Directions for Use

Directions for Use

NATRELLE®
Silicone-Filled Breast Implants

Smooth &
BIOCELL® Texture

ALLERGAN

THE SCIENCE OF REJUVENATION™

Caution: Federal (USA) law restricts this device to sale by or on the order of a physician.

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INTRODUCTION

• DIRECTIONS TO THE PHYSICIAN

The information supplied in this Directions for Use document is intended to provide an overview of essential information about *NATRELLE*® Silicone-Filled Breast Implants, including the indications for use, contraindications, warnings, precautions, important factors for a patient to consider, adverse events, other reported conditions, and a summary of Allergan's Core Study results.

Patient Counseling Information

You should review this document prior to counseling the patient about *NATRELLE*® Silicone-Filled Breast Implants and breast implant surgery. Please familiarize yourself with the content of this document and resolve any questions or concerns prior to proceeding with use of the device. As with any surgical procedure, breast implantation is NOT without risks. Breast implantation is an elective procedure, and the patient must be well counseled and understand the risk/benefit relationship.

Before making the decision to proceed with surgery, the surgeon or a designated patient counselor should instruct the patient to read the patient labeling, ***Breast Augmentation/ Reconstruction with NATRELLE® Silicone-Filled Breast Implants*** and discuss with the patient the warnings, precautions, important factors to consider, complications, and Allergan's clinical Core Study results listed in the patient labeling. The physician should advise the patient of the potential complications and that medical management of serious complications may include additional surgery and explantation.

Informed Decision

Each patient should receive Allergan's patient labeling during her initial visit/consultation to allow her sufficient time prior to surgery to read and adequately understand the important information on the risks, follow-up recommendations, and benefits associated with silicone gel-filled breast implant surgery.

Allow the patient at least 1-2 weeks after reviewing and considering this information before deciding whether to have primary breast surgery. In the case of a revision it may be medically necessary to perform surgery sooner.

In order to document a successful informed decision process, the ***Acceptance of Risk and Consent to Surgery*** document should be signed by both the patient and the surgeon and then retained in the patient's file.

NATRELLE® Silicone-Filled Breast Implant Physician Certification and Education via Allergan's ***Physician Certification Program*** is required in order to gain access to *NATRELLE®* Silicone-Filled Breast Implants. Physician certification provides documentation of training in the use of these devices. Allergan has developed an online certification process that may be accessed via **www.allerganacademy.com**. Please contact your local Breast Aesthetics Business Development Manager or the Allergan Customer Care Department for further information on the *NATRELLE®* Silicone-Filled Breast Implant Certification Program, the ALLERGAN ACADEMY™ or any other Allergan physician education initiatives.

Device Tracking

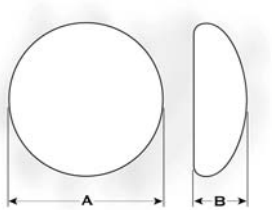
NATRELLE® Silicone-Filled Breast Implants are subject to Device Tracking per Federal Regulation. This means that the physician is required to report to Allergan the serial number of the implanted device(s), the date of surgery, information relating to the physician's practice and information on the patient receiving the implant(s). This information should be recorded on the ***Device Tracking Form*** supplied by Allergan with each silicone gel-filled breast implant. Return the top portion of the form to Allergan following surgery in the envelope provided.

The bottom portion of the form should be provided to the patient following surgery. The patient has the right to have her personal information removed from Allergan's Device Tracking program. However, Allergan strongly recommends that all patients receiving *NATRELLE®* Silicone-Filled Breast Implants participate in Allergan's Device Tracking program. This will help ensure that Allergan has a record of each patient's contact information. Patients should be encouraged to complete the Device Tracking Form and return it to Allergan in the postage paid business reply envelope provided so that they can be contacted in the event of a recall or other problems with the implants that they should be made aware of.

