An Advisory to Patients Considering Breast Augmentation

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On January 26, 2011, the FDA released an advisory updating the findings of its investigation and analysis of an extremely rare type of tumor that has been reported in a small number of women worldwide with breast implants. The following information summarizes what we know at this time regarding any possible association with breast implants. Please read this information thoroughly and write down any questions you have so that we can address those questions with you.

Over the past several years, there have been a very small number of cases of a rare type of lymphoma (anaplastic large cell lymphoma, ALCL) reported in women who have breast implants. This type of tumor also occurs in patients without breast implants, and with or without implants, the occurrence of this type of lymphoma is exceedingly rare, with some estimates of an occurrence rate of 0.2 cases per 100,000 person years. This potential rate of occurrence is miniscule compared to every woman's risk of developing breast cancer. In some of the reports, some of the patients who developed this lymphoma had implants that had a type of texturing on the surface of the implant that is the same as the texturing on the Allergan Style 410 implant. The Biocell™ textured surface is created during manufacturing using a lost salt process in which salt crystals are used to create the surface texturing and the salt crystals washed off the implant, leaving the textured surface.

From our review of data that is available, it is clear that many of these cases are very poorly documented, and much critical information is missing, information that would better help us determine what, if, any increased risks may be associated with Biocell™ texturing or other implant parameters. Whether this type of lymphoma occurs more commonly in patients with implants, or any specific type of implant, and whether it occurs at similar rates in women without implants is not yet known by valid scientific data. It is also not clear whether this entity really represents a lymphoma or whether it is some type of benign, excessive growth of lymphoid tissue (a lymphoproliferative disorder).
FDA Medical Device Safety Communication: Reports of Anaplastic Large Cell Lymphoma (ALCL) in Women with Breast Implants

Date Issued: January 26, 2011

Audience:
- Health care providers involved in the care of patients with breast implants
- Hospital tumor boards
- Breast implant patients and families of patients, including those that have received breast implants for aesthetic augmentation, revision, or reconstruction.
- Patients considering breast implant surgery

Medical Specialties: Radiology, Pathology, Plastic Surgery, General Surgery, Internal Medicine, Obstetrics/Gynecology, Oncology, Nursing, General Practice

Purpose:
The FDA is issuing this communication to inform health care providers and the public about a possible association between breast implants and a type of anaplastic large cell lymphoma (ALCL). Although ALCL is extremely rare, the FDA believes that women with breast implants may have a very small but increased risk of developing this disease in the scar capsule adjacent to the implant. The FDA is also asking health care providers to report confirmed cases of ALCL in women with breast implants to the FDA.

Summary of Issue:
The FDA is exploring a possible link between breast implants and ALCL. ALCL is a rare cancer of the immune system, which can occur anywhere in the body. According to the Surveillance, Epidemiology, and End Results (SEER) Program of the National Cancer Institute, an estimated 1 in 500,000 women per year in the U.S. is diagnosed with ALCL. ALCL in the breast is even more rare; approximately 3 in 100 million women per year in the U.S. are diagnosed with ALCL in the breast. As part of its analysis, the FDA conducted a thorough review of scientific literature published from January 1997 through May 2010. From this review, the FDA identified 34 unique cases of ALCL in women with breast implants throughout the world. In total, the FDA is aware of approximately 60 case reports of ALCL in women with breast implants worldwide. This number is difficult to verify because not all cases were published in the scientific literature. Some cases have been identified through the FDA’s contact with other regulatory authorities, scientific experts, and breast implant manufacturers, and it is not clear how many of these are duplicates of the ones found in the literature.

The number of identified cases is small compared to the estimated 5 to 10 million women who have received breast implants worldwide. But based on these data, the FDA believes that women with breast implants may have a very small but increased risk of ALCL. Because the risk of ALCL appears very small, FDA believes that the totality of evidence continues to support a reasonable assurance that FDA-approved breast implants are safe and effective when used as labeled.
The table below describes the characteristics of the 34 published cases of ALCL in women with breast implants:

**Characteristics of 34 Published Cases of ALCL in Women with Breast Implants**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Median</th>
<th>Range</th>
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</thead>
<tbody>
<tr>
<td><strong>Age (years)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>51</td>
<td>28-87</td>
</tr>
<tr>
<td><strong>Type of Implant</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Silicone</td>
<td>24</td>
<td></td>
</tr>
<tr>
<td>Saline</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>Not specified</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td><strong>Time from Implant to ALCL Diagnosis (years)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>8</td>
<td>1-23</td>
</tr>
<tr>
<td><strong>Reason for Implant</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reconstruction</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>Augmentation</td>
<td>19</td>
<td></td>
</tr>
<tr>
<td>Not specified</td>
<td>4</td>
<td></td>
</tr>
</tbody>
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FDA’s overview, review of the literature and discussion of these cases can be found in the document *Anaplastic Large Cell Lymphoma (ALCL) in Women with Breast Implants: Preliminary FDA Findings and Analyses*.

