -0.37 | 0.12 | [-0.63;-0.10] |
| | Diff. (Treatment-Placebo) | -0.06 | 0.16 | [-0.42;0.30] |
| PP | Treatment | -0.44 | 0.11 | [-0.70;-0.19] |
| | Placebo | -0.37 | 0.12 | [-0.63;-0.11] |
| | Diff. (Treatment-Placebo) | -0.08 | 0.16 | [-0.44;0.29] |
| ITT | Treatment | -0.40 | 0.11 | [-0.64;-0.15] |
| | Placebo | -0.36 | 0.11 | [-0.62;-0.10] |
| | Diff. (Treatment-Placebo) | -0.04 | 0.16 | [-0.39;0.32] |

Treatment Satisfaction Questionnaire for Medication (TSQM) scores were evaluated in the study. The TSQM score for effectiveness was statistically significantly higher in the active mode 1 arm compared to the placebo arm. The mean scores for side-effects, convenience, and global satisfaction were similar in both groups.

Change from baseline in quality of life using the Patient Assessment of Constipation Quality of Life Questionnaire (PAC-QOL) was evaluated in the V270 study. More subjects reported an improvement in quality of life from baseline (on the PAC-QOL) in the Active Mode 1 arm than in the placebo arm (77.9% of Active Mode 1 arm subjects versus 66.2% of placebo arm subjects).

**Safety Results**

The ITT data analysis set served as the principal set for the safety analysis (200 treatment subjects (37 from the Active Mode 2 arm and 163 from the Active Mode 1) and 149 control subjects). A total of 114 AEs were reported during the study: 74 AEs experienced by 62 treatment subjects (31.0.%), and 40 AEs experienced by 26 subjects (17.45%) in the control arm. Two (2) AEs, both in the control arm, were classified as serious adverse events (SAEs), but were not considered related to the study treatment. There were no SAEs reported in the treatment arms.

