

UPDATE: Potential Risks with Liquid-filled Intra-gastric Balloons - Letter to Health Care Providers

April 27, 2020

The U.S. Food and Drug Administration (FDA) is providing an update on the potential risks of over-inflation (spontaneous hyperinflation), acute pancreatitis, and deaths in patients with Orbera and ReShape liquid-filled intra-gastric balloons used for weight loss in adult patients with obesity.

The FDA first communicated on the potential risk of hyperinflation and acute pancreatitis with liquid-filled intra-gastric balloons in February 2017 ([/medical-devices/letters-health-care-providers/fda-alerts-health-care-providers-about-potential-risks-liquid-filled-intra-gastric-balloons](#)). Since then, the FDA provided updates in August 2017 ([/medical-devices/letters-health-care-providers/update-potential-risks-liquid-filled-intra-gastric-balloons-letter-health-care-providers](#)) and June 2018 ([/medical-devices/letters-health-care-providers/update-potential-risks-liquid-filled-intra-gastric-balloons-letter-health-care-providers-o](#)) about the potential risk of death with liquid-filled intra-gastric balloons, and in December 2019 announced the availability of the final data summary for the Reshape balloon post-approval study (PAS).

Now, the PAS for the Orbera intra-gastric balloon has been completed.

The current update describes the results from the post-approval studies for hyperinflation and acute pancreatitis for both the Orbera and ReShape devices, provides an update on adverse event reports received by the FDA, and provides our latest recommendations to health care providers.

Recommendations

The FDA recommends that health care providers:

- Consider the post-approval study results, including specifically hyperinflation and acute pancreatitis, when discussing the risks and benefits of liquid-filled intra-gastric balloons with patients.
- Carefully follow the product labeling which includes more information about possible risks associated with the use of these devices in the U.S.

The FDA continues to recommend that health care providers:

- Instruct patients about the symptoms of potentially life-threatening complications such as balloon deflation, gastrointestinal obstruction, ulceration, and gastric and esophageal

perforation and advise them when to seek medical attention.

- Monitor patients closely during the entire duration of treatment with liquid-filled intra-gastric balloon systems for potential complications, including acute pancreatitis, spontaneous hyperinflation, and other potentially life-threatening complications.
- Report any adverse events related to intra-gastric balloon systems through MedWatch, the FDA Safety Information and Adverse Event Reporting program ([/safety/medwatch-fda-safety-information-and-adverse-event-reporting-program/reporting-serious-problems-fda](https://www.fda.gov/safety/medwatch-fda-safety-information-and-adverse-event-reporting-program/reporting-serious-problems-fda)).

Background

In 2015, the FDA approved two liquid-filled intra-gastric balloon systems for use in the U.S., the Orbera and ReShape intra-gastric balloon systems. The Orbera Intra-gastric Balloon System is manufactured by Apollo Endosurgery and the ReShape Integrated Dual Balloon System, previously manufactured by ReShape Medical Inc., was acquired by Apollo Endosurgery in December 2018. In January 2019, Apollo Endosurgery stopped selling and distributing the ReShape intra-gastric balloon.

As a condition of approval for both the Orbera and ReShape intra-gastric balloons, the FDA required the manufacturers to conduct a post-approval study assessing their postmarket performance. The FDA's Post-Approval Study Database provides the study protocol parameters for the Orbera (https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma_pas.cfm?t_id=534908&c_id=3558) post-approval study and ReShape (https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma_pas.cfm?t_id=538679&c_id=3557) post-approval study. The primary endpoint in both studies was the rate of device- and procedure-related serious adverse events.

The FDA is issuing this current letter to health care providers to inform them of the final results from the post-approval studies, specifically for hyperinflation and acute pancreatitis. The final data summary for all other post-approval study results can be found on the respective post-approval study webpages for Orbera (https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma_pas.cfm?t_id=534908&c_id=3558) and ReShape (https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma_pas.cfm?t_id=538679&c_id=3557). In addition, the FDA is providing an update on our continued evaluation of reported deaths in patients with Orbera and ReShape liquid-filled intra-gastric balloons.

In 2016, the FDA approved the Obalon Balloon System (<https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=P160001>), which is a gas-inflated intra-gastric balloon system unlike Orbera and ReShape, which are liquid-filled. The

FDA also required its manufacturer to conduct a post-approval study assessing the postmarket performance of the device. To date, the FDA has not received any reports of death, hyperinflation or acute pancreatitis associated with the Obalon Balloon System in the U.S. The FDA will continue to monitor the results of the ongoing post-approval studies for the Obalon Balloon System (https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma_pas.cfm?t_id=586643&c_id=4124) and Obalon Navigation-Touch System (https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma_pas.cfm?t_id=648004&c_id=5158), as well as other sources of adverse event reports.

Risk of Hyperinflation

Hyperinflation involves the spontaneous filling of intra-gastric balloons with additional air or liquid while inside a patient's stomach, typically resulting in the need for early device removal.

