Directions for Use (DFU)

NATRELLE®

Silicone-Filled Breast Implants

Physician Labeling

Allergan™

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Introduction

DIRECTIONS TO THE SURGEON

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*® Gel-Filled Breast Implants, including the indications for use, contraindications, warnings, precautions, complications and summaries of clinical study 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 gel-filled breast implants and breast implant surgery.

Physician Education

Allergan offers a physician education program via the Allergan Academy™ to educate physicians on issues relevant to Allergan's breast implants. The primary goals of the Allergan Academy™ are to convey important information to physicians from Allergan's multicenter clinical studies and implant retrieval analyses, and to ensure that physicians are equipped with the most current clinical outcome and risk information to provide to their patients. Please contact your local Allergan Plastic Surgery Sales Representative or the Allergan Customer Care Department for further information on the Allergan Academy™ and other Allergan physician education initiatives.

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 bilingual ***Patient Planner for Breast Augmentation or Reconstruction with NATRELLE® Gel-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 in Allergan's **Patient Planner** (patient decision-making aid) on the risks, follow-up recommendations, and benefits associated with silicone gel-filled breast implant surgery.

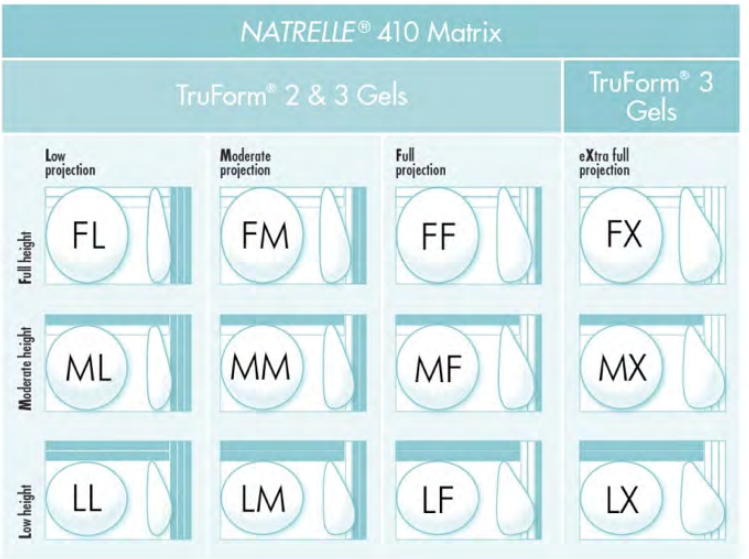
In order to document a successful informed consent process the Patient Planner also includes an *Acceptance of Risk and Consent to Surgery* document that should be signed by both the patient and the surgeon and then retained in the patient's file.

Device Descriptions

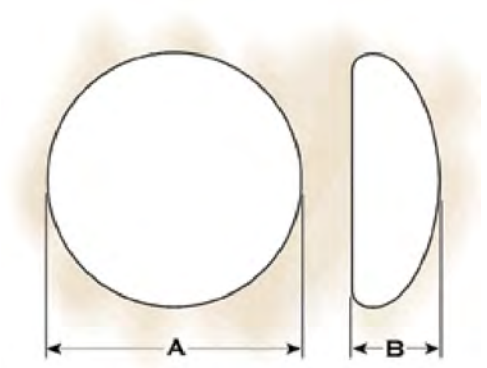
The gel-filled breast implants in the *NATRELLE®* Collection are constructed with barrier shell technology resulting in a low diffusion silicone elastomer shell and are filled with TruForm® gel. TruForm® is the specially formulated, premium quality gel used in the *NATRELLE®* Collection. TruForm® 1 is a soft cohesive gel that is responsive to movement with a shape that is influenced by the surrounding breast tissue, TruForm® 2 is a slightly firmer, form stable cohesive gel that retains a natural feel while helping to create the desired shape for more predictable long-term control, and TruForm® 3 is a form stable cohesive gel developed specifically for anatomical implants with a firmer feel for the ultimate shape control providing predictable aesthetic results over time.

The Collection includes TruForm® 1 (formerly known as Cohesive) Gel-Filled Breast Implants, TruForm® 2 (formerly known as Soft Touch™) Gel-Filled Breast Implants, TruForm® 3 (formerly known as Highly Cohesive) Gel-Filled Breast Implants, and INSPIRA® (implants that are filled to about 95% of volume with TruForm® 1 or TruForm® 2 gel). All styles consist of a shell, a patch, and silicone gel fill and are dry-heat sterilized.

NATRELLE® TruForm® Gel-Filled Breast Implants are available in both smooth and BIOCELL® textured surfaces.



NATRELLE® Round TruForm® 1 Style Number	**Breast Implant Description**	**Size Range**
Style 10	Smooth shell surface, moderate projection	120cc – 800cc
Style 15	Smooth shell surface, mid-range projection	155cc – 752cc
Style 20	Smooth shell surface, high projection	120cc – 800cc
Style 110	BIOCELL® Textured shell surface, moderate projection	90cc – 510cc
Style 115	BIOCELL® Textured shell surface, mid-range projection	150cc – 716cc
Style 120	BIOCELL® Textured shell surface, high profile	180cc – 650cc



A = Width; B = Projection

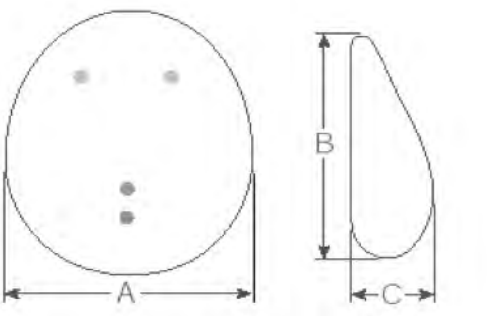
Round Breast Implant

NATRELLE® 410 TruForm® 2 and 3 Gel-Filled Breast Implants are manufactured with the BIOCELL® surface texture.

NATRELLE® 410 TruForm® 2 Style Number	**Breast Implant Description**	**Size Range**
410FL	Full height, low projection	130g – 350g
410FM	Full height, moderate projection	155g – 670g
410FF	Full height, full projection	120g – 740g
410ML	Moderate height, low projection	125g – 285g
410MM	Moderate height, moderate projection	95g – 450g
410MF	Moderate height, full projection	140g – 640g
410LL	Low height, low projection	135g – 300g
410LM	Low height, moderate projection	140g – 320g
410LF	Low height, full projection	125g – 595g

NATRELLE® 410 TruForm® 3 Style Number	Breast Implant Description	Size Range
410FL	Full height, low projection	140g – 320g
410FM	Full height, moderate projection	155g – 670g
410FF	Full height, full projection	160g – 740g
410FX	Full height, extra full projection	185g – 775g
410ML	Moderate height, low projection	125g – 285g
410MM	Moderate height, moderate projection	160g – 450g
410MF	Moderate height, full projection	140g – 640g
410MX	Moderate height, extra full projection	160g – 765g
410LL	Low height, low projection	135g – 300g
410LM	Low height, moderate projection	140g – 320g
410LF	Low height, full projection	125g – 595g
410LX	Low height, extra full projection	145g – 685g

NATRELLE® 410 implants are considered form stable as there is no migration of the gel. The device maintains its shape.



A = Width
B = Height
C = Projection

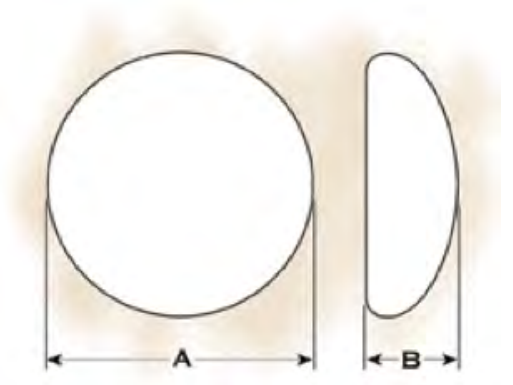
Shaped Breast Implant

NATRELLE® INSPIRA® TruForm® 1 Style Number	Breast Implant Description	Size Range
N-SRL	Smooth shell surface, responsive (TruForm® 1 gel), low profile	110 - 610 g
N-SRLP	Smooth shell surface, responsive (TruForm® 1 gel), low profile plus	125 - 640 g
N-SRM	Smooth shell surface, responsive (TruForm® 1 gel), moderate profile	140 - 755 g
N-SRF	Smooth shell surface, responsive (TruForm® 1 gel), full profile	180 - 770 g
N-SRX	Smooth shell surface, responsive (TruForm® 1 gel), extra full profile	200 - 800 g

NATRELLE® INSPIRA® TruForm® 2 Style Number	Breast Implant Description	Size Range
N-SSL	Smooth shell surface, soft Touch (TruForm® 2 gel), low profile	110 - 610g
N-SSLP	Smooth shell surface, soft Touch (TruForm® 2 gel), low profile plus	125 - 640g
N-SSM	Smooth shell surface, soft Touch (TruForm® 2 gel), moderate profile	140 - 755g
N-SSF	Smooth shell surface, soft Touch (TruForm® 2 gel), full profile	180 - 770g
N-SSX	Smooth shell surface, soft Touch (TruForm® 2 gel), extra full profile	200 - 800g

NATRELLE® INSPIRA® TruForm® 1 Style Number	Breast Implant Description	Size Range
N-TRL	Textured shell surface, responsive (TruForm® 1 gel), low profile	110 - 610g
N-TRLP	Textured shell surface, responsive (TruForm® 1 gel), low profile plus	125 - 640g
N-TRM	Textured shell surface, responsive (TruForm® 1 gel), moderate profile	140 - 685g
N-TRF	Textured shell surface, responsive (TruForm® 1 gel), full profile	180 - 745g
N-TRX	Textured shell surface, responsive (TruForm® 1 gel), extra full profile	205 - 800g

NATRELLE® INSPIRA® TruForm® 2 Style Number	Breast Implant Description	Size Range
N-TSL	Textured shell surface, soft Touch (TruForm® 2 gel), low profile	110 - 610g
N-TSLP	Textured shell surface, soft Touch (TruForm® 2 gel), low profile plus	125 - 640g
N-TSM	Textured shell surface, soft Touch (TruForm® 2 gel), moderate profile	140 - 685g
N-TSF	Textured shell surface, soft Touch (TruForm® 2 gel), full profile	180 - 745g
N-TSX	Textured shell surface, soft Touch (TruForm® 2 gel), extra full profile	205 - 800g



A = Width; B = Projection

INSPIRA® Breast Implant

NATRELLE® INSPIRA® TruForm® 1 and 2 Breast Implant Matrix

Indications

- **Breast Augmentation** - A woman must be at least 22 years old for breast augmentation
- **Breast Reconstruction**
- **Revision** of previous breast augmentation or reconstruction to correct or improve the result of the previous surgery

Contraindications

Patient Groups in which the product is contraindicated:

- Women with existing malignant or pre-malignant tumors of the breast without adequate treatment
- Women with an active infection anywhere in the body
- Women who are currently pregnant or nursing

Warnings

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

- **Alteration:** Do not alter the implant
- **Stacking of implants:** Do not place more than one implant per breast
- **Reuse:** Single use only. Do not resterilize or reuse explanted implants
- **Closed Capsulotomy:** Do not treat capsular contracture by forceful external compression, which will likely result in implant damage, rupture, folds and/or hematoma
- **Periumbilical approach:** Do not use the periumbilical approach for placement of the implant

Avoid Damage During Surgery

- ***Care should be taken to avoid the use of excessive force and to minimize handling of the implant during surgical insertion. The unique nature of the highly cohesive gel creates an implant with a precisely defined shape. Excessive force upon insertion of the implant may compromise this shape, potentially leading to an undesirable cosmetic outcome.***

  Data accumulated from Allergan's retrieval study analyses of explanted ruptured silicone gel-filled breast implants, observations of surgeries, and a review of the published literature, indicate that forcing an implant through too small an opening or applying concentrated, localized pressure on the implants may result in localized weakening of the breast implant shell potentially leading to shell damage and possible implant rupture.