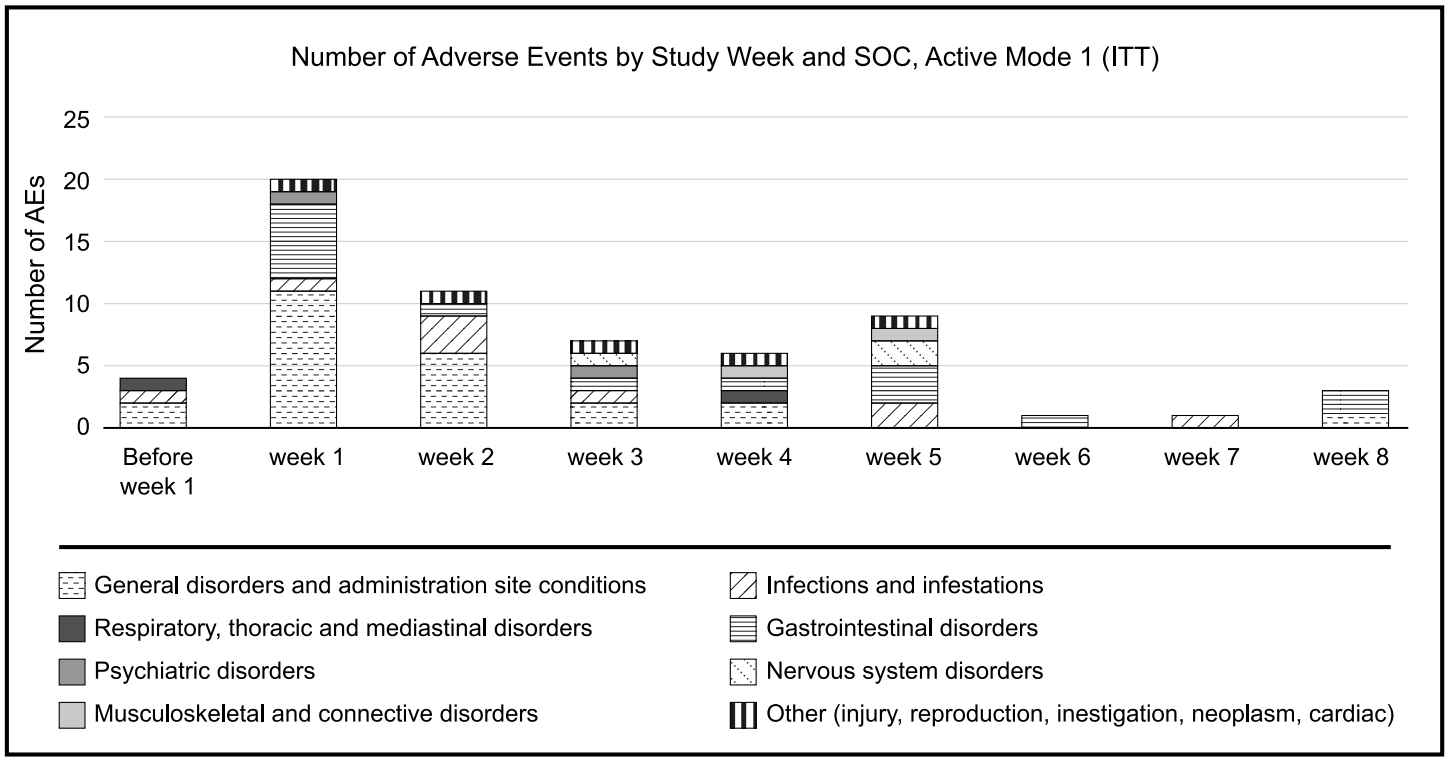
49 AEs were considered possibly, probably or definitely related to the study treatment or procedure (41 in the treatment arm, and 8 in the control arm). Device and procedure related AEs reported in the study included abdominal pain, abdominal distension, abdominal discomfort, vomiting, nausea, diarrhea, flatulence and proctalgia. Medical device discomfort events characterized as sensation of vibration were the most commonly reported device related AE, with 18 subjects (11.04%) in the Active Mode 1 arm reporting 20 such events and 1 subject in the Active Mode 2 arm (2.70%) reporting 1 such event (none in the placebo group).

