Reactie LivaNova (in 2 delen ontvangen)

Deel 1

While we are not able to participate in the broadcast planned for Monday, Nov. 26, we want to provide you with context and information related to your questions and broadcast plans.

Care for our patients and the quality of our products are at the forefront of everything we do. We have frequent interactions with the U.S. Food and Drug Administration (FDA) and various regulatory authorities around the world, ensuring that we comply with all required medical device reporting and taking appropriate action as necessary.

All of our efforts are focused on saving patients' lives and improving the quality of patients' lives. While a small percentage of patients may experience adverse events with any type of medical treatment, we are committed to developing treatments and therapies with the goal to positively impact all of our patients. LivaNova instills its quality processes with extreme rigor and care, working to treat every device with the special attention each patient deserves.

Jeanne Lenzer's book, *The Danger Within Us,* focuses on a small percentage of adverse effects and events. While unfortunate, adverse events can and do happen, but it is a tremendous disservice to dismiss effective treatments that provide positive, life-changing results for so many patients. In the case of adverse events, LivaNova works diligently and in tandem with appropriate regulatory authorities to effectively address and manage issues that arise for patients using our treatments and therapies.

LivaNova's VNS Therapy® is an important treatment option for patients with epilepsy who have tried and failed multiple medications. Uncontrolled epilepsy such as this can be life-threatening and puts patients at significant risk for accidental death and SUDEP (Sudden Unexpected Death in Epilepsy). VNS Therapy, in combination with patients' epilepsy medication, provides a safe and effective means of combating drug-resistant epilepsy for these patients.

Over the past 20 years, more than 100,000 patients worldwide have received VNS Therapy. VNS Therapy is the most proven implantable device solution for epilepsy with more than 1,000 clinical papers published. More than 6,000 of these patients have participated in clinical studies of VNS Therapy, including the two randomized controlled trials that resulted in PMA Approval. The treatment is effective, helping patients have fewer seizures, shorter seizures and faster recovery. Many of these patients have shared their remarkable stories with us, and can be seen on our website.

We also understand you have questions around a Field Safety Notice that was issued in June 2017. LivaNova takes great care to recognize and deal with any device-related issues quickly and with a high level of vigilance. On June 30, 2017, LivaNova issued a Voluntary Medical Device Correction, also known as a Field Safety Notice (FSN) related to a possible shorter than expected longevity (or battery life) on certain Model 105 AspireHC and Model 106 AspireSR VNS Therapy generators for the treatment of epilepsy. The FSN explained that although the lifespan of the device may be shorter, its functions are not affected and the administration of the therapy remains intact until the device reaches the end of its life (EOS). Also the status indicators of the device's battery were not affected and accurately reflected the device's battery status. The production problem has been resolved and does not affect devices produced after September 2015. The observed occurrence of premature EOS within the group of potentially affected devices is 10.1% for Model 105 and 11.8% for Model 106.

Recommended actions to be taken by providers included:

1) Monitoring patients on a regular basis and continuing to perform diagnostic tests on each visit to check the battery status.
2) Ensuring that epilepsy patients continue to regularly use their magnet to check if the stimulation is felt as described.

The FSN was issued to impacted hospitals and included a description of the problem, recommended action to be taken, as well as details on the affected devices potentially impacted by the issue. The FSN advised organizations receiving the information to communicate it to all personnel who need to be aware of it. LivaNova also routed a Customer Response Form to confirm receipt of the FSN.

LivaNova did recently expand this medical device correction in the U.S. for devices distributed prior to October 2015. A screening process was implemented for devices that had not yet been distributed at the time of the initial correction. Further analysis determined that some screened devices may have a shorter than expected battery longevity, although the issue is not as prominent as the devices associated with the field action from July 2017.

Deel 2

While we are not able to participate in the broadcast planned for Monday, Nov. 26, we want to provide you with context and information related to your questions and broadcast plans.

