

Directions for Use (DFU)

Natrelle[®] Saline-Filled Breast Implants

Physician Labeling



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Introduction

DIRECTIONS TO THE PHYSICIAN

This document contains information that is essential to the patient consultation process. Please familiarize yourself with the content of this document and resolve any questions or concerns prior to proceeding with the use of this device.

The information supplied in this *Directions for Use* document is intended to provide an overview of essential information about NATRELLE® Saline-Filled Breast Implants, including the indications for use, contraindications, warnings, precautions, complications, and a summary of Allergan’s clinical results.

Sections of this *Directions for Use* document indicated by “***Patient Counseling Information***” contain points that the physician should review when counseling the patient about breast implants and breast implant surgery.

INFORMATION TO BE DISCUSSED WITH THE PATIENT

WARNINGS, PRECAUTIONS, ADVERSE EVENTS

Patient Counseling Information

Breast implant surgery is known to provide satisfaction to patients, HOWEVER, as with any surgical procedure, it is NOT without risks. Breast implantation is an elective procedure, and the patient must be well counseled and understand the risk/benefit relationship.

Each patient should receive Allergan’s **Making an Informed Decision, Breast Surgery with NATRELLE® Saline-Filled Breast Implants** during her initial visit/consultation. The surgeon or a designated patient counselor should instruct the patient to read the patient information carefully and also discuss with the patient the warnings, precautions, and complications listed in this *Directions for Use* document. The physician should advise the patient of the potential complications and that medical management of serious complications may include additional surgery and explantation. Patients should understand that breast implant surgery can cause irreversible changes to the breast.

INFORMED CONSENT

Patient Counseling Information

Before making the decision to proceed with surgery, the patient should be allowed sufficient time to read and adequately understand the important patient information on the risks, follow-up recommendations, and benefits associated with saline-filled breast implant surgery.

Device Descriptions

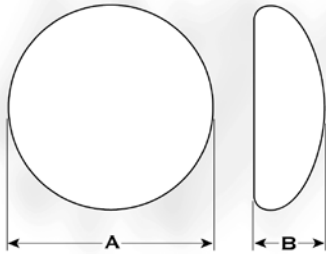
NATRELLE® Saline-Filled Breast Implants are constructed from Room Temperature Vulcanized (RTV) silicone elastomer, made of polydimethylsiloxane. The device is inflated to the desired size with sterile isotonic saline before implantation. Each implant is supplied sterile with a disposable fill tube and reflux valve.

Round Breast Implants:

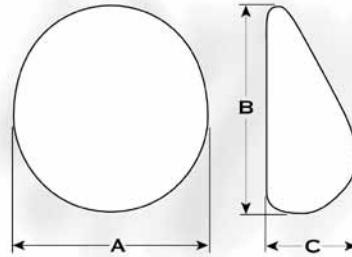
Style Number	Breast Implant Description	Size Range
Style 68LP	Smooth shell surface, anterior filling valve, low protection	125cc – 700cc
Style 68	Smooth shell surface, anterior filling valve, moderate protection	120cc – 850cc
Style 68HP	Smooth shell surface, anterior filling valve, high protection	160cc – 850cc
Style 168	BIOCELL® Textured shell surface, anterior filling valve, moderate projection	120cc – 850cc

Shaped Breast Implants:

Style Number	Breast Implant Description	Size Range
Style 468	BIOCELL® Textured shell surface, anterior filling valve, full height, moderate protection	195cc – 205cc



A = Width; B = Projection
ROUND BREAST IMPLANT



A = Width; B = Height; C = Projection
SHAPED BREAST IMPLANT

Indications

NATRELLE® Saline-Filled Breast Implants are indicated for females for the following:

- **Breast augmentation for women at least 18 years old.** Breast augmentation includes primary breast augmentation to increase the breast size, as well as revision surgery to correct or improve the result of a primary breast augmentation surgery.
- **Breast reconstruction.** Breast reconstruction includes primary reconstruction to replace breast tissue that has been removed due to cancer or trauma or that has failed to develop properly due to a severe breast abnormality. Breast reconstruction also includes revision surgery to correct or improve the result of a primary breast reconstruction surgery.

Contraindications

Breast implant surgery should not be performed in:

- Women with existing cancer or pre-cancer of their breast who have not received adequate treatment for those conditions.
- Women with active infection anywhere in their body.
- Women who are currently pregnant or nursing.

Warnings

Surgical Practices in which product use is contraindicated due to compromise of product integrity:

- **Adulterated Fill.** Do not place drugs or substances inside the implant other than sterile saline for injection.
- **Alteration.** Do not alter the implant or valve.
- **Do not inject** through the implant shell.
- **Stacking of implants:** Do not place more than one implant per breast pocket.
- Do not allow the implant to come into prolonged contact with povidone iodine.

Closed Capsulotomy

DO NOT treat capsular contracture by forceful external compression, which will likely result in implant damage, deflation, folds, and/or hematoma. Capsule firmness must not be treated by overexpansion of the device.

Reuse

Breast implants are intended for single use only. Do not resterilize.

Avoiding Damage during Surgery

- Care should be taken not to damage the prosthesis with surgical instruments.
- Do not insert or attempt to repair a damaged prosthesis.
- Use care in subsequent procedures such as open capsulotomy, breast pocket revision, hematoma/seroma aspiration, and biopsy/lumpectomy to avoid damage to the implant shell or valve.
- Do not contact the implant with disposable, capacitor-type cautery devices.

Proper Filling

Follow the recommended fill volume on the product data sheet; do not overfill or underfill the implant. Following recommended fill volumes may decrease the possibility of shell wrinkling and crease fold failure.

