檔　　號：
保存年限：

正本

衛生福利部食品藥物管理署　函

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受文者：台灣急診醫學會

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密等及解密條件或保密期限：
附件：Breast Implant Associated-Anaplastic Large Cell Lymphoma (BIA-ALCL) - Letter to Health Care Providers

主旨：檢送美國食品藥物管理局就「乳房植入物相關的間變性大細胞淋巴瘤(簡稱BIA-ALCL)」發布安全警訊1份，詳如附件，惠請轉知所屬會員，請查照。

說明：

一、美國食品藥物管理局近期重新檢視接獲「乳房植入物相關的間變性大細胞淋巴瘤(簡稱BIA-ALCL)」之案件，並提出下列建議事項予相關專科醫療人員，略述如下:

(一)籲請醫療照護者在進行乳房植入物手術前，應完整告知及教育被植入者其植入產品之資訊，並確保被植入者瞭解該類產品不同類型之使用風險與效益。

(二)在治療晚發及乳房植體周圍出現血清腫之病患，請優先考慮BIA-ALCL的可能性，因為部分案例中，被植入者之乳房植入物週邊出現腫塊。

(三)疑似BIA-ALCL病人應蒐集相關組織之血清液及組織液，並送去病理檢查相關細胞免疫組織及細胞生物標記(如CD30、ALK等)，以確認是否為BIA-ALCL。

(四)若患者診斷為BIA-ALCL，請醫療照護者組成跨領域醫療照護團隊，並參考相關臨床文獻擬定治療方案。

二、另依嚴重藥物不良反應通報辦法第3條規定略以，因藥物所引起之嚴重藥物不良反應發生時，醫療機構、藥局、藥商應依本辦法填具通報書，連同相關資料，向全國藥物不良反應通報中心通報(通報網頁入口:本署網站首頁>業務專區>通報及安全監視專區>通報入口(我要通報)>醫療器材不良事件通報)。違者，可依藥事法第92條處辦。

正本：台灣美容外科醫學會、台灣整形外科醫學會、台灣臨床腫瘤醫學會、中華民國

癌症醫學會、台灣乳房醫學會、台灣病理學會、台灣外科醫學會、台灣放射腫瘤學會、中華民國放射線醫學會、台灣內科醫學會、台灣婦產科醫學會、台灣急診醫學會、台灣家庭醫學醫學會、台灣醫院協會、中華民國公立醫院協會、中華民國血液病學會、中華民國美容醫學醫學會、中華民國醫師公會全國聯合會、台灣胸腔及心臟血管外科學會、台灣胸腔暨重症加護醫學會、中華民國重症醫學會、中華民國急重症護理學會、台灣臨床細胞學會、社團法人台灣細胞免疫醫學會、中華民國免疫學會

副本：財團法人藥害救濟基金會(含附件)

署長 吳秀梅

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Breast Implant Associated-Anaplastic Large Cell Lymphoma (BIA-ALCL) - Letter to Health Care Providers

February 6, 2019

Dear Health Care Providers of the following specialties:

- Radiology
- Pathology
- Plastic Surgery
- Cosmetic Surgery
- General Surgery
- Internal Medicine
- Obstetrics/Gynecology
- Oncology
- General Practice/Family Practice
- Nurse Practitioners
- Physician's Assistants
- Emergency Medicine

The Food and Drug Administration (FDA) wants to increase awareness about an association between all breast implants, regardless of filling or texture, and Breast Implant Associated- Anaplastic Large Cell Lymphoma (BIA-ALCL). The FDA received reports indicating that patients with breast implants have an increased risk of developing this disease within the scar capsule adjacent to the implant.

We want all healthcare providers to be aware of BIA-ALCL, particularly in patients with new swelling, lumps, or pain around breast implants, to expedite diagnosis of this malignancy. We are also asking health care providers to report to the FDA cases of BIA-ALCL in patients with breast implants. This includes reporting individual cases as well as rates you may have experienced during your practice.

BACKGROUND

BIA-ALCL is a type of lymphoma and is not a cancer of the breast tissue. When breast implants are placed in the body, they are inserted behind the breast tissue or under the chest muscle. Over time, a fibrous scar called a capsule develops around the implant, separating it from the rest of the breast. In patients with breast implants, reported cases of BIA-ALCL were generally found adjacent to the implant itself and contained within the fibrous capsule.

A significant body of medical literature has been published since the FDA's **2011 report on BIA-ALCL (https://www.fda.gov/downloads/medicaldevices/productsandmedicalprocedures/implantsandprosthetics/breast-implants/ucm260090.pdf)**, including additional case histories and comprehensive reviews of the natural history and long-term outcomes of BIA-ALCL. Current literature

reports various estimates for the incidence of BIA-ALCL. These estimated incidence rates range from a high of 1 per 3,817 patients to a low estimate of 1 in 30,000 (Clemens et al, 2017; Loch-Wilkinson et al, 2017; De Boer et al, 2018). While the majority of patients who develop BIA-ALCL have had textured implants, and most cases reported in the literature describe individuals who have had textured implants, there have been reports of BIA-ALCL in patients with smooth-surfaced implants and many reports do not include the surface texture of the implant at the time of diagnosis.

As of the latest **medical device reports (MDRs) update (https://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/ImplantsandProsthetics/BreastImplants/ucm481899.htm)**, the FDA has received a total of 660 MDRs of BIA-ALCL. The FDA has carefully reviewed the 660 MDRs to remove duplicate reports and to control for MDRs in which a BIA-ALCL diagnosis was confirmed by: a physician, positive pathology/cytology test results, or positive for biomarker CD30 and negative for biomarker ALK. The FDA's additional data analysis identified 457 unique MDRs for BIA-ALCL, including the death of nine patients which may be attributable to BIA-ALCL. However, 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.