**Table 7: Adverse Events by System Organ Class, Preferred Term and Relationship (ITT)**

| System Organ Class | Preferred Term | Relation to Device | Active (Combined) | | | Placebo | | |
|---|---|---|---|---|---|---|---|---|
| | | | # of reports | # of subjects | Incidence | # of reports | # of subjects | Incidence |
| Total | Total | Total | 41 | 29 | 14.50% | 8 | 5 | 3.36% |
| | | Possibly related | 12 | 7 | 3.50% | 7 | 4 | 2.68% |
| | | Probably related | 8 | 6 | 3.00% | 1 | 1 | 0.67% |
| | | Related | 18 | 15 | 7.50% | . | . | . |
| | | Related to procedure | 3 | 2 | 1.00% | . | . | . |
| Gastrointestinal disorders | Total | Possibly related | 9 | 5 | 2.50% | 7 | 4 | 2.68% |
| | | Probably related | 5 | 5 | 2.50% | 1 | 1 | 0.67% |
| | Abdominal pain | Possibly related | 1 | 1 | 0.50% | 2 | 2 | 1.34% |
| | Vomiting | Possibly related | 3 | 3 | 1.50% | . | . | . |
| | Nausea | Possibly related | 1 | 1 | 0.50% | . | . | . |
| | | Probably related | 1 | 1 | 0.50% | . | . | . |
| | Diarrhoea | Possibly related | 1 | 1 | 0.50% | . | . | . |
| | | Probably related | 1 | 1 | 0.50% | . | . | . |
| | Abdominal distension | Possibly related | 1 | 1 | 0.50% | 1 | 1 | 0.67% |
| | Flatulence | Possibly related | 1 | 1 | 0.50% | . | . | . |
| | Constipation | Possibly related | 1 | 1 | 0.50% | . | . | . |
| | Proctalgia | Possibly related | . | . | . | 1 | 1 | 0.67% |
| | | Probably related | 1 | 1 | 0.50% | . | . | . |
| | Abdominal discomfort | Probably related | 2 | 2 | 1.00% | . | . | . |
| | Anorectal discomfort | Possibly related | . | . | . | 2 | 1 | 0.67% |
| | Abdominal pain lower | Possibly related | . | . | . | 1 | 1 | 0.67% |
| | Abdominal pain upper | Probably related | . | . | . | 1 | 1 | 0.67% |
| General disorders and administration site conditions | Total | Possibly related | 1 | 1 | 0.50% | . | . | . |
| | | Probably related | 3 | 3 | 1.50% | . | . | . |
| | | Related | 16 | 14 | 7.00% | . | . | . |
| | | Related to procedure | 2 | 1 | 0.50% | . | . | . |
| | Medical device discomfort | Possibly related | 1 | 1 | 0.50% | . | . | . |
| | | Probably related | 3 | 3 | 1.50% | . | . | . |
| | | Related | 16 | 14 | 7.00% | . | . | . |
| | | Related to procedure | 1 | 1 | 0.50% | . | . | . |
| | Discomfort | Related to procedure | 1 | 1 | 0.50% | . | . | . |
| Reproductive system and breast disorders | Total | Possibly related | 1 | 1 | 0.50% | . | . | . |
| | Amenorrhoea | Possibly related | 1 | 1 | 0.50% | . | . | . |
| Nervous system disorders | Total | Possibly related | 1 | 1 | 0.50% | . | . | . |
| | Headache | Possibly related | 1 | 1 | 0.50% | . | . | . |
| Psychiatric disorders | Total | Related | 1 | 1 | 0.50% | . | . | . |
| | Sleep disorder | Related | 1 | 1 | 0.50% | . | . | . |
| Injury, poisoning and procedural complications | Total | Related | 1 | 1 | 0.50% | . | . | . |
| | Intentional device misuse | Related | 1 | 1 | 0.50% | . | . | . |
| Investigations | Total | Related to procedure | 1 | 1 | 0.50% | . | . | . |
| | Weight decreased | Related to procedure | 1 | 1 | 0.50% | . | . | . |

A post-hoc time to adverse event analysis demonstrated a higher prevalence of adverse events early in the study and a declining trend over the 8-week study.

**Figure 1: Adverse Events by Study Week and System Organ Class (ITT)**




**Additional Clinical Information**

Five (5) clinical trials were conducted prior to the V270 pivotal study. The studies included a total of 499 subjects and may have varied from the V270 study treatment protocol in the dosing regimen, number of Capsule vibration sets while passing through the large intestine, and the number of Capsule administered per week. The prior studies are unable to support effectiveness of the Vibrant System. However, FDA considered the cumulative safety data in these studies to support safety of the Vibrant System. Safety data from these prior studies are consistent in the type, severity and frequency of adverse events reported in the V270 pivotal study.

# 7. Pod Firmware Update

The information in this section is only being provided to inform the end user of the background update process.
Pod firmware updates can be performed at any time. Only authorized Vibrant staff are able to perform Pod firmware updates; updates are not intended to be performed by the end user.

As part of the daily communication initiated by the Pod, the Pod always provides its current firmware version number. In case there is a newer version, the cloud will identify it, and will instruct the Pod to start a firmware update process.
The update process starts with a download of the encrypted firmware file. Once the new firmware files are extracted, and only after Pod's verification, the new firmware will become active.
Note that the patient is not required to take any action as part of the above process.

# 8. Pod Cyber Security Guidelines

**Device Interface**

- The Pod device cannot interface with other devices using connectors, physical means, or Bluetooth or Wi-Fi.
- The device interfaces with the Capsule via short range RF antenna.
- The device interfaces with Vibrant Cloud via a secured encrypted cellular connection.