DEVICE DESCRIPTION

NATRELLE® Silicone-Filled Breast Implants are constructed with barrier shell technology resulting in a low diffusion silicone elastomer shell and are filled with a soft, cohesive silicone gel. All styles are single "lumen" round design and consist of a shell, a patch, and silicone gel fill. *NATRELLE*® Silicone-Filled Breast Implants are dry heat sterilized and are available in both smooth and BIOCELL® surface texture.

Style Number	Breast Implant Description	Size Range
Style 10	Smooth shell surface, moderate profile	120cc – 800cc
Style 15	Smooth shell surface, mid-range profile	155cc – 752cc
Style 20	Smooth shell surface, high profile	120cc – 800cc
Style 40	Smooth shell surface, moderate profile	80cc – 560cc
Style 45	Smooth shell surface, full profile	120cc – 800cc
Style 110	BIOCELL® Textured shell surface, moderate profile	90cc – 510cc
Style 115	BIOCELL® Textured shell surface, mid-range profile	150cc – 716cc
Style 120	BIOCELL® Textured shell surface, high profile	180cc – 650cc



A = Width; B = Projection
Round Breast Implant

INDICATIONS

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

- **Breast augmentation for women at least 22 years old**. Breast augmentation includes primary breast augmentation to increase the breast size, as well as revision surgery to correct or improve the result of a primary breast augmentation surgery.
- **Breast reconstruction.** Breast reconstruction includes primary reconstruction to replace breast tissue that has been removed due to cancer or trauma or that has failed to develop properly due to a severe breast abnormality. Breast reconstruction also includes revision surgery to correct or improve the result of a primary breast reconstruction surgery.

CONTRAINDICATIONS

Breast implant surgery should not be performed in:

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

WARNINGS

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.***

  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 the forcing of implants through too small an opening 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. This longer incision will reduce the potential for creating excessive stress to the implant during insertion.

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

  Silicone gel-filled breast implants are prone to unintended instrument trauma during implantation or during explantation.[1,2] 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.[3] Allergan's (retrieval study) analyses of explanted devices have identified unintended surgical instrument damage as one potential cause of implant rupture.

- Do not treat capsular contracture by closed capsulotomy or forceful external compression, which will likely result in implant damage, rupture, folds, and/or hematoma.

- ***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.***

- ***Do not immerse the implant in Betadine solution.*** If Betadine is used in the pocket, ensure that it is rinsed thoroughly so no residual solution remains in the pocket.

- Do not re-use or resterilize any product that has been previously implanted. Breast implants are intended for single use only.

- Do not place more than one implant per breast pocket.

- Do not use the periumbilical approach to place the implant.

MICROWAVE DIATHERMY

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

Precautions

Specific Populations

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

- Autoimmune diseases (e.g., lupus and scleroderma).
- A compromised immune system (for example, currently receiving immunosuppressive therapy).
- Conditions or medications 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. Please discuss any history of mental health disorders prior to surgery. Patients with a diagnosis of depression, or other mental health disorders, should wait until resolution or stabilization of these conditions prior to undergoing breast implantation surgery.

Surgical Precautions

- **Surgical technique** – The implantation of silicone gel-filled breast implants involves a variety of surgical techniques. Therefore, the surgeon is advised to use the method which her/his own practice and discretion dictate to be best for the patient, consistent with this product insert data sheet. It is advisable to have more than one size breast implant in the operating room at the time of surgery to allow for flexibility in determining the appropriate size implant to be used. A backup implant should also be available.

  Some of the important surgical and implant sizing variables that have been identified include the following:

- **Implant Selection**
  - The implant should be consistent in size with the patient's chest wall dimensions, including base width measurements, bearing in mind the laxity of the tissue and the projection of the implant.