From the Orbera post-approval study, 6 out of 258 patients (2.3%) experienced balloon hyperinflation. The onset of symptoms ranged from as early as within 1 week of balloon placement, to 23 weeks after balloon placement. Clinical symptoms included nausea, vomiting, and abdominal pain. In four of the six cases, these symptoms prompted the early removal of the balloons. In one patient, the balloon was removed at 24 weeks (6 months) after placement due to symptoms. For the remaining event, balloon hyperinflation was found at the time of removal and did not involve any clinical symptoms.

From the ReShape post-approval study, there were no events of hyperinflation reported.

The FDA has received over 200 adverse event reports of hyperinflation worldwide since the 2015 approvals of Orbera and ReShape, with over 99% of those reports received for Orbera. The FDA continues to work with Apollo Endosurgery to evaluate the root cause of hyperinflation with the Orbera intra-gastric balloon, as well as potential mitigation strategies. The FDA wants to ensure that you are aware of the incidence of this potential complication as observed in the post-approval studies.

Risk of Acute Pancreatitis

Acute pancreatitis may develop in patients with liquid-filled intra-gastric balloons. Although the precise pathophysiology is unknown, the mechanism could be related to pressure from the balloon and distended stomach causing direct injury to the pancreatic parenchyma, compression of the pancreatic duct, and/or indirect pancreatic injury through duodenal obstruction.

From the Orbera post-approval study, there were no events of acute pancreatitis reported.

From the ReShape post-approval study, two out of 159 patients (1.3%) had diagnosed acute pancreatitis. The onset of symptoms occurred at 3 days and two weeks after balloon placement, respectively. Clinical symptoms included nausea, vomiting, and abdominal pain. In both cases, the balloon was removed early.

The FDA has received nearly 30 adverse event reports of acute pancreatitis worldwide since the 2015 approvals of Orbera and ReShape, with over two-thirds of those reports received for Orbera. Although the focus of this communication is to highlight the adverse events observed in the post-approval studies for liquid-filled balloons, the FDA is aware of published cases of pancreatitis with air-filled intra-gastric balloons in patients outside of the U.S. The FDA will continue to work with the manufacturers of all available intra-gastric balloons in the U.S. to monitor this potential complication.

Risk of Death

There were no deaths reported in the Orbera and ReShape post-approval studies; however, it should be noted that neither of the studies were powered to detect rare events such as death. Additionally, there were no events of gastric or esophageal perforation reported in either study.

Since our update in June 2018 ([/medical-devices/letters-health-care-providers/update-potential-risks-liquid-filled-intra-gastric-balloons-letter-health-care-providers-o](https://www.fda.gov/medical-devices/letters-health-care-providers/update-potential-risks-liquid-filled-intra-gastric-balloons-letter-health-care-providers-o)), the FDA has received reports of one death in the U.S. associated with the Orbera device, four deaths outside of the U.S. associated with the Orbera device, and one death outside of the U.S. reported from the literature for the Orbera device. Of these, four deaths, including one in the U.S., occurred following gastric perforation, one day to 6 months after balloon placement. One reported death involved a patient outside the U.S. who died one day after balloon placement; however, the root cause and device relatedness of the death is not known. One death, outside of the U.S. was reported from the literature as a case of misdiagnosed Wernicke-Korsakoff Syndrome (Wernicke-Korsakoff syndrome is a neurodegenerative disorder resulting from a vitamin B1 deficiency) after intra-gastric balloon therapy.

Since the approvals of Orbera and ReShape, the FDA has received reports for a total of 18 deaths that occurred worldwide. Ten (10) of these 18 deaths occurred outside of the U.S. The remaining 8 deaths occurred in the U.S. (five with Orbera and three with ReShape). Additional clinical descriptions are as follows:

- Occurred following gastric perforation (n=3)
- Occurred following esophageal perforation (n=1)
- Occurred within a few days of balloon placement, but we do not know the root cause of death and we are unable to definitively attribute the death to the balloon therapy (i.e. unanticipated death) (n=2)

The FDA will continue to monitor the safety of liquid-filled intra-gastric balloons by working with manufacturers to monitor and evaluate death reports, assess possible risk factors and mitigations, and ensure that the products' labeling addresses this risk.

FDA Actions

The FDA will continue to work with Apollo Endosurgery to ensure that the Orbera product labeling includes the post-approval study findings. Since 2017, the FDA has worked with the manufacturers of all available intra-gastric balloons in the U.S. (liquid-filled and gas-filled) to update their labeling with more information about possible risks associated with use of their device in the U.S. including death, acute pancreatitis, and hyperinflation. We will continue to ensure that the products' labeling address these risks, as well as other potentially life-threatening complications.

The FDA will continue to keep health care providers and the public informed if new or additional information becomes available.

Reporting Problems to the FDA

The FDA encourages health care providers to report any adverse events or suspected adverse events related to intra-gastric balloons.

- Voluntary reports can be submitted through [MedWatch, the FDA Safety Information and Adverse Event Reporting program](#).
- Device manufacturers and user facilities must comply with the applicable [Medical Device Reporting \(MDR\) regulations](#).
- Health care personnel employed by facilities that are subject to the [FDA's user facility reporting requirements](#) should follow the reporting procedures established by their facilities.

Prompt reporting of adverse events can help the FDA identify and better understand the risks associated with medical devices.

Contact Information

If you have questions about this letter, contact the [Division of Industry and Consumer Education \(DICE\)](#):