  An incision should be of appropriate length to accommodate the style, size, and profile of the implant. The incision needed for silicone-filled breast implants will be longer than the one typically made for a saline breast augmentation. The unique nature of the more cohesive gel in the TruForm® 3 breast implant requires an even larger incision to reduce excessive stress on the implant during insertion and minimize the potential for implant damage or deformation (change in shape).

- ***Care should be taken when using surgical instruments in proximity with the breast implant, including scalpel, sutures, and dissection instrumentation.***

  Silicone-filled breast implants are prone to unintended instrument trauma during implantation or during explantation (Brandon et al. 2001, Young and Watson 2001). Shell failure can result from damage by scalpels, suture needles, hypodermic needles, hemostats, and Adson forceps, and has been observed in explanted device shells using scanning electron microscopy (Brandon et al. 2001). Allergan's analyses (retrieval study) of explanted devices have identified unintended surgical instrument damage as one potential cause of shell failure and thus implant rupture.

- ***Use care in subsequent procedures such as open capsulotomy, breast pocket revision, hematoma/seroma aspiration, and biopsy/lumpectomy to avoid damage to the implant.***

  Re-positioning of the implant during subsequent procedures should be carefully evaluated by the medical team and care taken to avoid contamination of the implant. Use of excessive force during any subsequent procedure can contribute to localized weakening of the breast implant shell potentially leading to decreased device performance.

- ***Do not contact the implant with disposable, capacitor-type cautery devices.***
- ***Do not alter the implants or attempt to repair or insert a damaged prosthesis.***

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.

Precautions

Specific Populations

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

- Autoimmune diseases (for example, lupus and scleroderma).
- A compromised immune system (for example, currently receiving immunosuppressive therapy).
- Conditions or medications that 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. Patients should be assessed for any history of mental health disorders and should be referred to a mental health professional for further follow up and treatment if necessary. Patients with a diagnosis of depression or other mental health disorder should not undergo surgery until these conditions resolve.

Mammography

Patient Counseling Information

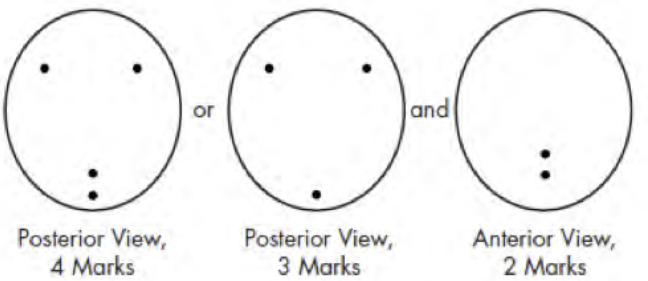
With breast implants, routine screening mammography will be more difficult. The patient should continue to perform monthly breast examinations for cancer screening; however, this may be more difficult. The implant may interfere with finding breast cancer during mammography. Because the breast and implant is squeezed during mammography, an implant may rupture during the procedure. More x-ray views are necessary for women with breast implants; therefore, a patient will receive more exposure to radiation. However, the benefit of having the mammogram to find cancer outweighs the risk of the additional x-rays.

Patients should be instructed to inform their mammographers about the presence, type and placement of their implants. Patients should be advised to request **diagnostic mammography** rather than **screening mammography**.

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.

Orientation Marks

Prior to mammography the radiologist should be alerted to the presence and location of the orientation marks on the TruForm® 2 and 3 implant as these may be visible on the mammographic images. These orientation marks are circular silicone elastomer dots located on the surface of the implant and are used to assist the physician with visual and tactile placement of the implant within the surgical pocket. The posterior surface of most sizes of the TruForm® 2 and 3 implant has 4 orientation marks; the posterior (back) surface of some smaller and/or shorter styles may have only 3 orientation marks. The front (anterior) surface of all TruForm® 2 and 3 implants has 2 orientation marks, as shown below.



Radiation to the Breast

Allergan has not tested the *in-vivo* effects of radiation therapy in patients who have breast implants. The literature suggests that radiation therapy does not compromise implant integrity, but may increase the likelihood of capsular contracture, necrosis, and extrusion.

Long-Term Effects

Patient Counseling Information

Allergan's clinical studies of the TruForm® 1 implants (the Core Study) and the TruForm® 3 implants (the Pivotal study) monitored the long-term (10 years) safety and effectiveness of these products. In addition, Allergan has initiated a separate large 10-year post approval study (the Breast Implant Follow-up Study, or BIFS) to address specific issues which the other studies were not designed to fully answer, as well as to provide a real-world assessment of some endpoints. Allergan will update its labeling on a regular basis with the results of these studies.

Important Factors to be Discussed with the Patient

Patient Counseling Information

The following information should be discussed with patients prior to their decision to proceed with surgery:

- ***Professional Care*** – Patients should be advised that follow-up exams as prescribed by their plastic surgeon are recommended to monitor the status of their breast implants.

- ***Avoiding Damage during Treatment*** – Patients should be instructed to inform other treating physicians of the presence of implants to minimize the risk of damage to the implants.

- ***Smoking*** – Patients should be informed that smoking may interfere with the healing process.

- ***Breast Examination Techniques*** – Patients should be instructed to follow the most current medical recommendations regarding breast examination and mammography frequency appropriate for their age and medical history. To maximize the effectiveness of breast self examinations for any palpable lesions, patients should be instructed how to distinguish the implant from breast tissue.

COMPLICATIONS

- ***Rupture*** – Patients should be informed that silicone gel-filled breast implants are not lifetime devices and that there is a potential for implant rupture. The decision to remove a ruptured or suspected ruptured implant should be undertaken following review of all available clinical information and after careful consideration between you and your patient. However, if implant rupture is diagnosed, it is recommended that the implant be removed.

- ***Clinical Management of Suspected and Confirmed Rupture*** – Patients should be informed that following a diagnosis of suspected or confirmed rupture that implant removal might be recommended by their surgeon, particularly in those instances where there may be evidence that silicone gel has moved beyond the confines of the fibrous capsule that typically forms around the device. Most surgeons in Allergan's clinical studies have chosen to remove implants suspected of rupture.

Patients should be aware that, rarely, an intracapsular rupture may progress to an extracapsular rupture. Studies of Danish women indicate that over a 2-year period, about 10% of the implants with intra-capsular rupture progressed to extracapsular rupture as detected by MRI, i.e. for women with silicone gel rupture within the scar tissue capsule detected via MRI after 2 years, 1 in 10 of these women will have progression of the gel outside the scar tissue capsule. In about half of these cases of progression from intra- to extra-capsular rupture, the women had experienced trauma or mammography. In the other half, no cause was given.

In the women with extracapsular rupture, after 2 years, the amount of silicone seepage outside the scar tissue capsule increased for about 14% of these women, i.e. for 100 women with silicone gel rupture outside the scar tissue capsule, the amount of gel outside the scar tissue capsule increased for 14 women 2 years later. This type of information is not available for Allergan-specific implants and it pertains to a variety of silicone implants from a variety of manufacturers and implant models. Given the greater cohesivity of TruForm® 3 implants, it is likely that they have less risk of extracapsular rupture than other silicone implants.

- ***Monitoring for Implant Rupture*** – Patients should be informed that periodic evaluation of the integrity of their breast implants is required to determine whether the implant has ruptured in the absence of any clinical symptoms. While there are various diagnostic methods available to evaluate for possible implant rupture including physical examination, mammogram, and ultrasound, FDA believes the best method for detection of rupture is Magnetic Resonance Imaging (MRI). In most cases, an

MRI diagnosis of rupture or possible rupture is consistent with a ruptured implant at explantation (Brown et al. 2000, Holmich et al. 2004). However, the scientific value of MRI is still developing. Allergan's clinical study results and other published reports have found that in some cases MRI may falsely show a breast implant rupture when there is none (false positive). In some cases MRI may also show no breast implant rupture when there is one (false negative). Scaranelo et al. (2004) found that the sensitivity and specificity of MRI to detect rupture in asymptomatic patients was 64% and 77%, respectively. Thus, MRI findings of rupture should not be considered definitive (Scaranelo et al. 2004).

Health Canada and the Canadian Expert Advisory Panel on silicone gel-filled breast implants advocate the following approach to monitor patients with breast implants. **In consideration of all the available scientific information, it has been suggested that the process for determining implant integrity (e.g. rupture) should be related to clinical signs and symptoms. Thus, the following 6-step process is recommended for screening for silicone gel-filled breast implant rupture:**

1. **Patient self-examination;**
2. **New symptom or sign suspected;**
3. **Physician physical examination, related to a periodic review or new symptoms and signs, suggests findings that warrant further investigation;**
4. **Ultrasound, mammogram, or both of the implant and the breast involved should be acquired;**
5. **MRI if ultrasound is negative or inconclusive. The MRI should be performed at a centre with a breast coil with a magnet of at least 1.5 Tesla. The MRI should be read by a radiologist who is familiar with looking for implant rupture; and**
6. **If signs of rupture are seen on MRI, then in consultation with the plastic surgeon, the implant(s) may be removed, with or without replacement.**

Rupture Rate Information on Allergan Implants

TruForm® 1 Breast Implants

In Allergan's Core Study, rupture was assessed for patients who had scheduled MRIs to screen for silent rupture (i.e., part of the MRI cohort) and those who were not assessed for rupture by MRI (i.e., part of the non-MRI cohort). The rupture rates in the MRI cohorts were 9.3% for primary augmentation, 5.4% for revision-augmentation, 35.4% for primary

reconstruction, and 0% for revision-reconstruction. The rupture rate for the combined overall MRI cohort in the Core Study through 10 years was 13.0% for patients and 7.7% for implants. Across all patients in the Core Study, all ruptures were intracapsular gel, but one rupture progressed to extracapsular gel following exploratory surgery to confirm the rupture and then implant replacement was delayed. There were no cases of migrated gel.

Further rupture rate information on TruForm® 1 implants is provided from a published European study known as the International MRI Study.[27] Silent rupture data were collected via a single MRI on 77 augmentation, 11 reconstruction, and 18 revision patients implanted with smooth and textured *NATRELLE*® implants by surgeons in 5 countries. The average age of the implants was approximately 11 years. Silent rupture was found in approximately 15% of the combined group of augmentation, reconstruction, and revision patients and 8% of the implants. There were three possible case of extracapsular rupture with the remainder classified as intracapsular ruptures. No cases of migrated gel were found.