- A thorough discussion should be conducted with the patient, employing appropriate visual aids such as imaging, sizing implants, or other options to clarify her objectives and reduce the incidence of reoperation for size change.
- The following may cause implants to be more palpable: textured implants, larger implants, subglandular placement, and an insufficient amount of skin/tissue available to cover the implant.
- Available tissue must provide adequate coverage of the implant.
- A recent report indicates that larger sized implants (>350cc) may increase the risk of developing complications such as implant extrusion, hematoma, infection, palpable implant folds, and visible skin wrinkling requiring surgical intervention to correct these complications.[4]

- Incision Site Selection
  - The periareolar site is typically more concealed, but it is associated with a higher likelihood of difficulties in successfully breastfeeding as compared to other incision sites.[5] A periareolar incision may result in changes in nipple sensation.
  - The inframammary incision is generally less concealed than the periareolar, but it is associated with less breastfeeding difficulty than the periareolar incision site.[6]
  - The axillary incision is less concealed than the periareolar site.
  - The periumbilical approach has not been studied in the *NATRELLE*® Core Study and should not be used for a wide variety of reasons, including potential damage to the implant shell.
- Implant Placement Selection
  - A well-defined, dry pocket of adequate size and symmetry must be created to allow the implant to be placed flat on a smooth surface.
  - Submuscular placement may make surgery last longer, may make recovery longer, may be more painful, and may make it more difficult to perform some reoperation procedures than subglandular placement. The possible benefits of this placement are that it may result in less palpable implants, less likelihood of capsular contracture,[7] and easier imaging of the breast for mammography. Also, submuscular placement may be preferable if the patient has thin or weakened breast tissue.

- Subglandular placement may make surgery and recovery shorter, may be less painful, and may be easier to access for reoperation than the submuscular placement. However, this placement may result in more palpable implants, greater likelihood of capsular contracture,[8,9] and increased difficulty in imaging the breast with mammography.

- **Explantation**
  If it is necessary to perform explantation of the implant, care must be taken to minimize manipulation of the product (particularly in regards to sharp-edged openings). Evaluation of the condition of the device upon explantation should be performed by the explanting surgeon and Allergan.

Important Factors to be Discussed with the Patient

Breast implantation is an elective procedure and the patient must be thoroughly counseled on the risks, as well as the benefits, of these products and procedures. You should advise your patient that she must read the patient labeling section of the Patient Planner for either augmentation or reconstruction, as applicable. The patient labeling is intended as the primary means to relate uniform risk and benefit information to assist your patient in making an informed decision about primary breast augmentation and revision-augmentation, or primary reconstruction and revision-reconstruction surgery (as applicable), but is not intended to replace consultation with you. The patient should be advised to wait at least 1-2 weeks after reviewing and considering this information, before deciding whether to have this surgery, unless an earlier surgery is deemed medically necessary.

Below are some of the important factors your patients need to be aware of when using silicone gel-filled breast implants. Section 1.4 of the patient labeling provides a more detailed listing of important factors for patients.

- **Rupture** – Rupture of a silicone gel-filled breast implant is most often silent (i.e., there are no symptoms experienced by the patient and no physical sign of changes with the implant) rather than symptomatic. The sensitivity of plastic surgeons familiar with implants to diagnose rupture is 30%[10] compared to 89% for MRI.[11] **Therefore, you should advise your patient that she will need to have regular MRIs over her lifetime to screen for silent rupture even if she is having no problems. The first MRI should be performed at 3 years postoperatively, then every 2 years, thereafter.** The importance of these MRI evaluations should be emphasized. You should provide her with a list of MRI facilities in her area that have at least a 1.5 Tesla magnet, a dedicated breast coil, and a radiologist experienced with breast implant

MRI films for signs of rupture. Diagnostic procedures will add to the cost of having breast implants, and patients should be told that these costs may exceed the cost of their initial surgery over their lifetime and that these costs may not be covered by their insurance carrier.

  - ***Clinical Management of Suspected Rupture*** – If rupture is identified via MRI, then you should advise your patient to have her implant removed.

