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June 7, 2019

## **Administrative Notice**

Pharmaceutical Safety Division,  
Pharmaceutical Safety and Environmental Health Bureau,  
Ministry of Health, Labour and Welfare

To: Commissioners of Prefectural Health Departments (Bureaus)

### **Revision of Precautions to the Package Inserts of Gel-filled Breast Implant**

This is to notify commissioners of prefectural health departments of the notification we have issued to the marketing authorization holder of the concerned product. A copy of the notification is attached to this notice as an appendix.



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## Appendix

June 7, 2019

## Notification

PSEHB Notification No. 0607-1

CEO  
Allergan Japan K. K.

Director of Medical Devices Safety Division,  
Pharmaceutical Safety and Environmental Health  
Bureau, Ministry of Health, Labour and Welfare

### **Revision of Precautions to the Package Inserts of Gel-filled Breast Implant**

Regarding gel-filled breast implants (Natrele Breast Implant (Approval Number: 22400BZX00354000), Natrele 410 Breast Implant (Approval Number: 22500BZX00460000)), alert to the development of breast implant-associated anaplastic large cell lymphoma (BIA-ALCL) has been in place under the Precautions in the product package inserts and other relevant materials.

Recently, the Japan Oncoplastic Breast Surgery Society has reported a case of BIA-ALCL diagnosed for the first time in Japan in a patient who had received a gel-filled breast implant that is not approved in Japan. Taking account of this case, we have concluded that precaution for BIA-ALCL is necessary in gel-filled implant products. Consequently, you are requested to revise the Precautions of the product package inserts as indicated below and properly to circulate the information among medical institutions and other relevant parties.

1. Precautions should be revised in the package insert.
  - (1) The following language should be added to the Warning section (revised language is underlined):



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Prior to the use of this product, patients should be adequately informed of the risk of breast implant-associated anaplastic large cell lymphoma (BIA-ALCL) in line with the information provided in the Breast Implant-associated Anaplastic Large Cell Lymphoma prepared by relevant academic societies. Patients should be continuously followed up after implantation of this product. (Precautions, see 2. Important Precautions section).

(Note): Information reported in the literature etc. should be noted in the specified bracket [ ] if available and data of literature should be listed in the Reference section under Reference and Contact.

- (2) Time to development of BIA-ALCL from implantation of the device should be added to the Precautions surgeons should take, Important Precautions section based on reports in literature and other proper sources. Necessity of continued follow-up of patients should also be added and the Breast Implant-associated Anaplastic Large Cell Lymphoma prepared by relevant academic societies should be suggested as reference for examination and treatment flowchart.
- (3) The following language should be added to the Important Precautions section, Precautions, as Precautions patients should be instructed (revised language is underlined):

Patients should be instructed to immediately contact their physicians if they experience symptoms as follows that could be adverse events.

<u>Adverse reaction /events</u>	<u>Symptoms (not inclusive)</u>
<u>Seroma (BIA-ALCL is suspected.)</u>	<u>Swelling surrounding the implant, pain, asymmetry, lumps in the breast or armpit, redness, hardening of the breast, etc.</u>



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- (4) A Clinically Significant Adverse Reactions subsection should be newly added to the Malfunctions and Adverse Reactions section, Precautions, to include the following language (revised language is underlined):

Breast implant-associated anaplastic large cell lymphoma (BIA-ALCL)

2. A new package insert revised according to 1. above should be uploaded in the Medical Device Package Insert Information page, in the home page of the Pharmaceuticals and Medical Devices Agency (PMDA).
3. Progress in the responses listed in 1. and 2, as well as in the circulation of information on the details of the revision of package inserts should be reported to the Division of Safety for Medical Devices, Office of Manufacturing Quality and Vigilance for Medical Devices, PMDA by July 8, 2019.