TruForm® 3 Breast Implants

In Allergan's pivotal study, rupture was assessed for patients who had scheduled MRIs to screen for silent rupture (i.e., part of the MRI cohort) and those who were not assessed for rupture by MRI (i.e., part of the non-MRI cohort). The rupture rates in the MRI cohorts were 17.7% for primary augmentation, 14.7% for revision-augmentation, 12.4% for primary reconstruction, and 19.6% for revision-reconstruction. The rupture rate for the whole MRI cohort in the pivotal study through 10 years was 16.4% for patients and 9.7% for implants. Across all patients in the pivotal study, all of the ruptures were intracapsular, with no cases of extracapsular rupture or migrated gel.

Further rupture information on TruForm® 3 implants is provided from a published study known as the 410 Swedish MRI Study.[28] Silent rupture data were collected via a single MRI on 124 augmentation and 20 revision patients implanted with *NATRELLE*® TruForm® 3 implants at one hospital. The average age of the implants was approximately 6 years. Silent rupture was found in approximately 2% of the combined group of augmentation and revision patients and 1% of the implants. All ruptures were classified as intracapsular with no cases of extracapsular rupture or migrated gel.

- ***Reoperation (Additional Surgeries)*** – Patients should be advised that additional surgery to their breast and/or implant may be necessary over the course of their lives.
- ***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 rupture, and it is one of the most common reasons for reoperation.

- ***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 lives. 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, displacement, incorrect size, unanticipated contour, 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 silicone gel-filled 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 of other conditions in women with breast implants. Many of these conditions which are listed below, have been studied to evaluate their potential association with breast implants. 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**

  Breast Cancer – Reports in the medical literature indicate that patients with breast implants are not at a greater risk than those without breast implants for developing breast cancer. Some reports have suggested that breast implants may interfere with or delay breast cancer detection by mammography and/or biopsy; however, other reports in the published medical literature indicate that breast implants neither significantly delay breast cancer detection nor adversely affect survival of women with breast cancer. A large follow-up study reported no evidence of an association between breast implants and cancer, and even showed a decreased incidence of breast cancer compared to the general population.

Brain cancer – One recent study has reported an increased incidence of brain cancer in women with breast implants as compared to the general population. The incidence of brain cancer, however, was not significantly increased in women with breast implants when compared to women who had other plastic surgeries. A recently published review of four large studies of women with cosmetic implants and an additional long-term follow-up study concluded that the evidence does not support an association between brain cancer and breast implants.

Respiratory/lung cancer – Studies have reported an increased incidence of respiratory/lung cancer in women with breast implants. Other studies of women in Sweden and Denmark have found that women who get breast implants are more likely to be current smokers than women who get breast reduction surgery or other types of cosmetic surgery.

Cervical/vulvar cancer – Two studies have reported an increased incidence of cervical/vulvar cancer in women with breast implants, while another long-term study showed equivalent incidences of cervical cancer in women with breast implants compared to the general population.

Other cancers – One study has reported an increased incidence of stomach cancer and leukemia in women with breast implants compared to the general population. This increase was not significant when compared to women who had other types of plastic surgeries.

Lymphomas, including anaplastic large T-cell lymphoma (ALCL) – Based on information reported to global regulatory agencies and found in medical literature, an association has been identified between breast implants and the development of anaplastic large cell lymphoma (ALCL), a type of non-Hodgkin's lymphoma. Women with breast implants may have a very small but increased risk of developing Breast Implant Associated ALCL (BIA-ALCL) in the fluid or scar capsule adjacent to the implant, with documented potential for local, regional, and distant spread of the cancer with mortality reported in rare cases.

BIA-ALCL has been reported globally in patients with an implant history that includes Allergan's and other manufacturers' breast implants with various surface properties, styles, and shapes. Most of the cases in the literature reports describe a history of the use of textured implants.

You should consider the possibility of BIA-ALCL when a patient presents with late onset, persistent peri-implant seroma. In some cases, patients presented with capsular contracture or masses adjacent to the breast implant. When testing for BIA-ALCL, collect fresh seroma fluid and representative portions of the capsule, and send to a laboratory with appropriate expertise for pathology tests to rule out ALCL, including immunohistochemistry testing for CD30 and ALK (anaplastic lymphoma kinase). If your patient is diagnosed with peri-implant BIA-ALCL, develop an individualized treatment plan in coordination with a multi-disciplinary care team. Because of the small number of cases worldwide, there is no worldwide consensus on the treatment regimen for peri-implant BIA-ALCL. However, the National Comprehensive Cancer Network (NCCN) recommends surgical treatment that includes implant removal and complete capsulectomy ipsilaterally as well as contralaterally, where applicable (NCCN Clinical Practice Guidelines in Oncology, T-cell Lymphomas. Version 1.2017).

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 informed of BIA-ALCL in the literature and provide appropriate therapy to patients as needed.

- **Neurological Disease, Signs, and Symptoms**

  Some women with breast implants have complained of neurological symptoms (such as difficulties with vision, sensation, muscle strength, walking, balance, thinking or remembering things) or diseases (such as multiple sclerosis), which they believe are related to their implants. A scientific expert panel report found that the evidence for a neurological disease or syndrome caused by or associated with breast implants is insufficient or flawed. Further review of the epidemiologic evidence also failed to find an association between implants and neurologic disease.

- **Mental Health Disorders**

  Patients should be encouraged to discuss any history of mental health disorders, including a clinical diagnosis of depression, body dysmorphic disorder or eating disorder with you during their consultation visit(s). Patients with a diagnosis of depression or other mental health disorder should be encouraged to wait to schedule surgery until these conditions resolve.

- **Suicide**

  In several studies, a higher incidence of suicide was observed in women with breast implants. The reason for the observed increase is unknown, but it was found that women with breast implants had higher rates of hospital admission due to psychiatric causes prior to surgery, as compared with women who had breast reduction or in the general population of Danish women.

- **Effects on Children**

  At this time, it is not known if a small amount of silicone may pass through from the breast implant silicone shell into breast milk during breastfeeding. Although there are no current established methods for accurately detecting silicone levels in breast milk, a study measuring silicon (one component in silicone) levels did not indicate higher levels in breast milk from women with silicone gel-filled implants when compared to women without implants.

  In addition, concerns have been raised regarding potential damaging effects on children born to mothers with implants. Two studies in humans have found that the risk of birth defects overall is not increased in children born after breast implant surgery. Although low birth weight was reported in a third study, other factors (for example, lower pre-pregnancy weight) may explain this finding. One of the authors of these human studies recommended further research on infant health. A review of the evidence did not find that offspring of women with implants were at an increased risk for esophageal disorders, rheumatic diseases, or congenital malformations.

- **Gel Diffusion and Potential Health Consequences**

  Small quantities of low molecular weight (LMW) siloxane compounds and platinum (in a zero valance/biocompatible state), have been found to diffuse (leak) through an intact implant shell. Studies on implants implanted for a long duration have suggested that such diffusion may be a contributing factor in the development of capsular contracture and lymphadenopathy. Other studies have shown evidence of silicone in scar tissue capsules surrounding the implant, in axillary lymph nodes, and in distant organs, which may be due to gel diffusion. The clinical significance of the presence of silicone in these tissues is unknown. Other studies have reported that certain silicones (for example, D4

and D5) and platinum leak from intact breast implants and are present in surrounding tissue. The clinical significance to humans of the presence of silicone in the body tissues is unknown. However, there has been no evidence in the medical literature or from Allergan's own testing associating gel diffusion with local complications in breast implant patients. Studies have demonstrated that the low concentration of platinum contained in breast implants is in the zero valence or most biocompatible state.

- **Delayed-type Hypersensitivity**

  While there is no scientific evidence that silicone can cause hypersensitivity reactions in humans, some animal testing reports in the literature suggest evidence of a delayed-type hypersensitivity to silicone. The biological mechanism and outcome for these findings in animal models remain unknown.

Preclinical Study Information

Preclinical study of the silicone-filled breast implants revealed that the materials of which the devices are made are biocompatible, the silicone elastomer shell is durable, and there is a low potential for gel diffusion (bleed). A summary of the preclinical studies conducted by Allergan, including chemistry, toxicology, and physical/mechanical testing can be found in the Summary Basis for Decision (SBD) document on Health Canada's website at **www.canada.ca/en/health-canada.html**

Allergan's Clinical Studies

Overview of Allergan's Core Clinical Study (TruForm® 1 Implants)

The Core Study was a 10-year study to assess safety and effectiveness in augmentation, reconstruction, and revision (revision-augmentation and revision-reconstruction) patients implanted with TruForm® 1 breast implants. *NATRELLE*® INSPIRA® implants were not included in the study. Patient follow-up was at 0-4 weeks, 6 months, 12 months, 24 months, and annually through 10 years. Safety was assessed by complications, such as implant rupture, capsular contracture, and reoperation. Benefit (effectiveness) was assessed by breast size change, patient satisfaction, and measures of body image/esteem and self-esteem.

The Core Study consisted of 715 patients. This included 455 augmentation patients, 147 revision-augmentation patients, 98 reconstruction patients, and 15 revision-reconstruction patients. The study is complete, and the final results through 10 years are reported in this brochure.

AUGMENTATION AND REVISION-AUGMENTATION PATIENTS

Described below are the benefits and complications reported in the Allergan Core Study for augmentation and revision-augmentation patients.

Allergan's results indicate that the risk of any complication at some point through 10 years after implant surgery was 32.9% for primary augmentation patients and 38.6% for revision-augmentation patients. However, the majority of women were satisfied with their implants. The results also indicate that the chance of additional surgery (reoperation) through the first 10 years was more than 1 in 3 for primary augmentation patients (with implant removal with replacement as the most common type of additional surgery), and about 1 in 2 for revision-augmentation patients (with the most common type of additional surgery being implant removal with replacement). The information below provides more details about the complications and benefits of TruForm® 1 breast implants.

Patient Accounting (Follow-Up Rates)

The Core Study enrolled 455 augmentation patients. Of the women expected to be seen at the 10-year follow-up visit, 67% were seen.

The Core Study enrolled 147 revision-augmentation patients. Of the women expected to be seen at the 10-year follow-up visit, 62% were seen.

Effectiveness Outcomes

The benefits of TruForm® 1 breast implants were assessed by a variety of outcomes, including bra cup size change and assessments of patient satisfaction, body image, body esteem, and self concept. Data were collected before implantation and at scheduled follow-up visits.

Primary Augmentation Patients:

For primary augmentation patients, 396 of the original 455 patients had a breast measurement within 18 months of surgery. Of these 396 patients, 41% increased by 1 cup size; 45% increased by 2 cup sizes; 8% increased by more than 2 cup sizes; and 5% had no increase or decrease.

Allergan patient satisfaction was based on a 5-point scale assessment of satisfaction with their implants at the time of the follow-up visits. Of the original 455 patients, 279 (61%) provided a satisfaction rating at 10 years after implantation, with 94% of these patients indicating that they were satisfied with their breast implants.

Quality of life assessments were made at 1, 2, 4, 6, 8, and 10 years post-implantation. For primary augmentation patients, the SF-36, which measures mental and physical health, showed a slight improvement in one scale and a slight worsening in some of the other scales after 10 years compared to before breast implantation, although all scales remained higher than the general U.S. female population. For patient responses to questions regarding overall self-concept/self-esteem, there was a decrease in self-concept on the Tennessee Self Concept Scale and no change in overall self-esteem on the Rosenberg Self Esteem Scale 10 years after receiving implants. Patient responses to questions on the Body Esteem Scale showed decreases regarding overall body image, weight concern, and physical condition, and an increase with regard to sexual attractiveness. On the Rowland Expectation Scale, patients showed significant improvement in self-image, social relations, and daily living. Breast satisfaction was significantly increased after 10 years, including satisfaction with breast size, shape, feel, and how well they matched.