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. Additional cases have been identified through the FDA's contact with other regulatory authorities, scientific experts, and breast implant manufacturers. Recent journal articles explore possible risk factors for developing BIA-ALCL, including the methods used to create the textured surface and the role of biofilm. Additionally, most of the published information about treatment describes removal of the implant and the capsule surrounding the implant, and in some patients, treatment with chemotherapy and radiation.

Though the number of identified cases of BIA-ALCL is small compared to the estimated 1.5 million patients who receive breast implants worldwide every year, confirmed data and published information reviewed to date suggests that patients with breast implants have an increased risk of BIA-ALCL.

RECOMMENDATIONS

In most of the cases reported to the FDA, patients were diagnosed with BIA-ALCL when they sought medical treatment for implant-related symptoms such as pain, lumps, swelling, or asymmetry that developed after their initial surgical sites were fully healed. These symptoms were due to collection of fluid (seroma), or masses surrounding the breast implant. Examination of the fluid and capsule surrounding the breast implant led to the BIA-ALCL diagnosis.

Therefore, the FDA is recommending that health care providers:

- Prior to implantation, provide all patients with the breast implant manufacturer's labeling, including the patient-specific labeling, as well as other educational material prior, and make sure they are aware of the benefits and risks of the different types of implants. Most confirmed cases of BIA-ALCL have occurred in patients with textured surface implants, although there are known cases in patients with only smooth-surface breast implants.
- Consider the possibility of BIA-ALCL when treating a patient with late onset, peri-implant seroma. In some cases, patients presented with a mass or masses adjacent to the breast implant. If you have a patient with suspected BIA-ALCL, refer the individual's case to a multidisciplinary team for evaluation.
- Collect fresh seroma fluid and representative portions of the capsule and send for pathology tests to rule out BIA-ALCL. Diagnostic evaluation should include cytological evaluation of seroma fluid or mass with Wright Giemsa stained smears

and cell block immunohistochemistry/flow cytometry testing for cluster of differentiation (CD30) and Anaplastic Lymphoma Kinase (ALK) markers.

- Develop an individualized treatment plan in coordination with the patient's multi-disciplinary care team. Consider current clinical practice guidelines, such as those from the Plastic Surgery Foundation or the National Comprehensive Cancer Network (NCCN) when choosing your treatment approach.
- **Report all confirmed cases of BIA-ALCL** in individuals with breast implants to **MedWatch, the FDA Safety Information and Adverse Event Reporting program (https://www.accessdata.fda.gov/scripts/medwatch/index.cfm?action=reporting.home)**.
  - Health care personnel employed by facilities that are subject to **FDA's user facility reporting requirements (https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/PostmarketRequirements/ReportingAdverseEvents/default.htm)** 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. In some cases, the FDA may contact you for additional information. The FDA will keep the identities of the reporter and the patient confidential.
- Submit case reports of BIA-ALCL to the **Patient Registry and Outcomes For breast Implants and anaplastic large cell Lymphoma etiology and Epidemiology (PROFILE) Registry (https://www.thepsf.org/research/registries/profile)** to contribute to a better understanding of the causes and treatments of BIA-ALCL.

FDA ACTIONS

The FDA continues to actively work alongside the American Society of Plastic Surgeons (ASPS), international regulatory agencies and other experts in the clinical and scientific communities to evaluate all available information to understand the nature and possible factors contributing to BIA-ALCL in patients with breast implants.

The FDA will keep the public informed as significant new information becomes available.

CONTACT US

If you have questions about this communication, please contact the Division of Industry and Consumer Education (DICE) at **DICE@FDA.HHS.GOV (mailto:DICE@FDA.HHS.GOV)**, 1-800-638-2041 or 301-796-7100.

Sincerely,
/s/
William Maisel, MD, MPH
Chief Medical Officer
Center for Devices and Radiological Health
U.S. Food and Drug Administration

ADDITIONAL RESOURCES

- **Medical Device Reports of Breast Implant-Associated Anaplastic Large Cell Lymphoma: FDA.gov (Last Updated: February 6, 2019) (https://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/ImplantsandProsthetics/BreastImplants/ucm481899.htm)**
- **Breast Implant-Associated Anaplastic Large Cell Lymphoma (BIA-ALCL): FDA.gov (Last Updated: February 6, 2019) (https://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/ImplantsandProsthetics/BreastImplants/ucm239995.htm)**
- **Frequent activating STAT3 mutations and novel recurrent genomic abnor-**

ma.. Oncotarget (November 16, 2018) (https://www.ncbi.nlm.nih.gov/pubmed/30546832)

- Bacterial Adhesion and Biofilm Formation on Textured Breast Implant Shell Materials.: Aesthetic Plastic Surgery (October 1, 2018) (https://www.ncbi.nlm.nih.gov/pubmed/30276456)
- The Functional Influence of Breast Implant Outer Shell Morphology on Bacterial Attachment and Growth.: Plastic and Reconstructive Surgery (October 2018) (https://www.ncbi.nlm.nih.gov/pubmed/30252806)
- Reports of Breast Implant-Associated Anaplastic Large Cell Lymphoma (BIA-ALCL) in Women with Breast Implants: FDA Safety Communication (January 26, 2011) (http://wayback.archive-it.org/7993/20170722214256/https:/www.fda.gov/MedicalDevices/Safety/AlertsandNotices/ucm240000.htm)

More in Letters to Health Care Providers (/MedicalDevices/Safety/LetterstoHealthCareProviders/default.htm)