Microwave Diathermy

The use of microwave diathermy in patients with breast implants is not recommended, as it has been reported to cause tissue necrosis, skin erosion, and extrusion of the implant.

Use of endoscopic instruments or the periumbilical approach for placement of the implant has not been studied in the Allergan clinical trial and is not recommended as damage to the device may occur.

Precautions

Specific Populations

Safety and effectiveness have not been established in patients with the following:

- Autoimmune diseases (e.g., lupus and scleroderma).
- A compromised immune system (for example, currently receiving immunosuppressive therapy).
- Conditions or medications which interfere with wound healing and blood clotting.
- Reduced blood supply to breast tissue.
- Radiation to the breast following implantation.
- Clinical diagnosis of depression or other mental health disorders, including body dysmorphic disorder and eating disorders. Please discuss any history of mental health disorders prior to surgery. Patients with a diagnosis of depression, or other mental health disorders, should wait until resolution or stabilization of these conditions prior to undergoing breast implantation surgery.

Important Factors to be Discussed with the Patient

Breast implantation is an elective procedure and the patient must be thoroughly counseled on the risks, as well as the benefits, of these products and procedures. You should advise your patient that she must read the patient labeling for either augmentation or reoperation, as applicable. The patient labeling is intended as the primary means to relate uniform risk and benefit information to assist your patient in making an informed decision about primary breast augmentation and revision-augmentation, or primary reconstruction and revision-reconstruction surgery (as applicable), but is not intended to replace consultation with you. The patient should review and consider this information before deciding whether to have this surgery.

Below are some of the important factors your patients need to be aware of when using saline-filled breast implants.

- **Reoperation** – Patients should be advised that additional surgery to their breast and/or implant will be likely over the course of their life.
- **Explantation** – Patients should be advised that implants are not considered lifetime devices and they will likely undergo implant removal, with or without replacement, over the course of their life. Patients should also be advised that the changes to their breast following explantation are irreversible.
- **Mammography** – Breast implants may complicate the interpretation of mammographic images by obscuring underlying breast tissue and/or by compressing overlying tissue. Accredited mammography centers and use of displacement techniques are needed to adequately visualize breast tissue in the implanted breast. Presurgical mammography with a follow-up mammogram 6 months to 1 year following surgery may be performed to establish a baseline for future routine mammography. Patients should be instructed to inform their mammographers about the presence of their implants.
- **Lactation** – Patients should be advised that breast implants may interfere with the ability to successfully breastfeed, either by reducing or eliminating milk production.
- **Breast Examination Techniques** – Patients should be instructed to perform breast self-examinations monthly and be shown how to distinguish the implant from their breast tissue. The patient should be instructed not to manipulate (i.e., squeeze) the valve excessively, which may cause valve leakage.
- **Avoiding Damage During Treatment** – Patients should inform other treating physicians of the presence of implants to minimize the risk of damage to the implants.
- **Smoking** – Smoking may interfere with the healing process.
- **Insurance Coverage** – Patients should be advised that health insurance premiums may increase, insurance coverage may be dropped, and/or future coverage may be denied based on the presence of breast implants. Treatment of complications may not be covered as well. Patients should check with their insurance company regarding coverage issues before undergoing surgery.
- **Mental Health and Elective Surgery** – It is important that all patients seeking to undergo elective surgery have realistic expectations that focus on improvement rather

than perfection. Request that your patient openly discuss with you, prior to surgery, any history that she may have of depression or other mental health disorders.

- **Long Term Effects**
Safety and effectiveness beyond 10 years has not been clinically evaluated.

Complications

Potential adverse events that may occur with saline-filled breast implant surgery include: implant deflation, capsular contracture, reoperation, implant removal, pain, changes in nipple and breast sensation, infection, scarring, asymmetry, wrinkling, implant displacement/migration, implant palpability/visibility, breastfeeding complications, hematoma/seroma, implant extrusion, necrosis, delayed wound healing, breast tissue atrophy/chest wall deformity, calcium deposits, and lymphadenopathy.

Below is a description of these adverse events. For specific adverse event rates/outcomes for *NATRELLE*[®] Saline-filled Breast Implants, refer to Allergan's Clinical Study section below.

- **Deflation** – *Breast implants are not lifetime devices.* Saline breast implants deflate when the shell develops a tear or hole. Deflation can occur at any time after implantation, but they are more likely to occur the longer the implant is implanted. The following things may cause implants to deflate: damage by surgical instruments; folding or wrinkling of the implant shell; excessive force to the chest (e.g., during closed capsulotomy, which is contraindicated); trauma; compression during mammographic imaging; and severe capsular contracture. Breast implants may also simply wear out over time. Laboratory studies have identified some of the causes of deflation for Allergan's product; however, it is not conclusively known whether these tests have identified all causes of deflation.
- **Reoperation** – Patients should be advised that additional surgery to their breast and/or implant will likely be necessary over the course of their life. Patients may decide to change the size or type of their implants, requiring a reoperation, or they may have a reoperation to improve or correct their outcome.
- **Capsular Contracture** – Patients should be advised that capsular contracture may be more common following infection, hematoma, and seroma, and the chance of it happening may increase over time. Capsular contracture occurs more commonly in revision patients than in primary augmentation or reconstruction patients. Capsular contracture is also a risk factor for implant deflation, and it is one of the most common reasons for reoperation.

Patients should also be advised that additional surgery may be needed in cases where pain and/or firmness are severe. This surgery ranges from removal of the implant capsule tissue to removal and possible replacement of the implant itself. This surgery may result in loss of breast tissue. Capsular contracture may happen again after these additional surgeries. Capsular contracture may increase the risk of deflation.