Revision-Augmentation Patients:

Revision-augmentation patients did not undergo a measurement of bra cup size change because they were undergoing replacement of an existing breast implant.

Patient satisfaction was based on a 5-point scale assessment of satisfaction with their implants at the time of the follow-up visits. Of the original 147 revision-augmentation patients, 74 (50%) provided a satisfaction rating at 10 years. Of these 74 patients, 73% indicated that they were satisfied with their breast implants.

For revision-augmentation patients, the SF-36, which measures mental and physical health, showed no significant changes in all but one of these scales after 10 years. Patient responses to questions on the Tennessee Self Concept Scale and Rosenberg Self Esteem Scale regarding overall self-concept/self-esteem showed no changes 10 years after receiving implants. Patient responses to questions on the Body Esteem Scale regarding overall body image showed no changes, but a decrease with regard to physical condition was shown. On the Rowland Expectation Scale, patients showed significant improvement in self-image, social relations, and daily living. Breast satisfaction was significantly increased after 10 years, including satisfaction with breast size, shape, feel, and how well they matched.

Safety Outcomes

Table 1 describes the complications experienced by primary augmentation and revision-augmentation patients in the Core Study.

Table 1
Core Study: Complications
10-Year Cumulative First Occurrence Kaplan-Meier Risk Rates, By Patient

Complication*	Primary Augmentation N = 455 Rate (%) (95% CI)	Revision-Augmentation N = 147 Rate (%) (95% CI)
Reoperation	36.1% (31.6%, 40.9%)	46.0% (38.0%, 54.9%)
Capsular Contracture Baker Grade III/IV	18.9% (15.4%, 23.1%)	28.7% (21.3%, 37.9%)
Implant Removal with Replacement	18.6% (15.0%, 22.8%)	30.1% (22.8%, 39.0%)
Breast Pain	11.5% (8.7%, 15.0%)	11.7% (7.1%, 18.8%)
Swelling	9.2% (6.8%, 12.4%)	8.2% (4.6%, 14.5%)
Implant Rupture (MRI cohort)	9.3% (5.3%, 15.8%)	5.4% (1.4%, 20.0%)
Implant Malposition	6.9% (4.8%, 9.7%)	6.0% (3.1%, 11.7%)
Nipple Complications	6.3% (4.3%, 9.1%)	1.4% (0.3%, 5.4%)
Scarring/Hypertrophic Scarring	4.2% (2.6%, 6.5%)	6.6% (3.5%, 12.3%)
Asymmetry	3.3% (2.0%, 5.6%)	6.5% (3.2%, 12.8%)
Implant Removal without Replacement	2.8% (1.6%, 5.0%)	4.0% (1.7%, 9.4%)
Ptosis	2.0% (1.0%, 3.9%)	4.9% (2.2%, 10.5%)
Seroma/Fluid Accumulation	1.8% (0.9%, 3.5%)	6.0% (3.0%, 11.7%)
Wrinkling/Rippling	1.8% (0.8%, 3.7%)	5.4% (2.6%, 11.0%)
Breast/Skin Sensation Changes	1.6% (0.8%, 3.3%)	2.2% (0.7%, 6.6%)
Hematoma	1.6% (0.7%, 3.2%)	2.1% (0.7%, 6.3%)
Implant Palpability/Visibility	1.6% (0.8%, 3.4%)	6.0% (3.0%, 11.6%)
Delayed Wound Healing	1.1% (0.5%, 2.7%)	<1%
Bruising	<1%	3.0% (1.1%, 7.8%)
Infection	<1%	1.4% (0.3%, 5.4%)
Capsule Calcification, Gel Migration, Implant Extrusion, Irritation, Lymphadenopathy, Lymphedema, Other Complications, Pneumothorax, Redness, Skin Rash, Tissue/Skin Necrosis	0% - <1%	0% - <1%

* Most events were assessed with severity ratings, and the rates shown in the table include only complications rated moderate, severe or very severe (excludes mild and very mild ratings). All occurrences of reoperation, implant removal, implant rupture, implant extrusion and pneumothorax are included.

Reasons for Reoperation

Table 2 provides the main reason for each reoperation performed through 10 years in primary augmentation and revision-augmentation patients.

Table 2
Core Study: Main Reason for Reoperation through 10 Years

Reason for Reoperation	Primary Augmentation n (% of 221 reoperations)	Revision-Augmentation n (% of 108 reoperations)
Capsular Contracture	55 (24.9%)	26 (24.1%)
Suspected Rupture	29 (13.1%)	7 (6.5%)
Need for Biopsy	28 (12.7%)	9 (8.3%)
Implant Malposition	27 (12.2%)	12 (11.1%)
Ptosis	25 (11.3%)	9 (8.3%)
Hematoma/Seroma	13 (5.9%)	13 (12.0%)
Patient Request for Style/Size Change	12 (5.4%)	3 (2.8%)
Scarring/Hypertrophic Scarring	8 (3.6%)	7 (6.5%)
Asymmetry	5 (2.3%)	3 (2.8%)
Breast Cancer Mass	4 (1.8%)	3 (2.8%)
Breast Pain	3 (1.4%)	1 (0.9%)
Delayed Wound Healing	3 (1.4%)	2 (1.9%)
Wrinkling/Rippling	3 (1.4%)	2 (1.9%)
Infection	2 (0.9%)	3 (2.8%)
Implant Palpability/Visibility	1 (0.5%)	1 (0.9%)
Implant Extrusion	1 (0.5%)	1 (0.9%)
Necrosis	1 (0.5%)	0
Nipple Complications	1 (0.5%)	3 (2.8%)
Breast Tissue Contour Deformity, Device Injury, Other	0	1 each (0.9%)
Total	221 (100%)	108 (100%)

Reasons for Implant Removal

The main reasons for implant removal among primary augmentation and revision-augmentation patients over the 10 years are shown in Table 3.

Table 3
Core Study: Main Reason for Implant Removal through 10 Years

Reason for Removal	Primary Augmentation n (% of 156 Explants)	Revision-Augmentation n (% of 78 Explants)
Capsular Contracture	50 (32.1%)	28 (35.9%)
Patient Request for Style/Size Change	31 (19.9%)	11 (14.1%)
Suspected Rupture	27 (17.3%)	6 (7.7%)
Ptosis	12 (7.7%)	6 (7.7%)
Implant Malposition	11 (7.1%)	14 (18.0%)
Asymmetry	7 (4.5%)	1 (1.3%)
Wrinkling/Rippling	6 (3.9%)	2 (2.6%)
Breast Pain	5 (3.2%)	1 (1.3%)
Breast Cancer Mass	2 (1.3%)	2 (2.6%)
Infection	2 (1.3%)	2 (2.6%)
Breast Tissue Contour Deformity, Implant Extrusion, Need for Biopsy	1 each (0.6%)	0
Scarring/Hypertrophic Scarring, Other	0	2 each (2.6%)
Implant Palpability/Visibility	0	1 (1.3%)
Total	156 (100%)	78 (100%)

Other Events

Through 10 years, events other than the complications described in the previous tables were collected in the Core Study for augmentation and revision-augmentation patients. Some of these events, such as breast cancer and CTD, can occur in non-implanted patients. Therefore, without a comparison group of women with similar characteristics (such as age, race, etc.) and without breast implants, no conclusions can be made about the relationship between breast implants and some of these other events.

Benign breast disease occurred in 18% of primary augmentation and in 20% of revision-augmentation patients. Malignant breast disease occurred in 1% of primary and 1% of revision-augmentation patients. CTD events occurred in 1% of primary and 1% of revision-augmentation patients.

RECONSTRUCTION AND REVISION-RECONSTRUCTION PATIENTS

Described below are the benefits and complications reported in the Core Study for reconstruction and revision-reconstruction patients.

Allergan's results indicate that the risk of any complication at some point through 10 years after implant surgery is 47% for primary reconstruction patients and 47% for revision-reconstruction patients. However, the majority of women were satisfied with their implants. The results also indicate that the chance of additional surgery (reoperation) through the first 10 years is about 3 in 4 for primary reconstruction patients (with implant removal and replacement as the most common type of additional surgery), and 1 in 2 for revision-reconstruction patients (with nipple reconstruction/tattoo as the most common type of additional surgery). The information below provides more details about the complications and benefits of TruForm® 1 breast implants.

Patient Accounting (Follow-Up Rates)

The Core Study enrolled 98 reconstruction patients. Of the women expected to be seen at the 10-year follow-up visit, 73% were seen.

The Core Study enrolled 15 revision-reconstruction patients. Of the women expected to be seen at the 10-year follow-up visit, 73% were seen.

Effectiveness Outcomes

The benefits of TruForm® 1 breast implants were assessed by a variety of outcomes, including assessments of patient satisfaction, body image, body esteem, and self-concept. Data were collected before implantation and at scheduled follow-up visits.

Primary Reconstruction Patients:

Patient satisfaction was based on a 5-point scale assessment of satisfaction with their implants at the time of the follow-up visits. Of the original 98 patients, 43 (44%) provided a satisfaction rating at 10 years after implantation, with 90% of these patients indicating that they were satisfied with their breast implants.

Quality of life assessments were made at 1, 2, 4, 6, 8, and 10 years post-implantation. For primary reconstruction patients, the SF-36, which measures mental and physical health, showed no changes after 10 years compared to before breast implantation. For patient responses to questions regarding overall self-concept/self-esteem, there was no change in self-concept on the Tennessee Self Concept Scale and no change in overall self-esteem on the Rosenberg Self Esteem Scale 10 years after receiving implants. Patient responses to questions on the Body Esteem Scale regarding overall self-esteem related specifically to one's body also did not show a change 10 years after receiving implants. On the Rowland Expectation Scale, patients showed significant improvement in self-image, social relations, and well being. Breast satisfaction was significantly increased after 10 years, including satisfaction with breast size, shape, feel, and how well they matched.

Revision-Reconstruction Patients:

Patient satisfaction was based on a 5-point scale assessment of satisfaction with their implants at the time of the follow-up visits. Of the original 15 revision-reconstruction patients, 8 (53%) provided a satisfaction rating at 10 years. Of these 8 patients, 88% indicated that they were satisfied with their breast implants.

For revision-reconstruction patients, responses were similar pre- and post-implantation on the SF-36, Tennessee Self Concept Scale, Rosenberg Self Esteem Scale and Body Esteem Scale. On the Rowland Expectation Scale, patients showed significant improvement in self-image, social relations, and daily living. Breast satisfaction was significantly increased after 10 years, including satisfaction with breast size, shape, feel, and how well they matched.

Safety Outcomes

Table 4 describes the complications experienced by primary reconstruction and revision-reconstruction patients in the Core Study.