**Cyber Security Protected Design**

The device and Cloud system are designed to provide several features that protect the system against cyber threads:

- Device firmware is encrypted to prevent any changes in firmware by uncertified personnel.
- The device does not store any patient sensitive data.
- The communication between the components (device and cloud) is encrypted.
- Device firmware can always be restored from the cloud via a firmware update process.
- The device works on propriety firmware and therefore very hard to access.
- The device is embedded with an Anti-Malware software that can be updated remotely and creates a protected firmware, such that in runtime, the mitigation code detects and block exploitation attempts.
- In case of exploitation attempt detection, the Anti-Malware transmits an alert to the Cloud server using the Pod cellular modem.
- The device firmware is not accessible to the user. Therefore, no access to any system log files is permitted for the user.

**Cloud Connectivity**

The device and Vibrant Cloud System are designed to provide several features that protect the system against cyber threads:

- The connection with the Vibrant Cloud system is initiated by the Pod and allowed with a valid security certificate.
- Vibrant Cloud is USA HIPAA legislation certified to provide maximal IT protection means.
- All device logs and data are stored in the cloud system and not locally on the device.
- The device and treatment configuration are kept at the cloud and can be restored.
- The system is ready for use. No system settings are required either for using the treatment or for connecting the Pod with Vibrant Cloud.

**Vulnerability Incident Instructions**

In case servicing via a secure network for servicing is required and in case you've detected cybersecurity vulnerability or incident, you should follow the below instructions:

- If you face difficulties operating the Pod and using the treatment that could be originated by a cyber-attack, please contact Vibrant support. Do not use the device until receiving further instructions.

# 9. Electromagnetic Compatibility

**Table 8: Declaration - Electromagnetic Emissions**

| Emissions Test | Compliance | Electromagnetic Environment – Guidance |
|---|---|---|
| Conducted and radiated RF emissions CISPR 11 | Group1 Class B | The Vibrant Capsule System uses RF energy only for its internal function. Therefore, its RF emissions are very low and are not likely to cause any interference in nearby electronic equipment. |
| Harmonic emissions IEC 61000-3-2 | Class A | The Vibrant Capsule System is suitable for use in home healthcare ("home use") and professional healthcare facility ("hospital use") environments. |
| Voltage Fluctuations and Flicker IEC 61000-3-3:2013 | Complies | |