- **Explantation (*Implant Removal*)** – Patients should be advised that implants are not considered lifetime devices, and they will potentially undergo implant removal, with or without replacement, over the course of their life. Patients should also be advised that the changes to their breast following explantation are irreversible.
- **Infection** – In rare instances, acute infection may occur in a breast with implants. The signs of acute infection include erythema, tenderness, fluid accumulation, pain, and fever. Very rarely, Toxic Shock Syndrome, a potentially life-threatening condition, has been reported in women after breast implant surgery. It is characterized by symptoms that occur suddenly and include high fever (102°F, 38.8°C or higher), vomiting, diarrhea, a sunburn-like rash, red eyes, dizziness, lightheadedness, muscle aches, and drops in blood pressure, which may cause fainting. Patients should be advised to contact a physician immediately for diagnosis and treatment for any of these symptoms.
- **Cosmetic Dissatisfaction (*Unsatisfactory Results*)** – Patients should be informed that dissatisfaction with cosmetic results related to such things as scar deformity, hypertrophic scarring, capsular contracture, asymmetry, wrinkling, implant displacement/migration, incorrect size, and implant palpability/visibility may occur. Careful surgical planning and technique can minimize, but not preclude, the risk of such results. Pre-existing asymmetry may not be entirely correctable. Physiological and behavioral differences among patients and variations in surgical techniques and medical treatments account for a wide variety of responses to breast implant surgery. Revision surgery may be indicated to maintain patient satisfaction but carries additional considerations and risks.
- **Breastfeeding** – Difficulties have been reported following breast surgery, including breast reduction and breast augmentation surgery. A periareolar surgical approach may further increase the chance of breastfeeding difficulties.
- **Additional Complications** – After breast implant surgery the following may occur and/or persist, with varying intensity and/or for a varying length of time: pain, hematoma/seroma, changes in nipple and breast sensation, implant extrusion,

necrosis, delayed wound healing, and breast tissue atrophy/chest wall deformity. Calcium deposits can form in the tissue capsule surrounding the implant with symptoms that may include pain and firmness. Lymphadenopathy has also been reported in some women with implants.

Other Reported Conditions

There have been reports in the literature of other conditions in women with breast implants. Many of these conditions have been studied to evaluate their potential association with breast implants. No cause-and-effect relationship has been established between breast implants and the conditions listed below. There is the possibility of risks, yet unknown, which in the future could be determined to be associated with breast implants.

- **Connective Tissue Disease (CTD)**

Connective tissue diseases include diseases such as lupus, scleroderma, and rheumatoid arthritis. There have been a number of published epidemiological studies which have looked at whether having a breast implant is associated with having a typical or defined connective tissue disease. The most recent of these concluded that the weight of the evidence did not support causal association between implants and definite or atypical CTD. The study size needed to conclusively rule out a smaller risk of connective tissue disease (≤ 2) would need to be very large. Published studies taken together show that breast implants are not significantly associated with a risk of developing a specific CTD. These studies do not distinguish between women with intact and ruptured implants. Only one study evaluated specific CTD diagnoses and symptoms in women with silent ruptured versus intact implants, but the study was too small to rule out a small risk.

- **Cancer**

Published studies indicate that breast cancer is no more common in women with implants than those without implants.

Lymphomas, including anaplastic large T-cell lymphoma (ALCL) – Information from the medical literature has suggested a possible association, without evidence of causation, between breast implants and the very rare occurrence of ALCL in the breast. This disease is exceptionally rare and occurs in women with and without breast implants. Specific testing is needed to identify ALCL from other cancers of

the breast. It is important to note that these findings are considered preliminary. The majority of the cases reported in patients with breast implants present as late occurring seromas and have an indolent clinical course, including some involving spontaneous remission without adjuvant therapy. No study has concluded a cause and effect relationship between ALCL and breast implants. All pertinent findings respecting cases associated with Allergan devices should be reported to Allergan (e.g. time to clinical presentation, signs or symptoms, immunohistological analysis, type of implant, texture, patient history with implants). Physicians should keep abreast of ALCL in the literature and provide appropriate therapy to patients as needed.

- **Effects on Children**

There have been concerns raised regarding potential damaging effects on children born of mothers with implants. A review of the published literature on this issue suggests that the information is insufficient to draw definitive conclusions.

Allergan's Clinical Studies

Clinical Studies Overview

Allergan's Saline-Filled Breast Implants were evaluated in four major open label, multicenter clinical studies: the Large Simple Trial (LST, which involved 2875 patients), the 1995 Augmentation Study (A95, which involved 901 patients), the 1995 Reconstruction Study (R95, which involved 237 patients), and the Post Approval Survey Study (PASS, which was a continuation of the A95/R95 studies).

Study Design

Patients studied were those seeking implant surgery for augmentation or reconstruction of the breast. The LST Study was designed as a one year study to assess the four safety outcomes of capsular contracture, infection, implant leakage/deflation, and implant removal for a large number of patients. As the results from that study were similar to those found in the larger studies, the data is not reported here.

The A95/R95 Studies were designed as 5 year studies to assess safety and effectiveness. Patient follow-up was yearly for 5 years. Safety assessments in the A95/R95 Studies consisted of adverse event rates and rates of secondary surgical treatment. Effectiveness assessments in the A95/R95 Studies consisted of patient satisfaction, breast size change,

and measures of body esteem/self esteem/body image. The PASS study utilized patient surveys for collection of specific risk/benefit information 6 through 10 years post implant.