Table 4
Core Study: Complications
10-Year Cumulative First Occurrence Kaplan-Meier Risk Rates, By Patient

Complication*	Primary Reconstruction N = 98 Rate (%) (95% CI)	Revision-Reconstruction N = 15 Rate (%)** (95% CI)
Reoperation	71.5% (61.2%, 81.0%)	46.7% (21.3%, 73.4%)
Implant Removal with Replacement	48.0% (37.1%, 60.1%)	13.3% (1.7%, 40.5%)
Implant Rupture (MRI cohort)	35.4% (22.1%, 53.6%)	0% ***
Capsular Contracture Baker Grade III/IV	24.6% (16.2%, 36.2%)	6.7% (0.2%, 31.9%)
Asymmetry	23.2% (15.4%, 33.9%)	6.7% (0.2%, 31.9%)
Implant Removal without Replacement	13.6% (7.1%, 24.9%)	6.7% (0.2%, 31.9%)
Wrinkling/Rippling	10.2% (5.2%, 19.6%)	0%
Swelling	7.1% (3.5%, 14.4%)	0%
Breast Pain	6.8% (2.8%, 16.1%)	0%
Implant Palpability/Visibility	6.4% (2.3%, 16.8%)	6.7% (0.2%, 31.9%)
Scarring/Hypertrophic Scarring	5.5% (2.3%, 12.7%)	0%
Nipple Complications	3.3% (1.1%, 9.8%)	0%
Infection	3.2% (1.0%, 9.5%)	0%
Implant Malposition	2.3% (0.6%, 8.9%)	13.3% (1.7%, 40.5%)
Seroma/Fluid Accumulation	2.3% (0.3%, 15.4%)	6.7% (0.2%, 31.9%)
Tissue/Skin Necrosis	2.3% (0.6%, 8.8%)	0%
Redness	2.1% (0.5%, 8.3%)	0%
Skin Rash	2.0% (0.5%, 7.9%)	6.7% (0.2%, 31.9%)
Hematoma	1.5% (0.2%, 10.4%)	0%
Bruising	1.0% (0.1%, 7.1%)	6.7% (0.2%, 31.9%)
Breast/Skin Sensation Changes, Delayed Wound Healing, Implant Extrusion, Other Complications	1.0% each (0.1%, 7.2%)	0%
Capsule Calcification, Gel Migration, Irritation, Lymphadenopathy, Lymphedema, Pneumothorax, Ptosis	0% NA	0%

* Most events were assessed with severity ratings, and the rates shown in the table include only complications rated moderate, severe or very severe (excludes mild and very mild ratings). All occurrences of reoperation, implant removal, implant rupture, implant extrusion and pneumothorax are included.
** Calculated as a percentage of enrolled with binomial confidence interval.
*** No ruptures were reported in the MRI cohort (n=5); 1 rupture was reported in the non-MRI cohort (n=10) .

Reasons for Reoperation

Table 5 provides the main reason for each reoperation performed through 10 years in primary reconstruction and revision-reconstruction patients.

Table 5
Core Study: Main Reason for Reoperation through 10 Years

Reason for Reoperation	Primary Reconstruction n (% of 94 reoperations)	Revision-Reconstruction n (% of 12 reoperations)
Implant Malposition	16 (17.0%)	0
Asymmetry	15 (16.0%)	2 (16.7%)
Suspected Rupture	14 (14.9%)	0
Capsular Contracture	12 (12.8%)	2 (16.7%)
Hematoma/Seroma	8 (8.5%)	0
Need for Biopsy	8 (8.5%)	1 (8.3%)
Ptosis	4 (4.3%)	1 (8.3%)
Breast Cancer Mass	3 (3.2%)	0
Patient Request for Style/Size Change	3 (3.2%)	0
Scarring/Hypertrophic Scarring	3 (3.2%)	1 (8.3%)
Breast Tissue Contour Deformity, Implant Extrusion	2 each (2.1%)	0
Nipple Complications	1 (1.1%)	5 (41.7%)
Delayed Wound Healing, Necrosis, Wrinkling/Rippling	1 each (1.1%)	0
Total	94 (100%)	12 (100%)

Reasons for Implant Removal

The main reasons for implant removal among primary reconstruction and revision-reconstruction patients over the 10 years are shown in Table 6.

Table 6
Core Study: Main Reason for Implant Removal through 10 Years

Reason for Removal	Primary Reconstruction n (% of 57 explants)	Revision-Reconstruction n (% of 3 explants)
Suspected Rupture	15 (26.3%)	0
Implant Malposition	12 (21.1%)	0
Asymmetry	12 (21.1%)	2 (66.7%)
Capsular Contracture	10 (17.5%)	1 (33.3%)
Patient Request for Style/Size Change	4 (7.0%)	0
Hematoma/Seroma, Implant Extrusion, Necrosis, Wrinkling/Rippling	1 each (1.8%)	0
Total	57 (100%)	3 (100%)

Other Events

Through 10 years, events other than the complications described in the previous tables were collected in the Core Study for reconstruction and revision-reconstruction patients. Some of these events, such as breast cancer and CTD, can occur in non-implanted patients. Therefore, without a comparison group of women with similar characteristics (such as age, race, etc.) and without breast implants, no conclusions can be made about the relationship between breast implants and some of these other events.

Benign breast disease occurred in 17% of primary reconstruction patients and in 7% of revision-reconstruction patients. Malignant breast cancer was detected in 18% of primary reconstruction patients, with none detected in revision-reconstruction patients. A 2% CTD rate (rheumatoid arthritis and undifferentiated CTD) occurred in primary reconstruction patients, with no CTDs detected in revision-reconstruction patients.

OVERVIEW OF ALLERGAN'S PIVOTAL STUDY (TRUFORM® 3 IMPLANTS)

The pivotal study was a 10-year study to assess safety and effectiveness in augmentation, reconstruction, and revision (revision-augmentation and revision-reconstruction) patients implanted with TruForm® 3 implants. Patient follow-up was at 0-4 weeks, 6 months, 12 months, and annually through 10 years. Safety was assessed by complications, such as implant rupture, capsular contracture, and reoperation. Benefit (effectiveness) was assessed by breast size change, patient satisfaction and measures of body image/esteem and self-esteem.

The pivotal study consisted of 941 patients. This included 492 augmentation patients, 156 revision-augmentation patients, 225 reconstruction patients, and 68 revision-reconstruction patients. The study is complete, with the final results through 10 years reported in this brochure.

AUGMENTATION AND REVISION-AUGMENTATION PATIENTS

Described below are the benefits and complications reported in the pivotal study for augmentation and revision-augmentation patients.

Allergan's results indicate that the risk of any complication at some point through 10 years after implant surgery is 39% for primary augmentation patients and 57% for revision-augmentation patients. However, the majority of women were satisfied with their implants. The results also indicate that the chance of additional surgery (reoperation) through the first 10 years is approximately 1 in 3 for primary augmentation patients (with implant removal and replacement as the most common type of additional surgery), and almost 1 in 2 for revision-augmentation patients (with implant removal and replacement as the most common type of additional surgery). The information below provides more details about the complications and benefits of TruForm® 3 implants.

Patient Accounting (Follow-Up Rates)

The pivotal study enrolled 492 augmentation patients. Of the women expected to be seen at the 10-year follow-up visit, 66% were seen.

The pivotal study enrolled 156 revision-augmentation patients. Of the women expected to be seen at the 10-year follow-up visit, 55% were seen.

Effectiveness Outcomes

The benefits of TruForm® 3 breast implants were assessed by a variety of outcomes, including bra cup size change and assessments of patient satisfaction, body image, body esteem, and self-concept. Data were collected before implantation and at scheduled follow-up visits for those patients who still had their original implants and who came back for these visits. Quality of life data were collected through the first 2 years after implantation.

Primary Augmentation Patients:

Of the 469 patients with both a valid pre- and post-implant bra size, the majority of patients increased the size of their breasts by either 1 cup size (38%) or 2 cup sizes (53%). The remaining patients increased by more than 2 cup sizes (6%) or maintained the same cup size (3%).

Patient satisfaction was based on a 5-point scale assessment of satisfaction with their implants at the time of the follow-up visits. Of the original 492 patients, 292 (59%) provided a satisfaction rating at 10 years after implantation, with 96% of these patients indicating that they were satisfied with their breast implants.

For primary augmentation patients, the SF-36, which measures mental and physical health, showed no significant changes after 2 years compared to before breast implantation, and all scales remained higher than the general U.S. female population. For patient responses to questions regarding overall self-concept/self-esteem, there was no change in self-concept on the Tennessee Self Concept Scale and no change in overall self-esteem on the Rosenberg Self Esteem Scale 2 years after receiving implants. Patient responses to questions on the Body Esteem Scale regarding overall body image did not show a change 2 years after receiving implants, but body esteem related to sexual attractiveness did show an increase. On the Rowland Expectation Scale patients showed significant improvement in self-image, social relations, and daily living. Breast satisfaction was significantly increased after 2 years, including satisfaction with breast size, shape, feel, and how well they matched.

Revision-Augmentation Patients:

Patient satisfaction was based on a 5-point assessment of satisfaction with their implants at the time of the follow-up visits. Of the original 156 revision-augmentation patients, 72 (46%) provided a satisfaction rating at 10 years. Of these 72 patients, 87% indicated that they were satisfied with their breast implants.

Effectiveness measures such as the SF-36 assess the effect of implantation on quality of life, which is not feasible for revision-augmentation patients with pre-existing implants prior to enrollment in the study. Therefore, these assessments were not performed for revision-augmentation patients.

Safety Outcomes

Table 7 describes the complications experienced by primary augmentation and revision-augmentation patients in the pivotal study.

Table 7
Pivotal Study: Complications
10-Year Cumulative First Occurrence Kaplan-Meier Risk Rates, By Patient

Complication*	Primary Augmentation N = 492 Rate (%) (95% CI)	Revision-Augmentation N = 156 Rate (%) (95% CI)
Reoperation	29.7% (25.6%, 34.3%)	47.3% (39.2%, 56.0%)
Implant Rupture (MRI Cohort)	17.7% (11.7%, 26.4%)	14.7% (5.4%, 36.4%)
Implant Removal with Replacement	16.8% (13.6%, 20.8%)	27.8% (21.0%, 36.2%)
Capsular Contracture Baker Grade III/IV	9.2% (6.7%, 12.6%)	11.9% (7.2%, 19.3%)
Implant Malposition	4.7% (3.1%, 7.3%)	9.1% (5.2%, 15.6%)
Breast Pain	4.5% (2.8%, 7.1%)	5.2% (2.3%, 11.5%)
Swelling	4.0% (2.5%, 6.3%)	2.7% (1.0%, 7.1%)
Implant Removal without Replacement	3.3% (1.9%, 5.7%)	5.9% (2.8%, 12.2%)
Ptosis	1.9% (0.9%, 3.7%)	0%
Infection	1.7% (0.8%, 3.3%)	2.1% (0.7%, 6.3%)
Other Complications	1.6% (0.8%, 3.3%)	3.5% (1.3%, 9.2%)
Seroma/Fluid Accumulation	1.6% (0.8%, 3.3%)	3.2% (1.2%, 8.4%)
Breast/Skin Sensation Changes	1.5% (0.7%, 3.1%)	0%
Scarring/Hypertrophic Scarring	1.4% (0.6%, 3.0%)	3.7% (1.5%, 8.8%)
Hematoma	1.3% (0.6%, 2.9%)	2.0% (0.6%, 6.0%)
Nipple Complications	1.3% (0.6%, 2.8%)	0%
Asymmetry	1.2% (0.5%, 2.9%)	6.9% (3.6%, 13.1%)
Delayed Wound Healing	1.1% (0.4%, 2.5%)	1.3% (0.3%, 5.1%)
Bruising	<1%	<1%
Gel Fracture	<1%	<1%
Implant Extrusion	<1%	1.5% (0.4%, 5.8%)

Complication*	Primary Augmentation N = 492 Rate (%) (95% CI)	Revision-Augmentation N = 156 Rate (%) (95% CI)
Implant Palpability/Visibility	<1%	1.4% (0.3%, 5.4%)
Redness, Skin Rash	<1%	0%
Wrinkling/Rippling	<1%	3.7% (1.5%, 8.6%)
Upper Pole Fullness	0%	<1%
Capsule Calcification, Irritation, Lymphadenopathy, Lymphedema, Palpable Orientation Mark, Pneumothorax, Tissue/Skin Necrosis	0%	0%

* Most events were assessed with severity ratings, and the rates shown in the table include only complications rated moderate, severe or very severe (excludes mild and very mild ratings). All occurrences of reoperation, implant removal, implant rupture, implant extrusion, and pneumothorax are included.