**ALCL is Lymphoma – Not 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 women with breast implants, the ALCL was generally found adjacent to the implant itself and contained within the fibrous capsule. ALCL is lymphoma, a type of cancer involving cells of the immune system. It is not cancer of the breast tissue. Most patients were diagnosed 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 (persistent seroma), hardening of breast area around the implant (capsular contracture), or masses surrounding the breast implant. Examination of the fluid and capsule surrounding the breast implant led to the ALCL diagnosis.

The FDA believes that women with breast implants may have an increased risk of developing ALCL, but also believes any potential risk is extremely low. Due to the rarity of ALCL, the small number of reports, and the incomplete and limited data from these reports, more information is needed to fully understand the possible link between breast implants and ALCL.
**Recommended Actions for Health Care Providers and Patients**

**Health Care Providers:**

If you have patients with breast implants, you should continue to provide them routine care and support. ALCL is a very rare condition; when it occurs, it has been identified most frequently in patients undergoing implant revision operations for late onset, persistent seroma. Because it has generally only been identified in patients with late onset of symptoms such as pain, lumps, swelling, or asymmetry, prophylactic breast implant removal in patients without symptoms or other abnormality is not recommended.

Current recommendations include the steps below. As the FDA learns more about ALCL in patients with breast implants, these recommendations may change.

- Consider the possibility of ALCL when you have a patient with late onset, persistent peri-implant seroma. In some cases, patients presented with capsular contracture or masses adjacent to the breast implant. If you have a patient with suspected ALCL, refer her to an appropriate specialist for evaluation. When testing for ALCL, collect fresh seroma fluid and representative portions of the capsule and send for pathology tests to rule out ALCL. Diagnostic evaluation should include cytological evaluation of seroma fluid with Wright Giemsa stained smears and cell block immunohistochemistry testing for cluster of differentiation (CD) and Anaplastic Lymphoma Kinase (ALK) markers.

- Report all confirmed cases of ALCL in women with breast implants to the FDA. In some cases, the FDA may contact you for additional information. The FDA will keep the identities of the reporter and the patient confidential.

- Develop an individualized treatment plan in coordination with the patient’s multi-disciplinary care team. Because of the small number of cases worldwide and variety of available treatment options, there is no single defined consensus treatment regimen.

**Patients:**

If you have breast implants, there is no need to change your routine medical care and follow-up. ALCL is very rare; it has occurred in only a very small number of the millions of women who have breast implants. Although not specific to ALCL, you should follow standard medical recommendations including:

- Monitoring your breast implants. If you notice any changes, contact your health care provider promptly to schedule an appointment. For more information on self breast exams, visit [Medline Plus: Breast Self Exam](https://medlineplus.gov/breastselfexam.html).

- Getting routine mammography screening.

- If you have silicone gel-filled breast implants, getting periodic magnetic resonance imaging (MRI) to detect ruptures as recommended by your health care provider. The FDA-approved product labeling for silicone gel-filled breast implants states that the first MRI should occur three years after implant surgery and every two years thereafter.

If you do not currently have breast implants but are considering breast implant surgery, discuss the risks and benefits with your health care provider. You may also visit [FDA’s Breast Implants website](https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Implants/BreastImplants) for additional information.
FDA Activities:
The FDA continues to evaluate all available information to understand the nature and possible factors contributing to ALCL in women with breast implants. In addition, the American Society of Plastic Surgeons (ASPS) and other experts in the clinical and scientific communities have agreed to pursue a collaboration with the FDA to develop a registry to gather additional information to better characterize ALCL in women with breast implants.

While the details of the collaboration are being developed, the FDA is advising health care professionals to test breast implant patients with suspected ALCL according to the recommendations above and to submit findings on confirmed ALCL cases to the FDA. The FDA is also asking breast implant manufacturers to report confirmed cases. The FDA will update the public as new information is obtained.