Five-year data from the A95/R95 study and 10-year data from the PASS study are presented in this brochure.

Patient Accounting and Baseline Demographic Profile

The A95 Study enrolled 901 augmentation patients. Of those A95 patients available to be seen for their 5-year follow-up visit, 81% returned and were seen at 5 years after implant surgery. The R95 Study enrolled 237 reconstruction patients. Of those R95 patients available to be seen for their 5-year follow-up visit, 80% returned and were seen at 5 years after implant surgery. Demographic information obtained from the 1995 Studies revealed that nearly 90% of both augmentation and reconstruction patients were Caucasian and more than half of study participants were married. The median age of the augmentation patients was 32 years (range 19-66); for reconstruction patients the median age was 47 years (range 25-77). With respect to surgical baseline factors in the 1995 Studies, for augmentation patients, the most frequently used devices were textured round, the most common incision sites were periareolar and inframammary, and the most frequent placement of the implant was submuscular. For reconstruction patients, the most frequently used devices were textured shaped, the most common incision site was the mastectomy scar, and the most frequent placement of the implant was submuscular.

The post-approval study transitioned patients from data collection via physicians (0-5 years post-implantation) to data collection via mailed patient-completed surveys (6-10 years post-implantation). 85% of the augmentation patients and 86% of the reconstruction patients expected for follow-up at 10 years returned surveys to Allergan according to study protocol.

Effectiveness Outcomes

The benefits of saline-filled breast implants were assessed by a variety of outcomes, including bra cup size change (augmentation patients only), body image, body esteem, self concept, and patient satisfaction. Bra cup size was measured within the first year and a half after surgery. Body image, esteem, and self concept were assessed for patients with both original and replacement saline devices before implantation and at 3 years after surgery. Satisfaction was measured at every follow-up visit through 5 years.

Augmentation

859 (95%) of the original 901 augmentation patients had a breast measurement within 18 months of surgery. Of these 859 patients, 38% increased by 1 cup size; 49% increased by 2 cup sizes; 9% increased by 3 cup sizes, and 4% had no increase.

Of the original 901 augmentation patients, 683 (76%) provided a satisfaction rating at 5 years, with 95% indicating they were satisfied with their breast implants. The patient surveys showed 88% of the augmentation patients who provided satisfaction scores were satisfied with their breast implants at 10 years post-implant.

Quality of life assessments were obtained prior to implantation and at 6 months, 1 year, and 3 years after surgery. Before implantation, augmentation patients scored higher (better) than the general U.S. female population on the SF-36 scales, which measure general health-related quality of life. After 3 years, augmentation patients showed a slight worsening in their SF-36 scores, although all scales remained higher than the general U.S. female population. The Rosenberg Self Esteem Scale (which measures overall self esteem) and the Tennessee Self Concept Scale (which measures overall self concept) showed slight improvements over the 3 years. The Body Esteem Scale (which measures overall body image) showed a slight worsening overall but a large improvement in body esteem related to sexual attractiveness the 3 years.

Breast satisfaction was significantly increased after 3 years, including satisfaction with breast shape, size, feel or touch, and how well they matched (Table 1).

Table 1. Change from Pre-Surgery in Breast Satisfaction Scale

Quality of Life Scale	Primary Augmentation	
	Year 1	Year 2
Satisfaction with Breast	Improved	Improved
How well Breast Matched	Improved	Improved
Satisfaction with Breast Shape	Improved	Improved
Satisfaction with Breast Size	Improved	Improved
Satisfaction with Breast Feel/Touch	Improved	Improved

Reconstruction

Of the original 237 reconstruction patients, 137 (58%) provided a satisfaction rating at 5 years, with 89% indicating they were satisfied with their breast implants. The patient surveys showed 86% of the reconstruction patients who provided satisfaction scores were satisfied with their breast implants at 10 years post-implant.

Before implantation, reconstruction patients scored higher (better) than the general U.S. female population before implantation on all but one of the SF-36 scales, which measure general health-related quality of life. After 3 years, reconstruction patients showed an improvement in that SF-36 score to above the rate for the general U.S. female population. The following three overall scales showed no change over the 3 years: Tennessee Self Concept Scale (which measures overall self concept), Rosenberg Self Esteem Scale (which measures overall self-esteem), and the Body Esteem Scale (which measures overall body image).

Breast satisfaction was significantly increased after 3 years, including overall satisfaction and how well they matched.

Safety Outcomes

The A95 Study and R95 Study safety outcomes for primary implantation are presented in Tables 1 through 6.

The cumulative Kaplan-Meier risk of first occurrence of adverse events (and 95% confidence interval) is shown in Table 1 for the A95/R95 Study and Table 2 for the PASS Study. The rates reflect the number of patients out of 100 who experienced the listed complication at least once within the first 5 or 10 years after their implantation. Some complications occurred more than once for some patients.