**Table 9: Declaration – Electromagnetic Immunity**

| Immunity Test | IEC 60601 Test Level | Compliance Level | Electromagnetic Environment – Guidance |
|---|---|---|---|
| Electrostatic discharge (ESD) IEC 61000-4-2 | Contact: ±8kV; Air: ±2kV, ±4kV, ±8kV, and ±15 kV | Contact: ±8kV; Air: ±2kV, ±4kV, ±8kV, and ±15 kV | Floors should be wood, concrete or ceramic tile. If floors are covered with synthetic material, the relative humidity should be at least 30%. |
| Electrical fast transient/ burst IEC 61000-4-4 | Contact: ±2kV Power input ports<br>Contact: ±1 kV Power input ports | Contact: ±2kV Power input ports<br>N/A | Mains power quality should be that of a typical commercial or hospital environment. |
| Surge IEC 61000-4-5 | ±0.5kV and ±1kV line to line<br>±2 kV line(s) to earth<br>±2 kV Signal (input/output)to earth | ±0.5kV and ±1kV line to line<br>N/A<br>N/A | Mains power quality should be that of a typical commercial or hospital environment. |
| Conducted RF IEC 61000-4-6 | 3V<br>0.15 MHz – 80 MHz<br>6V in ISM and amateur radio bands between 0.15 MHz and 80 MHz.<br>And 80% AM at 1 kHz | 3V<br>0.15 MHz – 80 MHz<br>6V in ISM and amateur radio bands between 0.15 MHz and 80 MHz.<br>And 80% AM at 1 kHz | Portable and mobile RF communications equipment should be used no closer to any part of the Vibrant Capsule System, including cables, than the recommended separation distance calculated from the equation applicable to the frequency of the transmitter.<br>$d = [\frac{3,5}{V_1}]\sqrt{P}$<br>$d = [\frac{12}{V_2}]\sqrt{P}$<br>$d = [\frac{12}{E_1}]\sqrt{P}$ 80 MHz to 800 MHz<br>$d = [\frac{23}{E_1}]\sqrt{P}$ 800 MHz to 2,5 GHz |
| Radiated RF IEC 61000-4-3 | 10 V/m<br>80 MHz – 2700 MHz<br>80% AM at 1 kHz<br>3V from 0.15 to 80MHz; 6V from 0.15 to 80MHz and 80% AM at 1kHz | 10 V/m<br>80 MHz – 2700 MHz<br>80% AM at 1 kHz<br>3V from 0.15 to 80MHz; 6V from 0.15 to 80MHz and 80% AM at 1kHz | **Recommended separation distance** where P is the maximum output power rating of the transmitter in watts (W) according to the transmitter manufacturer and d is the recommended separation distance in meters (m).<br>Field strengths from fixed RF transmitters, as determined by an electromagnetic site survey, should be less than the compliance level in each frequency range.<br>D Interference may occur in the vicinity of equipment marked with the following symbol:<br>  |
| Voltage dips, short interruptions and voltage variations on power supply input lines IEC 61000-4-11 | 0% UT; 0.5cycle at 0°, 45°, 90°, 135°,180°, 225°, 270° and 315° 0% UT; 1cycle and 70% UT; 25/30 cycles Single phase at 0° 0% UT; 250/300 cycle | 0% UT; 1cycle and 70% UT; 25/30 cycles Single phase at 0° 0% UT; 250/300 cycle | Mains power quality should be that of a typical commercial or hospital environment. If the user of the Vibrant Capsule System requires continued operation during power mains interruptions, it is recommended that the Vibrant Capsule System be powered from an uninterruptible power supply or a battery. |
| Power frequency (50/60 Hz) magnetic field IEC 61000-4-8 | 30 (A/m) | 30 (A/m) | Power frequency magnetic fields should be at levels characteristic of a typical location in a typical commercial or hospital environment. |
| **NOTE:** UT is the AC mains voltage prior to application of the test level. | | | |

**Table 10: Impact of Electromagnetic (EM) Disturbances**

| Function/ performance | Normal function/ performance | Lost/degraded performance due to EM disturbance |
|---|---|---|
| Turning on | "On" LED indication illuminates green + short audible tone | "On" LED indication does not illuminate green and tone is not heard |
| Capsule successful activation | "Ready" LED indication illuminates green + short "beep" audible tone | "Ready" LED indication does not illuminate green and tone is not heard |
| Capsule unsuccessful activation | "X" LED indication illuminates and flashes red + 5 short "beep" audible tones | "X" LED indication does not illuminate and 5 short audible tones are not heard |
| Capsule removal at the end of successful activation | "Ready" LED indication turns off | "Ready" or "X" LED indication stays illuminated |
| Capsule removal at the end of unsuccessful activation | "X" LED indication turns off | "X" LED indication stays illuminated |

**Table 11: Wireless Communication Specifications**

| | |
|---|---|
| **Intended Range** | 10mm |
| **RF Frequency** | 42.5KHz |
| **Maximum Transfer Power** | 0.6W |