- **Explantation** – Implants are not considered lifetime devices, and patients likely will undergo implant removal(s), with or without replacement, over the course of their life. When implants are explanted without replacement, changes to the patient's breasts may be irreversible. Complication rates are higher following revision surgery (removal with replacement).
- **Reoperation** – Additional surgeries to the patients' breasts will likely be required, either because of implant rupture, other complications, or unacceptable cosmetic outcomes. Patients should be advised that their risk of future complications increases with revision surgery as compared to primary augmentation or reconstruction surgery. There is a risk that implant shell integrity could be compromised inadvertently during reoperation surgery, potentially leading to product failure.
- **Breast Examination Techniques** – Patients should perform breast self-examinations monthly and be shown how to distinguish the implant from their breast tissue. The patient should not manipulate or squeeze the implant excessively. The patient should be told that the presence of lumps, persistent pain, swelling, hardening, or change in the implant shape may be signs of symptomatic rupture of the implant. If the patient has any of these signs, she should be told to report them, and possibly have an MRI evaluation to screen for rupture.
- **Mammography** – Patients should be instructed to undergo routine mammography exams as per their primary care physician's recommendations. The importance of having these exams should be emphasized. Patients should be instructed to inform their mammographers about the presence, type, and placement of their implants. Breast implants may complicate the interpretation of mammographic images by obscuring underlying breast tissue and/or by compressing overlying tissue. Accredited mammography centers, technicians with experience in imaging patients with breast implants, and use of displacement techniques are needed to adequately visualize breast tissue in the implanted breast. The current recommendations for preoperative/screening mammograms are no different for women with breast implants than for those women without implants. Presurgical mammography with a mammogram following the procedure may be performed to establish a baseline for routine future mammography in augmentation patients.
- **Lactation** – Breast implant surgery may interfere with the ability to successfully breastfeed, either

by reducing or eliminating milk production.

- **Avoiding Damage During Treatment** – Patients should inform other treating physicians of the presence of implants to minimize the risk of damage to the implants.
- **Smoking** – Smoking may interfere with the healing process.
- **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 may increase the likelihood of capsular contracture, necrosis, and implant extrusion.
- **Insurance coverage** – Patients should be advised that health insurance premiums may increase, insurance coverage may be dropped, and/or future coverage may be denied based on the presence of breast implants. Treatment of complications may not be covered as well. Patients should check with their insurance company regarding coverage issues before undergoing surgery.
- **Mental Health and Elective Surgery** – It is important that all patients seeking to undergo elective surgery have realistic expectations that focus on improvement rather than perfection. Request that your patient openly discuss with you, prior to surgery, any history that she may have of depression or other mental health disorders.
- **Long-Term Effects** - The *NATRELLE®* Core Study will continue to evaluate the long-term (10 years) safety and effectiveness of these products. In addition, Allergan has initiated a separate large 10-year postapproval study (the Breast Implant Follow-up Studies, or BIFS) to address specific issues which Allergan's Core Study was not designed to fully answer, as well as to provide a real-world assessment of some endpoints. The endpoints in the BIFS large postapproval study include long-term local complications, connective tissue disease (CTD), CTD signs and symptoms, neurological disease, neurological signs and symptoms, offspring issues, reproductive issues, lactation issues, cancer, suicide, mammography issues, and MRI compliance and results. Allergan will update their labeling on a regular basis with the results of these two studies.

Adverse Events

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

Below is a description of these adverse events. For specific adverse event rates/outcomes for *NATRELLE®* implants, refer to Allergan's Core Study section below.

- ***Rupture*** – *Breast implants are not lifetime devices*. Breast implants rupture when the shell develops a tear or hole. Rupture can occur at any time after implantation, but they are more likely to occur the longer the implant is implanted. The following things may cause implants to rupture: damage by surgical instruments; stressing the implant during implantation and weakening it; folding or wrinkling of the implant shell; excessive force to the chest (e.g., during closed capsulotomy, which is contraindicated); trauma; compression during mammographic imaging; and severe capsular contracture. Breast implants may also simply wear out over time. Laboratory studies have identified some of the types of rupture for Allergan's product; however, it is not conclusively known whether these tests have identified all causes of rupture. These laboratory studies will continue postapproval.