Care for our patients and the quality of our products are at the forefront of everything we do. We have frequent interactions with the U.S. Food and Drug Administration (FDA), EU notified bodies and competent authorities and various regulatory authorities around the world, ensuring that we comply with all required medical device reporting and taking appropriate action as necessary.

All of our efforts are focused on saving patients' lives and improving the quality of patients' lives. While a small percentage of patients may experience adverse events with any type of medical treatment, we are committed to developing treatments and therapies with the goal to positively impact all of our patients and decrease the risk of adverse events with each successive product generation. LivaNova instills its quality processes with extreme rigor and care, working to treat every device with the special attention each patient deserves.

Jeanne Lenzer's book, The Danger Within Us, focuses on a small percentage of adverse effects and events. While unfortunate, adverse events can and do happen, but it is a tremendous disservice to dismiss effective treatments that provide positive, life-changing results for so many patients. In the case of adverse events, LivaNova works diligently and in tandem with appropriate regulatory authorities to effectively address and manage issues that arise for patients using our treatments and therapies.

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Recommended actions to be taken by providers included:
1) Monitoring patients on a regular basis and continuing to perform diagnostic tests on each visit to check the battery status.
2) Ensuring that epilepsy patients continue to regularly use their magnet to check if the stimulation is felt as described.

The FSN was issued to impacted hospitals and included a description of the problem, recommended action to be taken, as well as details on the affected devices potentially impacted by the issue. The FSN advised organizations receiving the information to communicate it to all personnel who need to be aware of it. LivaNova also routed a Customer Response Form to confirm receipt of the FSN.

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Finally, we provide the following responses to the questions for LivaNova about VNS Dutch Broadcast Radar (AVROTROS) that were sent to LivaNova on Saturday, November 24, 2018

How many safety warnings, recalls, field safety notices were sent [please fill in a number] to how many countries [please fill in a number] concerning the VNS Aspire model 106 ?
A: We would be willing to provide these data, but given that we received the request on Saturday (November 24, 2018), we will be unable to provide it by the 11:30 am CET Monday (November 26, 2018) deadline.

According to Jeanne Lenzer: in early studies, about 20-30% of patients had more seizures with VNS and this was not reported.
What is your response to this?
A: Ms. Lenzer was provided these data during the drafting of her book. These data were included in the FDA Summary of Safety and Effectiveness during the Pre-Market Approval (PMA) review process. Since approval in 1997, these data are publicly available from the Physician Manual posted on our website, see Figure 87 on page 215.

What are the death rates with VNS before conditional approval by the FDA, meaning from trials performed in the EU. Please be as specific as you can, so numbers of deaths in Europe before the VNS got FDA approved (for indication epilepsy in the US).
A: As with the response to the prior question, the number of deaths prior to FDA approval were provided in the FDA Summary of Safety and Effectiveness during the PMA Review process and are publicly available from the Physicians Manual from our website, see Table 85, page 214.

About VNS Model 101: how many safety alerts were published worldwide about this model?
What was the problem with VNS model 101?
A: We would be willing to provide this information, but given that we received the request on Saturday (November 24, 2018), we will be unable to provide it by the 11:30 am CET Monday (November 26, 2018) deadline.

How many incident reports are reported globally about VNS devices (all models) in the last 10 years? Please give me an exact number.
A: We would be willing to provide these data, but given that we received the request on Saturday (November 24, 2018), we will be unable to provide it by the 11:30 am CET Monday (November 26, 2018) deadline.

The Models 300, 302 and 303: a 'global medical device competent authority report' was sent around.
- What happened with this report after it was sent around?
- How was this problem investigated?
- Were the models removed from the market?
- Were these models removed from the market in The Netherlands?
A: We would be willing to provide details, but it is unclear to which report you are referring. Please clarify with the dates of this report and the topic.

How many report you have received about incidents, reports and deaths from The Netherlands with VNS (all models)?
How many reports have you submitted to the Dutch Health Care Inspectorate about the VNS (all models)?

A: We would be willing to provide these data, but given that we received the request on Saturday (November 24, 2018), we will be unable to provide it by the 11:30 am CET Monday (November 26, 2018) deadline.