Reasons for Reoperation

Table 8 provides the main reason for each reoperation performed through 10 years in primary augmentation and revision-augmentation patients.

Table 8
Pivotal Study: Main Reason for Reoperation through 10 Years

Reason for Reoperation	Primary Augmentation n (% of 167 Reoperations)	Revision-Augmentation N (% of 83 Reoperations)
Patient Request for Style/Size Change	22 (13.2%)	7 (8.4%)
Capsular Contracture	19 (11.4%)	12 (14.5%)
Suspected Rupture	19 (11.4%)	10 (12.0%)
Implant Malposition	17 (10.2%)	12 (14.5%)
Scarring/Hypertrophic Scarring	15 (9.0%)	7 (8.4%)
Need for Biopsy	14 (8.4%)	11 (13.3%)
Ptosis	13 (7.8%)	7 (8.4%)
Hematoma/Seroma	12 (7.2%)	3 (3.6%)
Breast Cancer Mass	8 (4.8%)	0
Other	7 (4.2%)	0
Asymmetry	5 (3.0%)	4 (4.8%)
Infection	4 (2.4%)	4 (4.8%)
Delayed Wound Healing	4 (2.4%)	1 (1.2%)
Breast Pain	2 (1.2%)	3 (3.6%)
Breast Tissue Contour Deformity	2 (1.2%)	0
Gel Fracture	1 (0.6%)	0
Implant Extrusion	1 (0.6%)	1 (1.2%)
Nipple Complications, Wrinkling/Rippling	1 each (0.6%)	0 each
Implant Palpability/Visibility	0	1 (1.2%)
Total	167 (100%)	83 (100%)

Reasons for Implant Removal

The main reasons for implant removal among primary augmentation and revision-augmentation patients over the 10 years are shown in Table 9.

Table 9
Pivotal Study: Main Reason for Implant Removal through 10 Years

Reason for Removal	Primary Augmentation n (% of 153 Explants)	Revision-Augmentation n (% of 78 Explants)
Patient Request for Style/Size Change	52 (34.0%)	19 (24.4%)
Suspected Rupture	21 (13.7%)	13 (16.7%)
Ptosis	17 (11.1%)	4 (5.1%)
Capsular Contracture	15 (9.8%)	18 (23.1%)
Implant Malposition	7 (4.6%)	7 (9.0%)
Asymmetry	7 (4.6%)	5 (6.4%)
Unknown	7 (4.6%)	1 (1.3%)
Other	6 (3.9%)	0
Hematoma/Seroma	4 (2.6%)	0
Breast Tissue Contour Deformity	4 (2.6%)	0
Infection	3 (2.0%)	4 (5.1%)
Breast Pain	3 (2.0%)	3 (3.9%)
Breast Cancer Mass	3 (2.0%)	0
Gel Fracture	1 (0.7%)	0
Implant Extrusion	1 (0.7%)	1 (1.3%)
Need for Biopsy, Wrinkling/Rippling	1 each (0.7%)	0
Implant Palpability/Visibility	0	2 (2.6%)
Scarring/Hypertrophic Scarring	0	1 (1.3%)
Delayed Wound Healing	0	0
Total	153 (100%)	78 (100%)

Other Events

Through 10 years, events other than the complications described in the previous tables were collected in the pivotal study for augmentation and revision-augmentation patients. Some of these events, such as breast cancer and CTD, can occur in non-implanted patients. Therefore, without a comparison group of women with similar characteristics (such as age, race, etc.) and without breast implants, no conclusions can be made about the relationship between breast implants and some of these other events.

Benign breast disease occurred in 5.3% of primary augmentation patients and in 9.7% of revision-augmentation patients. Malignant breast disease occurred in 2.4% and 0.8% of primary augmentation and revision-augmentation patients, respectively. A CTD rate of 0.6% occurred in primary augmentation patients (sclerosis/scleroderma, Graves disease, and positive ANA-specific diagnosis). A 2% CTD rate (fibromyalgia in two patients and Hashimoto thyroiditis in one patient) occurred in revision-augmentation patients.

RECONSTRUCTION AND REVISION-RECONSTRUCTION PATIENTS

Described below are the benefits and complications reported in the pivotal study for reconstruction and revision-reconstruction patients.

Allergan's results indicate that the risk of any complication at some point through 10 years after implant surgery is 65% for primary reconstruction patients and 71% for revision-reconstruction patients. However, the majority of women were satisfied with their implants. The results also indicate that the chance of additional surgery (reoperation) through the first 10 years is slightly more than 1 in 2 for primary reconstruction patients (with implant removal and replacement as the most common type of additional surgery), and 1 in 2 for revision-reconstruction patients (with implant removal and replacement as the most common type of additional surgery). The information below provides more details about the complications and benefits of TruForm® 3 breast implants.

Patient Accounting (Follow-Up Rates)

The pivotal study enrolled 225 reconstruction patients. Of the women expected to be seen at the 10-year follow-up visit, 81% were seen.

The pivotal study enrolled 68 revision-reconstruction patients. Of the women expected to be seen at the 10-year follow-up visit, 77% were seen.

Effectiveness Outcomes

The benefits of TruForm® 3 implants were assessed by a variety of outcomes, including assessments of patient satisfaction, body image, body esteem, and self-concept. Data were collected before implantation and at scheduled follow-up visits. Quality of life data were collected through the first 2 years after implantation.

Primary Reconstruction Patients:

Patient satisfaction was based on a 5-point scale assessment of satisfaction with their implants at the time of the follow-up visits. Of the original 225 patients, 134 (60%) provided a satisfaction rating at 10 years after implantation, with 93% of these patients indicating that they were satisfied with their breast implants.

For primary reconstruction patients, the SF-36, which measures mental and physical health, showed a slight worsening in one scale after 2 years compared to before breast implantation. For patient responses to questions regarding overall self-concept/self-esteem, there was no change in self-concept on the Tennessee Self Concept Scale and no change in overall self-esteem on the Rosenberg Self Esteem Scale 2 years after receiving implants. Patient responses to questions on the Body Esteem Scale regarding overall body image also did not show a change 2 years after receiving implants. On the Rowland Expectation Scale patients showed significant improvement in well-being. Breast satisfaction was increased after 2 years, including satisfaction with breast size, shape, feel, and how well they matched.

Revision-Reconstruction Patients:

Patient satisfaction was based on a 5-point scale assessment of satisfaction with their implants at the time of the follow-up visits. Of the original 68 revision-reconstruction patients, 40 (59%) provided a satisfaction rating at 10 years. Of these 40 patients, 90% indicated that they were satisfied with their breast implants.

Effectiveness measures such as the SF-36 assess the effect of implantation on quality of life which is not feasible for revision-reconstruction patients who have pre-existing implants prior to enrollment in the study. Therefore, these assessments were not performed for revision-reconstruction patients.

Safety Outcomes

Table 10 describes the complications experienced by primary reconstruction and revision-reconstruction patients in the pivotal study.

Table 10
Pivotal Study: Complications
10-Year Cumulative First Occurrence Kaplan-Meier Risk Rates, By Patient

Complication*	Primary Reconstruction N = 225 Rate (%)(95% CI)	Revision-Reconstruction N = 68 Rate (%)(95% CI)
Reoperation	54.6% (47.9%, 61.6%)	48.5% (37.0%, 61.5%)
Implant Removal with Replacement	34.3% (28.0%, 41.6%)	39.3% (28.2%, 52.9%)
Capsular Contracture Baker Grade III/IV	14.5% (10.1%, 20.6%)	26.8% (16.8%, 41.1%)
Asymmetry	12.4% (8.4%, 18.1%)	17.4% (9.6%, 30.3%)
Implant Rupture (MRI Cohort)	12.4% (6.0%, 24.4%)	19.6% (7.8%, 44.4%)
Breast Pain	8.2% (4.9%, 13.7%)	7.8% (2.9%, 20.4%)
Implant Removal without Replacement	6.7% (3.8%, 11.7%)	4.9% (1.2%, 18.7%)
Wrinkling/Rippling	6.2% (3.3%, 11.4%)	12.8% (6.1%, 25.6%)
Infection	6.1% (3.5%, 10.7%)	8.5% (3.6%, 19.5%)
Other Complications	6.0% (3.3%, 10.7%)	3.6% (0.9%, 13.8%)
Implant Malposition	5.7% (3.1%, 10.5%)	8.0% (3.0%, 20.5%)
Swelling	5.3% (2.8%, 9.7%)	3.2% (0.8%, 12.4%)
Hypertrophic/Other Abnormal Scarring	4.8% (2.6%, 8.7%)	3.2% (0.8%, 12.3%)
Upper Pole Fullness	4.2% (2.2%, 7.8%)	1.5% (0.2%, 10.1%)
Seroma/Fluid Accumulation	2.8% (1.1%, 6.6%)	6.2% (2.4%, 15.8%)
Implant Palpability/Visibility	1.2% (0.3%, 4.7%)	4.2% (1.0%, 16.5%)
Hematoma	1.0% (0.3%, 4.0%)	0%
Delayed Wound Healing	<1%	2.9% (0.7%, 11.3%)
Nipple Complications	<1%	1.7% (0.2%, 11.2%)
Redness	<1%	4.9% (1.6%, 14.7%)
Implant Extrusion, Capsule Calcification, Skin Rash	<1%	0%

Complication*	Primary Reconstruction N = 225 Rate (%)(95% CI)	Revision-Reconstruction N = 68 Rate (%)(95% CI)
Tissue/Skin Necrosis	<1%	1.5% (0.2%, 10.0%)
Bruising	0%	1.5% (0.2%, 10.0%)
Breast/Skin Sensation Changes, Gel Fracture, Irritation, Lymphadenopathy, Lymphedema, Palpable Orientation Mark, Pneumothorax, Ptosis	0%	0%

* Most events were assessed with severity ratings, and the rates shown in the table include only complications rated moderate, severe or very severe (excludes mild and very mild ratings). All occurrences of reoperation, implant removal, implant rupture, implant extrusion, and pneumothorax are included.

Reasons for Reoperation

Table 11 provides the main reason for each reoperation performed through 10 years in primary reconstruction and revision-reconstruction patients.