  Silicone gel-filled implant ruptures are most often silent. (MRI examination is currently the best method to screen for silent rupture.) This means that most of the time neither you nor your patient will know if the implant has a tear or hole in the shell. This is why MRI is recommended at 3 years and then every 2 years, thereafter, to screen for rupture. Sometimes there are symptoms associated with gel implant rupture. These symptoms include hard knots or lumps surrounding the implant or in the armpit, change or loss of size or shape of the breast or implant, pain, tingling, swelling, numbness, burning, or hardening of the breast.

  When MRI signs of rupture are found (such as subcapsular lines, characteristic folded wavy lines, teardrop sign, keyhole sign, noose sign), or if there are signs or symptoms of rupture, you should remove the implant and any gel you determine your patient has, with or without replacement of the implant. It also may be necessary to remove the tissue capsule, as well as the implant, which will involve additional surgery, with associated costs. If your patient has symptoms such as breast hardness, a change in breast shape or size, and/or breast pain, you should recommend that she has an MRI to determine whether rupture is present.[12,13]

There are also consequences of rupture. If rupture occurs, silicone gel may either remain within the scar tissue capsule surrounding the implant (intracapsular rupture), move outside the capsule (extracapsular rupture), or gel may move beyond the breast (migrated gel). There is also a possibility that rupture may progress from intracapsular to extracapsular and beyond. There have also been health consequences reported in the literature. See below for details.

Rupture Rate Information on Allergan 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 8.6% for primary augmentation, 0% for revision-augmentation, 11.4% for primary reconstruction, and 0% for revision-reconstruction. The rupture rate for the whole MRI cohort in the Core Study (including augmentation, revision-augmentation, reconstruction, and revision-reconstruction patients) through 7 years was 7.3% for patients and 4.5% for implants. Across all patients in the NATRELLE® Core Study, all ruptures were intracapsular with 1 case of 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 Allergan implants is provided from a published European study known as the International MRI Study.[14] 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 five surgeons. 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 was one possible case of extracapsular rupture with the remainder classified as intracapsular ruptures. No cases of migrated gel were found.

Additional information on rupture will be collected through Allergan's postapproval Core and BIFS studies.

Additional Information on Consequences of Rupture from Literature

Studies of Danish women evaluated with MRI involving a variety of manufacturers and implant models showed that about three-fourths of implant ruptures are intracapsular and the remaining one-fourth is extracapsular.[15] Additional studies of Danish women indicate that over a 2-year period, about 10% of the implants with intracapsular rupture progressed to extracapsular rupture as detected by MRI.[16] In about half of these cases of progression from intracapsular

to extracapsular rupture, the women had had trauma or mammography. In the other half, no cause was given. In the women with extracapsular rupture, after 2 years, the amount of silicone outside the scar tissue capsule increased for about 14% of these women. This type of information pertains to a variety of silicone implants from a variety of manufacturers and implant models, and it is not specific to *NATRELLE*® implants.

Below is a summary of information related to the health consequences of implant rupture, which have not been fully established. These reports were in women who had implants from a variety of manufacturers and implant models.

- Local breast complications reported in the published literature which were associated with rupture include breast hardness, a change in breast shape or size, and breast pain.[17] These symptoms are not specific to rupture, as they also are experienced by women who have capsular contracture.
- There have been rare reports of gel movement to nearby tissues such as the chest wall, armpit, or upper abdominal wall, and to more distant locations down the arm or into the groin. This has led to nerve damage, granuloma formation and/or breakdown of tissues in direct contact with the gel in a few cases. There have been reports of silicone presence in the liver of patients with silicone breast implants. Movement of silicone gel material to lymph nodes in the axilla also has been reported, even in women without evidence of rupture, leading to lymphadenopathy, as discussed below.[18]
- Concerns have been raised over whether ruptured implants are associated with the development of connective tissue or rheumatic diseases and/or symptoms such as fatigue and fibromyalgia.[19, 20, 21, 22] A number of epidemiology studies have evaluated large populations of women with breast implants. These studies do not, taken together, support a significant association of breast implants with a typical, diagnosed rheumatic disease. Other than one small study,[23] these studies do not distinguish whether the women had ruptured or intact implants.

