

FAQ on CE Mark Non-Renewal of Textured Breast Implants and Textured Tissue Expanders

December 19, 2018

1. What happened?

Allergan's breast implant portfolio is regulated in Europe by the French Notified Body, GMED. Like other manufacturers of medical devices, Allergan is periodically required to submit for re-certification of its CE mark in order to continue manufacturing and supplying its devices, including the family of breast implant products. On Friday, December 14th, 2018, Allergan was informed by GMED that a routine review and renewal of the CE mark for textured breast implants and tissue expanders had not been completed. Allergan's current certificates for its family of textured breast implant products expired on December 16, 2018.

The company has suspended sales of textured breast implants and tissue expanders in CE Mark countries and is withdrawing any remaining supply in European markets following a compulsory recall request from Agence Nationale de Sécurité du Médicament (ANSM), the French regulatory authority. The action stems from the expiration of the company's CE Mark for these products, which is regulated by Allergan's Notified Body, LNE-GMED. Allergan will continue to work through the CE Mark renewal with GMED, and is planning an appeal to ensure that appropriate patients have access to the products that their surgeons recommend. This decision does not impact sales in the United States. This action only pertains to the textured implant products and does not impact the smooth implant products, which will continue to be available for sale. Patient safety and product quality are of highest priority at Allergan and we are committed to strict adherence to all regulatory requirements and to the highest industry standards for our products.

Although Allergan disagrees with ANSM's request, the Company is fully cooperating with the authority. Allergan stands behind the benefit/risk profile of our breast implant products. The ANSM request, and this action, are not based on any new scientific evidence regarding these products. Furthermore, ANSM has not identified any immediate risk to the health of women with textured breast implants. Allergan stands behind the safety and benefit-risk profile of the entire portfolio of breast implants.

2. Have any safety issues been identified that are associated with incompleteness of the CE mark renewal?

No new safety issues have been identified. Allergan is confident in the safety of the products on the market.

3. Why is there a recall being conducted in the EU?

ANSM, the French regulatory authority, has issued a compulsory recall of Allergan textured breast implants and tissue expanders. Allergan has halted sales of the textured implants in CE Mark countries and is withdrawing any remaining supply from European markets. It is important to note that the ANSM request is not based on any new scientific evidence regarding these products.

4. What is the timing to resolve this issue?

Allergan is working directly with GMED to allow for re-issuance of the CE mark for these products so that the Company can resume manufacturing and supply as quickly as possible.

5. What is the potential sales impact?

On a FY 2018 basis, textured implant sales from CE mark countries represent approximately \$60 million in net revenues.

6. Does this issue impact 2018 full year guidance?

No, FY 2018 non-GAAP guidance provided during our Q3 2018 earnings call is not affected by this issue.

7. Does this issue impact your expectations for non-GAAP performance net income per share growth in FY2019 over FY2017?

We will provide 2019 guidance as we typically do during our 4Q 2018 earnings call.

8. Please comment on Allergan's potential liability risks associated with this recall and provide some relevant background information in BIA-ALCL.

- a. Historically, liability risk has been greater in the U.S., compared to ex-U.S. In contrast to the European market, where the majority of implants used are textured, the U.S. market utilizes predominantly smooth implants, which are not known to be associated with an increased risk of BIA-ALCL.
- b. Allergan is and has been fully committed to investing in, and supporting work, to further understand and increase awareness of BIA-ALCL. Allergan's proactive efforts on this issue have included:
 - i. Funding for external research and scientific advisory panels to work toward understanding the disease and potential causes;
 - ii. Development of product labeling regarding BIA-ALCL in close partnership with the FDA and international regulatory authorities;
 - iii. Partnering with plastic surgery societies to (1) help create the PROFILE Registry, and (2) develop a patient assistance fund;
 - iv. Updating product websites with additional BIA-ALCL information, including links to plastic surgery society pages on the topic; and
 - v. Creating and distributing patient education tools on the topic to surgeons for use with their patients.
- c. **BIA-ALCL (Breast Implant Associated-Anaplastic Large Cell Lymphoma)**
 - i. In 2011, the FDA identified a possible association between breast implants and the development of a type of non-Hodgkin's lymphoma (cancer of the immune system) known as anaplastic large cell lymphoma (ALCL).
 - ii. As recently as September 2018, the FDA issued a statement highlighting their commitment to studying breast implant safety <https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm620589.htm>. Editorial:

https://journals.lww.com/annalsofsurgery/Citation/2019/01000/Assessing_the_Risks_of_Breast_Implants_and_FDA_s.8.aspx

- d. BIA-ALCL is a lymphoma with very low incidence that to date has been noted to occur more often in patients with a history of a textured breast implant device. When identified early based on recognizable signs and symptoms in routine examination, it is curable in most patients.
<https://surgery.org/sites/default/files/BIA-ALCL-FAQ-3.pdf>
- e. Current recommendations for the treatment of BIA-ALCL call for total capsulectomy, removal of the breast implant, as well as excision of any associated lumps or masses. BIA-ALCL is a highly curable condition. A majority of those early stage patients who received a total capsulectomy required no additional treatment (<https://www.plasticsurgery.org/for-medical-professionals/health-policy/bia-alcl-physician-resources/frequently-asked-questions>).
- f. Current literature reported various estimates that BIA-ALCL may develop in 1 in between 3,817 to 30,000 women with textured breast implants ([Clemens et al, 2017](#); [Loch-Wilkinson et al, 2017](#); De Boer et al, 2018).
<https://www.fda.gov/medicaldevices/productsandmedicalprocedures/implantsandprosthetics/breastimplants/ucm239995.htm>
- g. **BACKGROUND INFORMATION:**
<https://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/ImplantsandProsthetics/BreastImplants/ucm481899.htm>
 - i. As of September 30, 2017, the FDA had received a total of 414 medical device reports (MDRs) of BIA-ALCL, including the death of nine patients.
 - ii. 272 of the 414 reports included information on the surface information of the implant at the time of the report, including 242 with textured surfaces and 30 with smooth surfaces.
 - iii. 413 of the 414 reports included information on implant fill types. Of these, 234 reported implants filled with silicone gel and 179 reported implants filled with saline.
 - iv. Limitations: While the MDR reports provide information regarding the implant at the time of BIA-ALCL diagnosis, they do not typically give information about a patient's history of breast implants. In the MDR reports, half of the reported cases were diagnosed within 7-8 years of implantation. It is important to note that at the time of diagnosis, patients may have their original breast implants, or they may have had one or more replacements.