Table 1
Complications
A95/R95: 5-Year Cumulative First Occurrence Kaplan-Meier Risk Rates, By Patient

Complication*	Augmentation (N=901)		Augmentation (N=237)	
	5-Year		5-Year	
	Rate (%)	(95% CI)	Rate (%)	(95% CI)
Reoperation	25.9	(23.0, 28.9)	44.5	(37.9, 51.0)
Breast Pain	17.0	(14.5, 19.5)	17.7	(12.4, 23.0)
Wrinkling	13.7	(11.3, 16.1)	24.6	(18.6, 30.6)
Asymmetry	12.2	(10.0, 14.4)	39.0	(32.1, 45.8)
Implant Palpability/Visibility	12.1	(9.8, 14.3)	27.1	(20.6, 33.5)
Implant Removal for Any Reason	11.8	(9.6, 14.0)	28.0	(22.1, 34.0)
Capsular Contracture Baker Grade III/IV	11.4	(9.2, 13.5)	35.7	(29.0, 42.4)
Loss of Nipple Sensation	9.9	(7.8, 11.9)	18.1	(12.5, 23.8)
Nipple Paresthesia	9.8	(7.8, 11.8)	<1	(0.0, 1.2)
Implant Malposition	9.2	(7.3, 11.2)	16.9	(11.7, 22.2)
Skin Paresthesia	7.6	(5.9, 9.4)	6.3	(2.9, 9.6)
Implant Deflation	6.8	(5.0, 8.5)	7.5	(3.8, 11.2)
Scarring Complications	6.5	(4.9, 8.2)	6.0	(2.7, 9.2)
Irritation/Inflammation	3.2	(2.0, 4.3)	6.6	(3.3, 9.8)
Seroma	2.6	(1.6, 3.7)	3.9	(1.4, 6.4)
Skin Rash	1.9	(1.0, 2.8)	3.3	(0.9, 5.7)
Capsular Calcification	1.8	(0.9, 2.7)	5.4	(2.3, 8.6)
Hematoma	1.7	(0.8, 2.5)	1.3	(0.0, 2.8)
Infection	1.0	(0.3, 1.6)	6.0	(2.8, 9.2)
Delayed Wound Healing	<1	<1	2.7	(0.6, 4.9)
Implant Extrusion	<1	<1	3.2	(0.9, 5.6)
Tissue/Skin Necrosis	<1	<1	3.6	(1.1, 6.0)

* Many events were assessed with severity ratings, and for these complications the rates shown in the table include only complications rated moderate, severe, or very severe (excludes mild and very mild ratings). All occurrences are included for reoperation, implant removal, leakage/deflation, scarring complications, irritation/inflammation, seroma, hematoma, skin rash, infection, implant extrusion and tissue/skin necrosis.

Table 2
Complications
Post Approval: 10 Year First Occurrence Kaplan-Meier Risk Rates, By Patient

Complication	10-Year Risk			
	Augmentation (N=901)		Augmentation (N=237)	
	Rate (%)	95% CI	Rate (%)	95% CI
Reoperation	36.5	(33.4, 39.9)	54.6	(48.1, 61.5)
Breast Pain	29.7	(26.6, 33.0)	33.0	(26.4, 40.7)
Capsular Contracture Baker Grade III/IV	20.8	(18.1, 23.8)	51.7	(44.6, 59.2)
Implant Replacement/Removal	20.2	(17.7, 23.1)	39.5	(33.3, 46.5)
Implant Deflation	13.8	(11.5, 16.4)	22.5	(16.8, 29.7)

Reasons for Reoperations

Table 3 shows the reasons for augmentation reoperation 5 years post-implantation from the A95 Study and 10 years post-implantation from the PASS Study based on the total number of reoperations.

Of the 901 augmentation patients in the A95 Study, at least one reoperation was performed on 225 patients (25%) through 5 years. A total of 293 reoperations were performed. The primary reason for reoperation through 5 years was implant deflation at 18.1%.

In the PASS Study, at least one reoperation was performed on 315 patients (36.5%) through 10 years. A total of 424 reoperations were performed. The primary reason for reoperation through 10 years on augmentation patients was implant deflation at 21.7%.

Table 3**Augmentation: Reasons for Reoperation Through 5 and 10 Years**

Reasons for Reoperation	5 years		10 years	
	N = 293		N = 424	
	n	%	n	%
Implant Deflation	53	18.1	92	21.7
Capsular Contracture	52	17.7	59	13.9
Patient Choice for Style/Size Change	45	15.3	88	20.7
Implant Malposition	28	9.6	36	8.5
Hematoma/Seroma	26	8.9	31	7.3
Lump/Mass/Cyst	25	8.5	66	15.6
Scarring	21	7.2	22	5.2
Ptosis	17	5.8	31	7.3
Asymmetry	14	4.8	14	3.3
Add/Remove Saline	14	4.8	21	5.0
Wrinkling	8	2.7	8	1.9
Unsatisfactory Nipple Result	5	1.7	5	1.2
Implant Palpability	4	1.4	5	1.2
Delayed Wound Healing	4	1.4	4	0.9
Infection	4	1.4	4	0.9
Skin Lesion/Cyst	3	1.0	3	0.7
Breast Pain	2	0.7	3	0.7
Irritation, Implant Extrusion, Capsule Calcification	1 each	0.3 each	1 each	0.2 each
Cancer	0	0	4	0.9
Total	328	111.9*	499	117.5*

* Total is greater than 100% because some reoperations were performed for multiple reasons.

Table 4 shows the reasons for reconstruction reoperation through 5 years in the R95 Study and 10 years in the PASS Study based on the total number of reoperations.

Of the 237 patients in the R95 Study, at least one reoperation was performed on 99 patients (42%) for a total of 125 reoperations through 5 years. The primary reason for reoperation through 5 years was capsular contracture at 27.2%.

In the PASS Study, at least one unplanned reoperation was performed on 120 patients (50.6%) through 10 years. A total of 159 reoperations were performed. The primary reason for reoperation through 10 years on reconstruction patients was also capsular contracture at 23.3%.