- ***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.

Patients should also be advised that additional surgery may be needed in cases where pain and/or firmness are severe. This surgery ranges from removal of the implant capsule tissue, to removal and possible replacement of the implant itself. This surgery may result in loss of breast tissue. Capsular contracture may happen again after these additional surgeries. Capsular contracture may increase the risk of rupture.[24]

- ***Reoperation*** – Patients should be advised that additional surgery to their breast and/or implant will likely be necessary over the course of their life. Patients may decide to change the size or type of their implants, requiring a reoperation, or they may have a reoperation to improve or correct their outcome.
- ***Implant Removal*** – Patients should be advised that implants are not considered lifetime devices, and they will potentially undergo implant removal, with or without replacement, over the course of their life. Patients should also be advised that the changes to their breast following explantation are irreversible.
- ***Pain*** – Pain of varying intensity and length of time may occur and persist following breast implant surgery. In addition, improper size, placement, surgical technique, or capsular contracture may result in pain. The surgeon should instruct his or her patient to inform them if there is significant pain or if pain persists.
- ***Changes in Nipple and Breast Sensation*** – Feeling in the nipple and breast can increase or decrease after implant surgery, and are typically lost after complete mastectomy where the nipple itself is removed, and can be severely lessened by partial mastectomy. Radiation therapy also can significantly reduce sensation in the remaining portions of the breast or chest wall. The placement of breast implants for reconstruction may further lessen the sensation in the remaining skin or breast tissue. The range of changes varies from intense sensitivity to no feeling in the nipple or breast following surgery. While some of these changes can be temporary, they can also be permanent, and may affect the patient's sexual response or ability to nurse.
- ***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.

- ***Unsatisfactory Results*** – Patients should be informed that dissatisfaction with cosmetic results related to such things as scar deformity, hypertrophic scarring, capsular contracture, asymmetry, wrinkling, implant displacement/migration, incorrect size, and implant palpability/visibility may occur. Careful surgical planning and technique can minimize, but not preclude, the risk of such results. Pre-existing asymmetry may not be entirely correctable. Revision surgery may be indicated to maintain patient satisfaction but carries additional considerations and risks.
- ***Breastfeeding Complications*** – Difficulties have been reported following breast surgery, including breast reduction and breast augmentation. 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: hematoma/seroma, implant extrusion, necrosis, delayed wound healing, and breast tissue atrophy/chest wall deformity. Calcium deposits can form in the tissue capsule surrounding the implant with symptoms that may include pain and firmness. Lymphadenopathy has also been reported in some women with implants.

OTHER REPORTED CONDITIONS

There have been reports in the literature of other conditions in women with silicone gel-filled breast implants. Many of these conditions have been studied to evaluate their potential association with breast implants. No cause and effect relationship has been established between breast implants and the conditions listed below. Furthermore, there is the possibility of risks, yet unknown, which in the future could be determined to be associated with breast implants. It should also be noted that the cited references include data from augmentation and/or reconstruction patients, as well as from a variety of manufacturers and implant models.

- ***Connective Tissue Disease (CTD)***

Connective tissue diseases include diseases such as lupus, scleroderma, and rheumatoid arthritis. Fibromyalgia is a disorder characterized by chronic pain in the muscles and soft tissues surrounding joints, with tenderness at specific sites in the body. It is often accompanied by fatigue. 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.[25, 26, 27, 28, 29 30, 31, 32, 33, 34] The published studies overall show that breast implants are not significantly associated with a risk of developing a typical or defined connective tissue disease.[35, 36, 37, 38] However, the study size needed to conclusively rule out a small risk of connective tissue

disease among women with silicone gel-filled implants would need to be very large. These studies do not distinguish between women with intact and ruptured implants. Only one study evaluated specific connective tissue disease diagnoses and symptoms in women with silent ruptured versus intact implants, but the study was too small to rule out a small risk.[39]