In an effort to ensure that patients receiving breast implants are informed of the possible link between ALCL and breast implants, the FDA will be working with breast implant manufacturers in the coming months to update their product labeling materials for patients and providers.

As part of its ongoing surveillance of all breast implants, the FDA plans to provide an update on the state of the science on silicone gel-filled breast implants in the spring of 2011. This update will include interim findings from ongoing post-approval studies for silicone gel-filled breast implants currently sold in the United States, adverse event reports submitted to the FDA, and a review of the scientific literature on these products.

How to Report Information to the FDA:
If you are a health care provider and you have identified ALCL in breast implant patients, please file a voluntary report through MedWatch, the FDA’s Safety Information and Adverse Event Reporting Program online, or at 1-800-332-1088.

To help us learn as much as possible about ALCL in women with breast implants, please include the following information in your reports, if available:

- The term “ALCL Case Report” in section B5 (Describe Event, Problem or Product Use Error) of the MedWatch form
- Patient age, gender, race/ethnicity
- ALCL diagnosis: date of diagnosis, anatomic site of ALCL, whether ALCL was primary in this site and pathologically confirmed
- Clinical presentation
- Detailed pathology findings
- Breast implant exposure: date implanted, brand and type of implant (saline or silicone-filled), type of implant surface (smooth or textured), complications, length of time from implant insertion, and history of subsequent revision surgeries
- Treatment(s) the patient received
- Name, contact information and medical specialty of reporter

All reports to the FDA are strictly confidential and protect individual patient privacy.

Contact Information:
If you have questions about this communication, please contact the Division of Small Manufacturers, International and Consumer Assistance (DSMICA) at DSMICA@FDA.HHS.GOV, 800-638-2041 or 301-796-7100.

This document reflects the FDA’s current analysis of available information, in keeping with our commitment to inform the public about ongoing safety reviews of medical devices. The FDA will provide updates as more information becomes available.
As we pursue more detailed data from the reported cases around the world, a process which will likely take many months to years, we believe the following:

1) It is every patient's best interest to make decisions based on scientifically valid data

2) Scientifically valid data to specify any risk or potential cause and effect relationship of ALCL associated with breast implants does not exist at this time.

3) IF ANY PATIENT HAS ANY CONCERN WHATEVER ABOUT ANY POTENTIAL RISK OF ALCL OR ANY OTHER RISK ASSOCIATED WITH ANY TYPE OF BREAST IMPLANT, THE PATIENT SHOULD STRONGLY CONSIDER NOT HAVING A BREAST AUGMENTATION.

4) IF ANY PATIENT HAS ANY CONCERN THAT A SPECIFIC TYPE OF IMPLANT OR TYPE OF TEXTURING ON AN IMPLANT MAY POSE ANY INCREASED RISK OF ANY TYPE, THE PATIENT SHOULD STRONGLY CONSIDER CHOOSING ANOTHER TYPE OF BREAST IMPLANT THAT DOES NOT HAVE TEXTURING OR CHOOSE NOT TO HAVE A BREAST AUGMENTATION.
I, _______________________ have read this document and understand its contents. I have had an opportunity to ask questions and have received answers to my questions to best of Dr. Tebbetts' and his staff's knowledge of facts relating to issues of breast implants and the rare type of lymphoma called ALCL.

Please initial each paragraph below, and sign and date at the conclusion of this document.

_____ I understand that there have been case reports of a type of lymphoma (ALCL) in patients with breast implants and in patients who have breast implants with a Biocell™ textured surface which is the type of textured surface on the Allergan Style 410 implant.

_____ Although there may not be any proved or scientifically valid association of ALCL with breast implants or Biocell™ textured surface implants, there MAY be a very small incidence of this type of lymphoma in patients with breast implants or patients with Biocell™ textured surface breast implants.

_____ Understanding that some association MAY exist between ALCL and breast implants or Biocell™ textured breast implants, but is not proved at this time, I have carefully and thoroughly considered these potential risks and I choose to have breast augmentation.

Patient: (Please Print Name and Sign Below)

    Print Name: ______________________
    Sign: ____________________________
    Date: ____________________________

Witness: (Please Print Name and Sign Below)

    Print Name: ______________________
    Sign: ____________________________
    Date: ____________________________