Table 4
Reconstruction: Reasons for Reoperation Through 5 and 10 Years

Reasons for Reoperation	5 years		10 years	
	N = 125		N = 159	
	n	%	n	%
Capsular Contracture	34	27.2	37	23.3
Asymmetry	25	20.0	25	15.7
Patient Choice for Style/Size Change	13	10.4	22	13.8
Implant Deflation	11	8.8	29	18.2
Implant Malposition	11	8.8	14	8.8
Lump/Mass/Cyst	10	8.0	16	10.1
Scarring	10	8.0	11	6.9
Infection	9	7.2	9	5.7
Tissue/Skin Necrosis	6	4.8	6	3.8
Hematoma/Seroma	6	4.8	6	3.8
Breast Pain	6	4.8	6	3.8
Wrinkling	5	4.0	5	3.1
Implant Extrusion	5	4.0	5	3.1
Add/Remove Saline	4	3.2	5	3.1
Implant Palpability	3	2.4	3	1.9
Delayed Wound Healing	2	1.6	2	1.3
Skin Lesion/Cyst	2	1.6	2	1.3
Unsatisfactory Nipple Result	1	0.8	2	1.3
Cancer	0	0	1	0.6
Total	163	130.4*	206	129.6*

* Total is greater than 100% because some reoperations were performed for multiple reasons.

Reasons for Implant Removal

Of the 901 augmentation patients in A95, there were a total of 98 patients (10.9%) who had 166 implants removed through 5 years. Of the 166 augmentation implants removed through 5 years, 94% were replaced. The most common reason for implant removal was patient choice for style/size change (43.4%). Through 10 years, 300 implants were removed from 170 patients. The most common reason was also patient choice for style/size change (41.3%).

The primary reason for implant removal in augmentation patients based on the number of implants removed is shown in Table 5 below.

Table 5
Augmentation: Reasons for Implant Removal Through 5 and 10 Years

Primary Reason for Implant Removal	5 years		10 years	
	N = 166		N = 300	
	n	%	n	%
Patient Choice for Size/Sytle Change	72	43.4	124	41.3
Implant Deflation*	54	32.5	100	33.3
Capsular Contracture	17	10.2	27	9.0
Wrinkling	6	3.6	8	2.7
Implant Palpability/Visibility	6	3.6	6	2.0
Asymmetry	3	1.8	8	2.7
Breast Pain	3	1.8	3	1.0
Malposition	2	1.2	16	5.3
Iatrogenic Injury	1	0.6	1	0.3
Infection	1	0.6	2	0.7
Implant Extrusion	1	0.6	1	0.3
Breast Mass/Lump/Cyst	0	0	4	1.3
Total	166	100	300	99.9

* Includes unreported/unknown (n=1 augmentation)

Of the 237 reconstruction patients in R95, there were 62 patients (26.2%) who had 70 implants through 5 years. Of the 70 reconstruction implants removed through 5 years, 70% were replaced. The most common reason for implant removal was capsular contracture (31.4%). Through 10 years, there were 104 implants removed from 85 patients. The most common reason for implant removal was implant leakage/deflation (32.7%).

The main reasons for implant removal in reconstruction patients are shown in Table 6 below.

Table 6
Reconstruction: Reasons for Implant Removal Through 5 and 10 Years

Primary Reason for Implant Removal	5 years		10 years	
	N = 70		N = 104	
	n	percent	n	percent
Capsular Contracture	22	31.4	22	21.2
Patient Choice for Style/Size Change	15	21.4	26	25.0
Implant Deflation*	12	17.1	34	32.7
Infection	7	10.0	7	6.7
Implant Extrusion	4	5.7	4	3.8
Implant Malposition	3	4.3	3	2.9
Other**	3	4.3	3	2.9
Wrinkling	2	2.9	2	1.9
Asymmetry	1	1.4	2	1.9
Recurrent Breast Cancer	1	1.4	1	1.0
Total	70	100	104	100.0

* Includes unreported/unknown (n=2 reconstruction)

** Other reasons as reported by the physician were: Abnormally on CT Scan at Mastectomy Site (n=1), Tissue Expansion Went Poorly Due to Radiation (n=1), Second Stage Breast Recon (n=1)

As additional safety information, Table 7 shows the 5-year cumulative Kaplan-Meier adverse event risk rates of first occurrence following implant replacement (i.e., revision) on a by implant basis for the A95 and R95 Studies. There were 126 augmentation implants and 40 reconstruction implants in the A95/R95 Studies that were removed and replaced with Allergan study devices.

Table 7
A95/R95: 5 Year Cumulative First Occurrence Kaplan Meier Risk Rates
Following Implant Replacement, by Implant

Complication Following Replacement of Implants	Augmentation N = 126 Implants		Reconstruction N = 40 Implants	
	%	95% CI	%	95% CI
Removal/Replacement	18.3	(12.7, 25.9)	28.2	(17.2, 44.0)
Capsule Contracture Baker Grade III/IV	13.2	(8.3, 20.6)	42.4	(27.8, 60.6)
Leakage/Deflation	9.0	(5.4, 14.6)	15.4	(6.9, 32.3)

Other Clinical Data Findings

This section summarizes post-implant observations from the A95 and R95 Studies pertaining to connective tissue/autoimmune (CTD) disease and breast disease (including breast carcinoma). These data should be interpreted with caution in that there was no comparison group of similar women without implants. Confirmed reports were based on a diagnosis by a physician. Data pertaining to effects on offspring and mammographic detection of tumors/lesions were not collected in these studies.

Breast Disease

Through 5 years, there were 81 reports of breast disease for augmentation patients; eighty (80) were benign and one incident was malignant.

For the reconstruction patients, there were 99 reports of breast disease; 75 were benign and 24 were malignant.