- *CTD Signs and Symptoms*

Literature reports have also been made associating silicone breast implants with various rheumatological signs and symptoms such as fatigue, exhaustion, joint pain and swelling, muscle pain and cramping, tingling, numbness, weakness, and skin rashes. Scientific expert panels and literature reports have found no evidence of a consistent pattern of signs and symptoms in women with silicone breast implants.[40, 41, 42, 43, 44] Having these rheumatological signs and symptoms does not necessarily mean that a patient has a connective tissue disease; however, you should advise your patient that she may experience these signs and symptoms after undergoing breast implantation. If a patient has an increase in these signs or symptoms, you should refer your patient to a rheumatologist to determine whether these signs or symptoms are due to a connective tissue disorder or autoimmune disease.

- *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.[45, 46, 47, 48, 49] 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 cancer survival of women with breast implants.[50, 51, 52, 53, 54]

Brain cancer – One recent study has reported an increased incidence of brain cancer in women with breast implants as compared to the general population.[55] The incidence of brain cancer, however, was not significantly increased in women with breast implants when compared to women who had other plastic surgeries. Another recently published review of four large studies in women with cosmetic implants concluded that the evidence does not support an association between brain cancer and breast implants.[56]

Respiratory/lung cancer – One study has reported an increased incidence of respiratory/lung cancer in women with breast implants.[57] 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.[58, 59, 60]

Cervical/vulvar cancer – One study has reported an increased incidence of cervical/vulvar cancer in women with breast implants.[61] The cause of this increase is unknown.

Other cancers – One study has reported an increased incidence of stomach cancer and leukemia in women with breast implants compared to the general population.[62] This increase was not significant when compared to women who had other types of plastic surgeries.

- *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.[63]

- *Suicide*

In several studies, a higher incidence of suicide was observed in women with breast implants.[64, 65, 66, 67] 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.[68]

- *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.[69]

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.[70, 71] Although low birth weight was reported in a third study, other factors (for example, lower pre-pregnancy weight) may explain this finding.[72] This author recommended further research on infant health.

- *Potential Health Consequences of Gel Bleed*

Small quantities of low molecular weight (LMW) silicone compounds, as well as platinum (in zero oxidation state), have been found to diffuse ("bleed") through an intact implant shell.[73,74] The evidence is mixed as to whether there are any clinical consequences associated with gel bleed. For instance, studies on implants implanted for a long duration have suggested that such bleed may be a contributing factor in the development of capsular contracture[75] and lymphadenopathy.[76] However, evidence against gel bleed being a significant contributing factor to capsular contracture and other local complications is provided by the fact that there are similar or lower complication rates for silicone gel-filled breast implants than for saline-filled breast implants. Saline-filled breast implants do not contain silicone gel and, therefore, gel bleed is not an issue for those products. Furthermore, toxicology testing has indicated that the silicone material used in Allergan's implants does not cause toxic reactions when large amounts are administered to test animals. It should also be noted that studies reported in the literature have demonstrated that the low concentration of platinum contained in breast implants is in the zero oxidation (most biocompatible) state.[77, 78, 79, 80]

Allergan provided testing to identity the gel constituents (including the platinum species [or other catalysts]), the rate that the gel constituents bleed, and how that rate changes over time. Allergan's test method, which was designed to mimic in-vivo exposure to silicone gel-filled breast implants, involved the incubation of smooth implants in bovine serum at 37°C. At specific timepoints, samples of the solution were withdrawn for analysis for low molecular weight (LMW) silicones and platinum. The testing indicated that the diffusion of measured constituents ceased by 90 days. Measurable amounts of silicones from D4 to D21 and from MD2M to MD19M diffused into the serum over that period. The maximum cumulative amount of LMW silicones was 48.1μg (micrograms) after 90 days. The maximum cumulative amount of platinum was 1.1μg after 90 days. Over 99% of the LMW silicones and platinum stayed in the implant. The overall body of available evidence supports that the extremely low level of gel bleed is of no clinical consequence.