Table 11
Pivotal Study: Main Reason for Reoperation through 10 Years

Reason for Reoperation	Primary Reconstruction n (% of 163 Reoperations)	Revision-Reconstruction n (% of 40 Reoperations)
Scarring/Hypertrophic Scarring	31 (19.0%)	1 (2.5%)
Capsular Contracture	20 (12.3%)	9 (22.5%)
Implant Malposition	20 (12.3%)	4 (10.0%)
Suspected Rupture	16 (9.8%)	3 (7.5%)
Asymmetry	13 (8.0%)	2 (5.0%)
Need for Biopsy	12 (7.4%)	2 (5.0%)
Patient Request for Style/Size Change	12 (7.4%)	4 (10.0%)
Infection	9 (5.5%)	3 (7.5%)
Ptosis	6 (3.7%)	0
Breast Tissue Contour Deformity	5 (3.1%)	1 (2.5%)
Breast Pain	4 (2.5%)	0
Breast Cancer Mass	4 (2.5%)	0
Hematoma/Seroma	3 (1.8%)	1 (2.5%)
Wrinkling/Rippling	3 (1.8%)	3 (7.5%)
Implant Extrusion	2 (1.2%)	0
Other	2 (1.2%)	2 (5.0%)
Necrosis	1 (0.6%)	0
Delayed Wound Healing	0	3 (7.5%)
Nipple Complications	0	2 (5.0%)
Total	163 (100%)	40 (100%)

Reasons for Implant Removal

The main reasons for implant removal among primary reconstruction and revision-reconstruction patients in the pivotal study over the 10 years are shown in Table 12.

Table 12
Pivotal Study: Main Reason for Implant Removal through 10 Years

Reason for Removal	Primary Reconstruction % (of 115 Explants)	Revision-Reconstruction % (of 40 Explants)
Patient Request for Style/Size Change	24 (20.9%)	8 (20.0%)
Capsular Contracture	18 (15.7%)	10 (25.0%)
Suspected Rupture	17 (14.8%)	3 (7.5%)
Implant Malposition	13 (11.3%)	3 (7.5%)
Asymmetry	13 (11.3%)	1 (2.5%)
Infection	6 (5.2%)	3 (7.5%)
Wrinkling/Rippling	6 (5.2%)	6 (15.0%)
Breast Pain	4 (3.5%)	0
Other	3 (2.6%)	0
Breast Cancer Mass, Implant Extrusion, Hematoma/Seroma, Ptosis	2 each (1.7%)	0
Unknown	2 (1.7%)	4 (10.0%)
Breast Tissue Contour Deformity	1 (0.9%)	1 (2.5%)
Delayed Wound Healing	0	1 (2.5%)
Total	115 (100%)	40 (100%)

Other Events

Through 10 years, events other than the complications described in the previous tables were collected in the pivotal study for reconstruction and revision-reconstruction patients. Some of these events, such as breast cancer and CTD, can occur in non-implanted patients. Therefore, without a comparison group of women with similar characteristics (such as age, race, etc.) and without breast implants, no conclusions can be made about the relationship between breast implants and some of these other events.

There were 17 Reconstruction patients (7.6%) and no Revision-Reconstruction patients with recurrence of breast cancer through 10 years, respectively. CTD events after implantation were 1.5% or less.

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.

Surgical Planning

Allergan relies on the surgeon to know and follow the proper surgical procedures with *NATRELLE*® Gel-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 should be aware that the unique nature of the highly cohesive TruForm® 3 gel may require a larger incision compared to the incision size required for other silicone-filled implants to avoid skin edge trauma or implant deformation. Excessive force upon insertion of the implant may compromise the precisely defined shape of the device, potentially leading to an undesirable cosmetic outcome. The surgeon must carefully evaluate breast implant size and contour, incision placement, pocket dissection, and implant placement criteria with respect to the patient's anatomy and desired physical outcome.

The surgeon should be aware that more upper pole fullness may be maintained by the TruForm® 3 implant than with other breast implants. 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 disfiguring, reactions, bearing in mind the importance of pocket dissection in minimizing implant rotation for the shaped TruForm® 2 and TruForm® 3 implants.

Preliminary Product Examination

How to Open Sterile Product Package

Remove the sterile breast implant from its package in an aseptic environment and using talc-free gloved hands. DO NOT expose the breast implant to lint, talc, sponges, towels, skin oils, or other contaminants.

1. Peel open the lid of the outer thermoform package.
2. Invert the outer thermoform package over the sterile field, allowing the sealed inner thermoform package to gently fall into the field.
3. Peel open the lid of the inner thermoform package using the pull-tab.
4. Gently retrieve the breast implant. Prior to use, keep the breast implant in the inner thermoform package to prevent contact with airborne and surgical field particulate contaminants.

Examination of Silicone-Filled Breast Implants

Prior to use, examine the breast implant for evidence of any particulate contamination, damage, or loss of shell integrity. If satisfactory, return the breast implant to the inner thermoform tray and cover it with the lid until implanted to prevent contact with airborne contaminants.

DO NOT implant any device that may appear to have particulate contamination, damage, or loss of shell integrity. A sterile back-up implant must be readily available at the time of surgery.

DO NOT implant any device that may appear to have leaks or nicks.

DO NOT implant damaged or contaminated breast implants.

Sterile Product

Each sterile silicone-filled breast implant is supplied in a sealed, double primary package. 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 from its package 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 resterilize the product.

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

Method for Removing Ruptured Silicone Gel from the Surgical Pocket

In the event of breast implant rupture, the following technique is useful for removal of the silicone mass. Wearing double talc-free surgical gloves on one hand, use the index finger to penetrate the silicone mass. With the other hand, exert pressure on the breast to facilitate manipulation of the silicone mass into the double-gloved hand. Once the silicone is in hand, pull the outer glove over the silicone mass and remove. To remove any residual silicone, blot the surgical pocket with gauze sponges. Avoid contact between surgical instruments and the silicone. If contact occurs, use isopropyl alcohol to remove the silicone from the instruments. Ruptured breast implants must be reported and should be returned to Allergan. In the event of breast implant rupture, contact Allergan's Product Support Department at 1.800.624.4261.

Surgical Procedure Placement

Ensure incision is sufficiently large to facilitate insertion without excessive manipulation and handling of the device and to avoid damage to the device. Inadequate pocket dissection increases the risk of rupture and implant malposition.

Orientation Dots

TruForm® 2 and 3 breast implants have orientation marks that are circular silicone elastomer dots located on the surface of the implant. They are used to assist with visual and tactile placement of the implant within the surgical pocket. The posterior surface of most sizes of TruForm® 2 and 3 implants has 4 orientation marks; the posterior surface of some smaller and/or shorter styles may have only 3 orientation marks. The anterior surface of all TruForm® 2 and 3 implants has 2 orientation marks.

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

DO NOT use excessive force during breast implant placement.

DO NOT manipulate the implant for either radial expansion, compression or dissection of the pocket.

Breast augmentation with silicone-filled implants can be carried out through several different incisions including inframammary, periareolar, or transaxillary. 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 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 are available to cover the implant and that the implant be properly sized and positioned based upon careful preoperative planning.

Allergan Academy™ Educational Materials are available through **www.allerganacademy.com** or **www.allerganacademy.ca** to supplement surgical knowledge of the dimensional techniques intended for use with *NATRELLE®* breast implants.

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.

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:

- Bilingual ***Patient Planner for Breast Augmentation or Reconstruction with NATRELLE® Gel-Filled Breast Implants***
  This planner should be used to facilitate patient education on the risks and benefits of silicone gel-filled breast implant surgery. The entire planner should be given to the patient during her initial visit/consultation to allow sufficient time for review. You should verify that the patient has an adequate understanding of the information provided by evaluating the Patient Self Assessment and using this as a foundation for subsequent preoperative discussion.
- ***Device Identification Card***
  Enclosed with each silicone-filled breast implant is Allergan's Device Identification Card. To complete the 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 Plastic Surgery Sales Representative or through the Customer Care Department at 1.866.653.9308. 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®* Premier Warranty provides lifetime replacement and limited financial reimbursement in the event of shell leakage or breakage resulting in implant rupture, subject to certain conditions as fully discussed in the *ConfidencePlus®* Premier literature. Our standard *ConfidencePlus®* Premier Warranty program applies automatically to every *NATRELLE®* breast implant recipient subject to the conditions discussed in the *ConfidencePlus®* literature. For more information, please visit www.cppwarranty.ca or contact Allergan's Product Support Department at 1.800.624.4261.

Product Ordering

To order directly in Canada or for product information, please contact your local Allergan Plastic Surgery Sales Representative or the Allergan Customer Care Department at 1.866.653.9308.

LITERATURE REFERENCES

1. Alobeid, B., et al. 2009. Aggressive presentation of breast implant-associated ALK-1 negative anaplastic large cell lymphoma with bilateral axillary lymph node involvement. Leuk. Lymphoma 50(5):831-833.
2. Baker, J.L. Augmentation mammoplasty. In: Owsley, J.Q. and Peterson, R., Eds. Symposium on aesthetic surgery of the breast. St. Louis, MO: Mosby, 1978:256-263.
3. Bengston BP, et al. 2007. Style 410 Highly Cohesive Silicone Breast Implant Core Study results at 3 years. Plast Reconstr Surg. 120(1):40-48s.
4. Berner, I., M., et al. 2002. Comparative examination of complaints of patients with breast-cancer with and without silicone implants. Eur. J. Obstet. Gynecol. Reprod. Biol. 102(1):61-6.
5. Bishara, M.R., et al. 2009. Case report: Primary anaplastic large cell lymphoma of the breast arising in reconstruction mammoplasty capsule of saline filled breast implant after radical mastectomy for breast cancer: An unusual presentation. Diagn. Pathol. 4:11-16.
6. Bondurant, S., V.L. Ernster and R. Herdman, Eds. 2000. Safety of silicone breast implants. Committee on the Safety of Silicone Breast Implants, Division of Health Promotion and Disease Prevention, Institute of Medicine. Washington, D.C.: National Academy Press.
7. Breiting, V.B., et al. 2004. Long-term health status of Danish women with silicone breast implants. Plast. Reconstr. Surg. 114:217-26.
8. Brinton, L.A., et al. 2001a. Mortality among augmentation mammoplasty patients. Epidemiology. 12(3):321-6.
9. Brinton, L.A., et al. 2000. Breast cancer following augmentation mammoplasty (United States). Cancer Causes Control. 11(9):819-27.
10. Brinton, LA., et al. 2001b. Cancer risk at sites other than the breast following augmentation mammoplasty. Ann. Epidemiol. 11(4):248-56.
11. Brinton, L.A., et al. 2004. Risk of connective tissue disorders among breast implant patients. Am. J. Epidemiol. 160(7):619-27.
12. Brown, S.L., et al. 2001. Silicone gel breast implant rupture, extracapsular silicone, and health status in a population of women. J. Rheumatol. 28(5):996-1003.
13. Bryant, H., and Brasher, P. 1995. Breast implants and breast cancer--reanalysis of a linkage study. N. Engl. J. Med. 332(23):1535-9.
14. Cook, L.S. 1997. Characteristics of women with and without breast augmentation. JAMA. 277(20):1612-7.
15. Daneshbod, Y., et al. 2010. Primary ALK-positive anaplastic large cell lymphoma of the breast: A case report and review of the literature. J. Pediatr. Hematol. Oncol. 32:e75-e78.