**Table 12: Test Specifications for Enclosure Port Immunity to RF Wireless Communications Equipment**

| Test frequency (MHz) | Band a) (MHz) | Service a) | Modulation b) | Maximum power (W) | Distance (m) | Immunity Test Level (V/m) | Compliance level (V/m) |
|---|---|---|---|---|---|---|---|
| 385 | 380–390 | TETRA 400 | Pulse modulation[b)] 18 Hz | 1.8 | 0.3 | 27 | 27 |
| 450 | 430–470 | GMRS 460, FRS 460 | FM[c)] ± 5 kHz deviation 1 kHz sine | 2 | 0.3 | 28 | 28 |
| 710 745 780 | 704–787 | LTE Band 13, 17 | Pulse modulation[b)] 217 Hz | 0.2 | 0.3 | 9 | 9 |
| 810 870 930 | 800–960 | GSM 800/900, TETRA 800, iDEN 820, CDMA 850, LTE Band 5 | Pulse modulation[b)] 18 Hz | 2 | 0.3 | 28 | 28 |
| 1720 1845 1970 | 1,700 – 1,990 | GSM 1800; CDMA 1900; GSM 1900; DECT; LTE Band 1, 3, 4, 25; UMTS | Pulse modulation[b)] 18 Hz | 2 | 0.3 | 28 | 28 |
| 2450 | 2,400 – 2,570 | Bluetooth, WLAN, 802.11 b/g/n, RFID 2450, LTE Band 7 | Pulse modulation[b)] 217 Hz | 2 | 0.3 | 28 | 28 |
| 5240 5500 5785 | 5,100 – 5,800 | WLAN 802.11 a/n | Pulse modulation[b)] 217 Hz | 0.2 | 0.3 | 9 | 9 |

NOTE: If necessary to achieve the IMMUNITY TEST LEVEL, the distance between the transmitting antenna and the ME EQUIPMENT or ME SYSTEM may be reduced to 1 m. The 1 m test distance is permitted by IEC 61000-4-3

a) For some services, only the uplink frequencies are included.
b) The carrier shall be modulated using a 50 % duty cycle square wave signal.
c) As an alternative to FM modulation, 50 % pulse modulation at 18 Hz may be used because while it does not represent actual modulation, it would be worst case.

**Warning**
Use of this equipment adjacent to or stacked with other equipment should be avoided because it could result in improper operation. If such use is necessary, this equipment and the other equipment should be observed to verify that they are operating normally.

**Warning**
Use of accessories, transducers and cables other than those specified or provided by the manufacturer of this equipment could result in increased electromagnetic emissions or decreased electromagnetic immunity of this equipment and result in improper operation.

**Warning**
Portable RF communications equipment (including peripherals such as antenna cables and external antennas) should be used no closer than 30 cm (12 inches) to any part of the [ME EQUIPMENT or ME SYSTEM], including cables specified by the manufacturer. Otherwise, degradation of the performance of this equipment could result."

**Table 13: FCC Compliance**

| FCC Test | Compliance | FCC Guidance |
|---|---|---|
| FCC Part 15, Subpart B | Class B | This equipment has been tested and found to comply with the limits for a Class B digital device, pursuant to part 15 of the FCC Rules. These limits are designed to provide reasonable protection against harmful interference in a residential installation. This equipment generates, uses and can radiate radio frequency energy and, if not installed and used in accordance with the instructions, may cause harmful interference to radio communications. However, there is no guarantee that interference will not occur in a particular installation. If this equipment does cause harmful interference to radio or television reception, which can be determined by turning the equipment off and on, the user is encouraged to try to correct the interference by increase the separation between the equipment and receiver. |
| **NOTE:** "Harmful interference" is defined in 47 CFR § 2.12 by the FCC as follows: Interference which endangers the functioning of a radionavigation service or of other safety services or seriously degrades, obstructs, or repeatedly interrupts a radio communication service operating in accordance with the [ITU] Radio Regulations. | | |

# 10. Symbols

| | |
|---|---|
| ℞ ONLY | Federal (U.S.) law restricts this device to sale by or on the order of a physician |
| 2 | The Capsule component is intended for single use |
| | Keep dry |
| IP22 | Protected from touch by fingers and objects greater than 12 mm |
| | Type BF applied part |
| | For additional information on how to use the Vibrant System, please call Toll Free 866-359-7532 |
| | For additional information regarding the Vibrant System, you may visit our website at www.vibranthcp.com |

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