CTD

For augmentation patients through 5 years, there were 7 confirmed reports of CTD disease (3 instances of Graves' Disease, and 2 instances each of hyperthyroiditis and chronic fatigue syndrome/fibromyalgia).

For reconstruction patients through 5 years, there was one confirmed report of Graves' disease.

Instructions for Use

NOTE: Back-up breast implants should be available during the procedure.

DO NOT use more than one implant per breast.

SINGLE USE

This product is intended for **single use only**. Do not reuse explanted implants.

PRODUCT IDENTIFICATION

Product identification stickers accompanying each device are provided within the internal product packaging. The stickers provide product-specific information and are designed to be attached to the patient's chart for identification purposes. The Device Identification Card should be provided to the patient for personal reference.

SURGICAL PLANNING

Allergan relies on the surgeon to know and follow the proper surgical procedures with *NATRELLE*® Saline-Filled breast implants. Proper surgical planning such as allowance for adequate tissue coverage, implant placement (i.e., submuscular vs. subglandular), incision site, implant type etc., should be made preoperatively. The surgeon must carefully evaluate implant size and contour, incision placement, pocket dissection, and implant placement criteria with respect to the patient's anatomy and desired physical outcome. Planning should include clear delineation of aesthetic goals to ensure mutual understanding between surgeon and patient. The surgeon should observe current and accepted techniques to minimize the risk of adverse and potentially unattractive reactions.

STERILE PRODUCT

Each sterile saline-filled breast implant is supplied in a sealed, double primary package. Style-specific sterile product accessories are also supplied within the product packaging. Sterility of the implant is maintained only if the thermoform packages, including the package seals, are intact. Use standard procedures to maintain sterility during transfer of the breast implant to the sterile field. Remove the breast implant and accessories from their packages in an aseptic environment and using talc-free gloved hands.

DO NOT use the product if the thermoform packages or seals have been damaged.

DO NOT implant damaged or contaminated breast implants.

DO NOT store the breast implant with the fill tube in place, which may damage the integrity of the valve seal.

DO NOT resterilize the product.

NEVER, under any circumstances, attempt to resterilize using ethylene oxide, which is known to cause adverse tissue reaction if not completely removed from the device. Avoid unnecessary exposure of the breast implant to lint, talc, sponge, towel, skin oils, and other contaminants.

Prior to use, keep the breast implant in the inner thermoform and covered to prevent contact with airborne and surgical field particulate contaminants.

1. Peel open the lid of the outer thermoform package.
2. Invert the outer thermoform over the sterile field, allowing the sealed inner thermoform to gently fall into the field.
3. Peel open the lid of the inner package using the pull tab.
4. Gently retrieve the breast implant.

SURGICAL PROCEDURE

Breast augmentation with saline-filled implants can be carried out through several different incisions including inframammary, periareolar, or transaxillary. The transumbilical incisional approach is not recommended. Some surgeons advocate a "no-touch" technique, which requires significant attention to minimizing contact between the patient's skin and the implant.

Pocket dissection should be planned out preoperatively and be performed accurately and with minimal trauma. Excellent hemostasis is important to avoid postoperative hematoma. The implant may be placed subglandularly or subpectorally depending upon the balance of cosmetic and medical considerations in any given patient. The size and shape of the device may be determined preoperatively by means of dimensional planning or intraoperatively with the help of temporary sizer devices. The implant may be filled with saline either before or after insertion. If inserted without saline, the implant may be inserted as received (i.e., filled with air), or the air may be evacuated prior to insertion. Regardless of which insertion technique is used, it is important to ultimately evacuate as much air from the implant as possible. It is also important to maintain proper orientation of any BioDIMENSIONAL® implant. The incision for the placement of the implant should be securely closed and in several layers, whenever possible. Drains are optional.

Breast reconstruction is generally carried out in the mastectomy scar. Special care must be used in breast reconstruction to make sure that appropriate amounts of healthy tissue is available to cover the implant and that the implant be properly sized and positioned based upon careful preoperative planning. Educational materials are available through the Allergan Customer Care Department to supplement surgical knowledge of the dimensional techniques intended for use with BioDIMENSIONAL® styles.

Maintaining Hemostasis/Avoiding Fluid Accumulation

Postoperative hematoma and seroma may be minimized by meticulous attention to hemostasis during surgery, and possibly also by postoperative use of a closed drainage system. Persistent, excessive bleeding must be controlled before implantation.

Any postoperative evacuation of hematoma or seroma must be conducted with care to avoid breast implant contamination, or damage from sharp instruments.

Technique for Using Breast Implants with Diaphragm Valve

The fill volume range is specified on the product package labeling and data sheet. Following recommended fill volumes can decrease the possibility of shell wrinkling and crease fold failure.

DO NOT underfill or overfill the breast implant beyond the range specified.

DO NOT use excessive force during any of the steps in the following procedure.

DO NOT damage the breast implant with sharp surgical instruments such as needles and scalpels, or by excessive handling and manipulation during introduction into the surgical pocket.

1. Fill tube insertion

Prepare the fill tube by attaching the reflux valve to the Luer adapter of the fill tube as shown in **Figure 1**. The reflux valve prevents back-flow during intraoperative filling. This two-way valve opens when a syringe is attached, and closes when the syringe is removed.

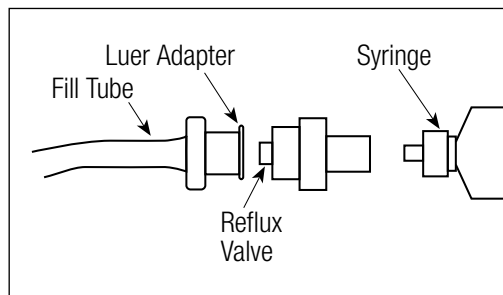


Figure 1

Figure 2 shows a cross section of the diaphragm valve with the strap closure in place and the valve closed. To insert the fill tube, wet the tip of the fill tube in sterile saline for injection and push the strap closure to one side of the valve entrance.