16. Deapen, D.M., et al. 1997. Are breast implants anticarcinogenic? A 14-year follow-up of the Los Angeles Study. Plast. Reconstr. Surg. 99(5):1346-53.
17. Deapen, D., et al. 2000. Breast cancer stage at diagnosis and survival among patients with prior breast implants. Plast. Reconstr. Surg. 105(2):535-40.
18. Deapen, D.M., et al. 2007. Cancer risk among Los Angeles women with cosmetic breast implants. Plast. Reconstr. Surg. 119(7):1987-92.
19. de Jong, D., et al. 2008. Anaplastic large-cell lymphoma in women with breast implants. JAMA 300(17):2030-2035.
20. Flassbeck, D.B., et al. 2003. Determination of siloxanes, silicon, and platinum in tissues of women with silicone gel-filled implants. 375(3):356-62.
21. Fritzsche, F.R., et al. 2006. Anaplastic large-cell non-Hodgkins lymphoma of the breast in periprosthetic localization 32 years after treatment for primary breast cancer – A case report. Virchows Arch 449:561-564.
22. Fryzek, J.P., et al. 2000. Characteristics of women with cosmetic breast augmentation surgery compared with breast reduction surgery patients and women in the general population of Sweden. Ann. Plast. Surg. 45(4):349-56.
23. Fryzek, J.P., et al. 2001. Self-reported symptoms among women after cosmetic breast implant and breast reduction surgery. Plast. Reconstr. Surg. 107(1):206-13.
24. Gaudet, G., et al. 2002. Breast lymphoma associated with breast implants: case-reports and a review of the literature. Leukemia Lymphoma 43:115-119.
25. Gualco, G., et al. 2009. Primary and secondary T-cell lymphomas of the breast: clinic-pathologic features of 11 cases. Appl. Immunohistochem. Mol. Morphol. 17(4):301-306.
26. Gualco, G., and C.E. Bacchi. 2008. B-cell and T-cell lymphomas of the breast: Clinical-pathological features of 53 cases. Int.J. Surg. Path. 16(4):407-413.
27. Guo, H.Y., et al. 2008. Primary non-Hodgkin's lymphoma of the breast: Eight-year follow-up experience. Hematol. 87(5):491-497.
28. Hedén, P., et al. 2006. Prevalence of rupture in Inamed silicone breast implants. Plast. Reconstr. Surg. 118(2):303-8.
29. Hedén, P., et al. 2006. Style 410 cohesive silicone breast implants: safety and effectiveness at 5 to 9 years after implantation. Plast. Reconstr. Surg. 118(6):1281-7.
30. Hemminki, E., et al. 2004. Births and perinatal health of infants among women who have had silicone breast implantation in Finland, 1967-2000. Acta Obstet. Gynecol. Scand. 83(12):1135-40.
31. Henriksen, T.F., et al. 2005. Surgical intervention and capsular contracture after breast augmentation: a prospective study of risk factors. Ann. Plast. Surg . 54(4):343-51.
32. Herdman, R.C., et al. 2001. Silicone breast implants and cancer. Cancer Invest. 19(8):821-32.

33. Hölmich, L.R., et al. 2005a. The diagnosis of silicone breast implant rupture: clinical findings compared with findings at magnetic resonance imaging. Ann. Plast. Surg. 54(6):583-9.
34. Hölmich, L.R., et al. 2005b. The diagnosis of breast implant rupture: MRI findings compared with findings at explantation. 2005. Eur. J. Radiol. 53:213-25.
35. Hölmich, L.R., et al. 2001. Prevalence of silicone breast implant rupture among Danish women. Plast. Reconstr. Surg. 108(4):848-58.
36. Hölmich, L.R., et al. 2003a. Incidence of silicone breast implant rupture. Arch. Surg. 138:801-6.
37. Hölmich, L.R., et al. 2003b. Self-reported diseases and symptoms by rupture status among unselected Danish women with cosmetic silicone breast implants. Plast. Reconstr. Surg. 111(2):723-32.
38. Hölmich, L.R., et al. 2004. Untreated silicone breast implant rupture. Plast. Reconstr. Surg. 114(1):204-14.
39. Hull, W.E. 1999. A critical review of MR studies concerning silicone breast implants. Magn. Reson. Med. 42:984-95.
40. Hurst, N.M. 1996. Lactation after augmentation mammoplasty. Obstet. Gynecol. 87(1):30-4.
41. Jacobsen, E. 2006. Anaplastic large-cell lymphoma, T-/null-cell type. Oncologist. 11(7):831-40.
42. Jacobsen, P.H., et al. 2004. Mortality and suicide among Danish women with cosmetic breast implants. Arch. Int. Med. 164(22):2450-5.
43. Jakubietz, M.G., et al. 2004. Breast augmentation: Cancer concerns and mammography – A literature review. Plast. Reconstr. Surg. 113(7):117e 22e.
44. Janowsky, E.C., et al. 2000. Meta-analyses of the relation between silicone breast implants and the risk of connective-tissue diseases. N. Engl. J. Med. 342(11):781-90.
45. Katzin, W.E., et al. 2005. Pathology of lymph nodes from patients with breast implants: a histologic and spectroscopic evaluation. Am. J. Surg. Pathol. 29(4):506-11.
46. Keech, J.A., Jr. and B.J. Creech. 1997. Anaplastic T-cell lymphoma in proximity to a saline-filled breast implant. Plast. Reconstr. 100(2):554-555.
47. Kennan, J.J. and Taylor, R.B. 1999. Migration and chemical modification of silicone in women with breast prostheses. Magn. Reson. Med. 42:982-3.
48. Kjøller, K., et al. 2002. Health outcomes in offspring of Danish mothers with cosmetic breast implants. Ann. Plast. Surg. 48(3):238-45.
49. Kjøller K., et al. 2003. Characteristics of women with cosmetic breast implants compared with women with other types of cosmetic surgery and population-based controls in Denmark. Ann. Plast. Surg. 50(1):6-12.

50. Kjøller, K., et al. 2004. Self-reported musculoskeletal symptoms among Danish women with cosmetic breast implants. Ann. Plast. Surg. 52(1):1-7.
51. Knight, C.T. 1999. Migration and chemical modification of silicone in women with breast prostheses. Magn. Reson. Med. 42:979-80.
52. Koot, V., et al. 2003. Total and cause specific mortality among Swedish women with cosmetic breast implants: prospective study. BMJ. 326(7388):527-8.
53. Kulmala, I., et al. 2004. Local complications after cosmetic breast implant surgery in Finland. Ann. Plast. Surg. 53(5):413-9.
54. Li, S. and A.K. Lee. 2010. Case report: Silicone implant and primary breast ALK1-negative anaplastic large cell lymphoma, fact or fiction? Int. J. Clin. Exp. Pathol. 3(1):117-127.
55. Lipworth, L., et al. 2004. Silicone breast implants and connective tissue disease: An updated review of the epidemiologic evidence. Ann. Plast. Surg. 52(6):598-601.
56. Lipworth, L., et al. 2009. Cancer among Scandinavian women with cosmetic breast implants: A pooled long-term follow-up study. Int. J. Cancer. 124(2):490-3.
57. Lipworth, L., et al. 2009. Breast implants and lymphoma risk: A review of the epidemiologic evidence through 2008. Plast. Reconstr. Surg. 123(3):790-3.
58. Lugowski, S.J., et al. 2000. Analysis of silicon in human tissues with special reference to silicone breast implants. J. Trace Elem. Med. Biol. 14(1):31-42.
59. Macdonald, P.M. 1999. Migration and chemical modification of silicone in women with breast prostheses. Magn. Reson. Med. 42:981-2.
60. McLaughlin, J., et al. 2007. The Safety of Silicone Gel-Filled Breast Implants: A Review of the Epidemiologic Evidence. Ann. Plast. Surg. 59(5): 569-80.
61. McLaughlin, J.K. and Lipworth, L. 2004. Brain cancer and cosmetic breast implants: A review of the epidemiological evidence. Ann. Plast. Surg. 52(2):15-17.
62. Miglioretti, D.L., et al. 2004. Effect of breast augmentation on the accuracy of mammography and cancer characteristics. JAMA. 291(4):442-50.
63. Miranda, R.N., et al. 2009. Anaplastic large cell lymphoma involving the breast: clinicalpathologic study of 6 cases and review of the literature. Arch. Pathol. Lab. Med. 133(9):1383-1390.
64. NCCN Clinical Practice Guidelines in Oncology, T-cell Lymphomas. Version 1.2017, December 7, 2016. NCCN.org.
65. Newman, M.K., et al. 2008. Primary breast lymphoma in a patient with silicone breast implants: A case report and review of the literature. J. Plast. Reconstr. Aesthet. Surg. 61(7):822-825.
66. Olack, B., et al. 2007. Anaplastic large cell lymphoma arising in a saline breast implant capsule after tissue expander breast reconstruction. Ann. Plast. Surg. 59(1):56-57.

67. Pukkala, E., et al. 2002. Incidence of breast and other cancers among Finnish women with cosmetic breast implants, 1970-1999. J. Long Term Eff. Med. Implants. 12(4):271-9.
68. Pukkala, E., et al. 2003. Causes of death among Finnish women with cosmetic breast implants, 1971-2001. Ann. Plast. Surg. 51(4):339-42.
69. Roden, A.C., et al. 2008. Seroma-associated primary anaplastic large-cell lymphoma adjacent to breast implants: An indolent T-cell lymphoproliferative disorder. Mod. Pathol. 21(4):455-463.
70. Sahoo, S., et al. 2003. Anaplastic large cell lymphoma arising in a silicone breast implant capsule: A case report and review of the literature. Arch. Pathol. Lab. Med. 127(3):e115-e118.
71. Seify, H., et al. 2005. Preliminary (3 years) experience with smooth wall silicone gel implants for primary breast augmentation. Ann. Plast. Surg. 54(3):231-5.
72. Signorello, L.B., et al. 2001. Offspring health risk after cosmetic breast implantation in Sweden. Ann. Plast. Surg. 46(3):279-86.
73. Tugwell, P., et al. 2001. Do silicone breast implants cause rheumatologic disorders? A systematic review for a court-appointed national science panel. Arthritis Rheum. (11):2477-84.
74. Weisman, M.H., et al. 1988. Connective-tissue disease following breast augmentation: A preliminary test of the human adjuvant tissue hypothesis. Plast. Reconstr. Surg. 82(4):626-30.
75. Williams, H.J., et al. 1997. Breast implants in patients with differentiated and undifferentiated connective tissue disease. Arthritis Rheum. 40(3):437-40.
76. Wolfe, F. and Anderson, J. 1999. Silicone filled breast implants and the risk of fibromyalgia and rheumatoid arthritis. J. Rheumatol. 26(9):2025-28.
77. Wong, A.K., J. et al. 2008. Anaplastic large cell lymphoma associated with a breast implant capsule: a case report and review of the literature. Am. J. Surg. Pathol. 32(8):1265-1268.
78. Stein, J., et al. 1999. In situ determination of the active catalyst in hydrosilylation reactions using highly reactive Pt(0) catalyst precursors. J. Am. Chem. Soc. 121(15):3693-3703.
79. Chandra, G., et al. 1987. A convenient and novel route to bis(alkyne)platinum(0) and other platinum(0) complexes from Speier's hydrosilylation catalyst. Organometallics. 6:191-2.
80. Lappert, M.F. and Scott, F.P.A. 1995. The reaction pathway from Speier's to Karstedt's hydrosilylation catalyst. J. Organomet. Chem. 492(2):C11-C13.
81. Lewis, L.N., et al. 1995. Mechanism of formation of platinum(0) complexes containing silicon-vinyl ligands. Organometallics. 14:2202-13.

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