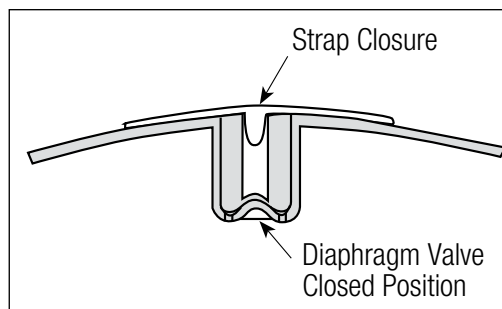


Figure 2

Insert the fill tube by gently pushing the fill tube tip into the valve entrance. Do not use excessive force while inserting the fill tube tip. When the fill tube flange nears or makes contact with the implant shell, the fill tube is in the proper position and the diaphragm valve is open (**Figure 3**).

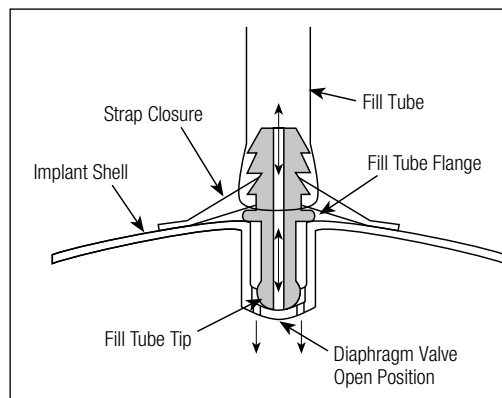


Figure 3

2. Air aspiration

After the fill tube is properly inserted, remove any air from the breast implant by aspiration with an empty sterile syringe attached to the reflux valve on the fill tube.

DO NOT use lubricants to facilitate placement, which create the risk of pocket contamination. Lubricants may also affect tissue adherence.

DO NOT use the breast implant for expansion or dissection of the pocket.

3. Filling

Use a syringe filled with sterile, pyrogen-free Sodium Chloride U.S.P. Solution for Injection to fill the prosthesis and fill to a volume within the recommended fill range specified on the product package labeling and data sheet. Only sterile pyrogen-free Sodium Chloride U.S.P. Solution for Injection drawn from its original container should be used. As it is known that bacterial infections may result from contaminated saline, it is recommended that a new sterile saline container be used with each surgery and implant-filling procedure.

NOTE: The order of filling, placement, and orientation may vary with surgeon preference and technique.

4. Residual Air

After filling is completed, aspirate any residual air bubbles. Then use gentle traction to remove the fill tube from the valve, taking care to avoid damage to shell or valve.

5. Diaphragm Valve Closure

Use gentle traction to remove the fill tube from the valve, taking care to avoid damage to shell or valve. Verify that the diaphragm valve is clear of particulates. Once the fill tube tip is removed the diaphragm valve is closed. To help retard tissue ingrowth or fluid accumulation in the valve entrance, engage the strap closure as follows: using the thumb and forefinger, compress the valve seat and the strap to snap the valve plug into place as shown in **Figure 2**.

Documentation the Physician Should Provide to the Patient

Breast implantation is an elective procedure and the patient must be well counseled on the risk-benefit relationship. The surgeon should provide each prospective patient with the following:

- ***Patient Labeling***

Allergan's bilingual **Patient Planner for Breast Augmentation or Reconstruction with NATRELLE® Saline-Filled Breast Implants** should be used to facilitate patient education on the risks and benefits of saline-filled breast implant surgery. It should be given to the patient during her initial visit/consultation to allow sufficient time for review prior to making the decision to proceed with surgery. You should verify that the patient has an adequate understanding of the information in subsequent preoperative discussions.

- ***Device Identification Card***

Enclosed with each saline-filled breast implant is a Device Identification Card. To complete Allergan's Device Identification Card, place one device identification sticker for each implant on the back of the card. Stickers are located on the internal product packaging attached to the label. If a sticker is unavailable, the lot number, catalog number and description of the device may be copied by hand from the device label. Patients should be provided with these cards for personal reference.

Additional Specific Product Information

Returned Goods Policy

Product returns should be handled through an Allergan Breast Aesthetics Surgical Sales Representative or through the Customer Care Department at 1.800.668.6427. Return value is based on time limitations. All package seals must be intact to be eligible for return. Returned products may be subject to a restocking charge.

Reporting and Return of Explanted Devices

The reason for explantation should be reported and the explanted device returned to Allergan. In the event of an explantation, please contact Allergan's Product Support Department at 1.800.624.4261 for an Explant Kit and explant return instructions.

ConfidencePlus® LIMITED WARRANTIES

The *ConfidencePlus®* Limited Warranties provide lifetime replacement and limited financial reimbursement in the event of loss of shell integrity resulting in implant deflation, subject to certain conditions as fully discussed in the *ConfidencePlus®* literature. For more information, please contact Product Support at 1.800.624.4261.

PRODUCT ORDERING

To order directly in Canada or for product information, please contact your local Allergan Breast Aesthetics Surgical Sales Representative or the Allergan Customer Care Department at 1.800.668.6427.

These products are covered by one or more of the following U.S. Patents: 5,480,430; 5,007,929; 4,889,744 and 4,859,712 and/or foreign patents corresponding thereto.

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