Allergan's Core Study

Overview of Allergan's Core Study

The Allergan Core Study is a 10-year study to assess safety and effectiveness in augmentation, reconstruction, and revision (revision-augmentation and revision-reconstruction) patients. Patient follow-up is at 0-4 weeks, 6 months, 12 months, 24 months, and annually through 10 years. Safety is assessed by complications, such as implant rupture, capsular contracture, and reoperation. Benefit (effectiveness) is assessed by breast size change, patient satisfaction and measures of quality of life (QoL). Allergan's Core Study results indicate that the risk of any complication (including reoperation) at some point through 7 years after implant surgery is 45% for primary augmentation patients, 57% for revision-augmentation patients, 70% for primary reconstruction patients, and 73% for revision-reconstruction patients.

The Allergan Core Study consists of 715 patients. This includes 455 primary augmentation patients, 147 revision-augmentation patients, 98 primary reconstruction patients, and 15 revision-reconstruction patients. Of these, 158 primary augmentation patients, 50 revision-augmentation patients, 51 primary reconstruction patients, and 5 revision-reconstruction patients are in the MRI cohort, which means that they are assessed for silent rupture by MRI at years 1, 3, 5, 7, and 9. At this time, MRIs have been performed at years 1, 3, 5, and 7, and the follow-up rates for the MRI cohort ranged from 63% to 80% at the 7-year timepoint across indications. As a whole, data are available through 7 years, and overall follow-up rates for each indication are provided below.

Demographic information for the Allergan Core Study with regard to race is as follows: 86% of the Allergan Core Study patients were Caucasian; 5% were Hispanic; 3% were Asian; <1% were African American; and 5% were other or unknown. The median age at surgery was 34 years for primary augmentation patients, 42 for revision-augmentation patients, 48 years for primary reconstruction patients, and 54 years for revision-reconstruction patients. Approximately 56% of the Core Study patients were married. Approximately 83% had some college education.

With respect to surgical baseline factors in the Allergan Core Study, for primary augmentation patients, the most frequently used devices were smooth implants (59%), the most common incision site was inframammary (46%), and the most frequent site of placement was submuscular (70%). For revision-augmentation patients, the most frequently used devices were smooth implants (57%), the most common incision site was inframammary (64%), and the most frequent site of placement was submuscular (60%). For primary reconstruction patients, the most frequently used devices were textured implants (64%), the most common incision site was the mastectomy scar (59%), and the most frequent site of placement was submuscular (83%). For revision-reconstruction patients,

the most frequently used devices were textured implants (56%), the most common incision site was mastectomy scar (52%), and the most frequent site of placement was submuscular (76%).

As a note, supplemental safety information was also obtained from Allergan's Adjunct Study, the Danish Breast Implant Registry, an international clinical MRI study, and the literature to help assess long-term rupture rate and the consequences of rupture for this product. The literature, which had the most available information on the consequences of rupture, was also used to assess other potential complications associated with silicone gel-filled breast implants. The key literature information is referenced in this document.

The Core Study is currently ongoing, with the results through 7 years reported in this document. Allergan will periodically update this document as more information becomes available. The information below provides more details about the complications and benefits of the *NATRELLE®* Silicone-Filled Breast Implants for primary augmentation and revision-augmentation patients, followed by primary reconstruction and revision-reconstruction patients, through 7 years.

PRIMARY AUGMENTATION AND REVISION-AUGMENTATION PATIENTS

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

Patient Accounting (Follow-Up Rates)

Allergan's Core Study enrolled 455 augmentation patients. Of the women expected to be seen at the 7-year follow-up visit, 74% were seen.

Allergan's Core Study enrolled 147 revision-augmentation patients. Of the women expected to be seen at the 7-year follow-up visit, 72% were seen.

Effectiveness Outcomes

The benefits of silicone gel-filled breast implants were assessed by a variety of outcomes, including bra cup size change and assessments of patient satisfaction and QoL. Allergan's patient satisfaction was based on a 5-point scale assessment of satisfaction with their implants at the time of the follow-up visits. The QoL measures were the Rosenberg Self Esteem Scale, the Body Esteem Scale, the Tennessee Self Concept Scale, and the SF-36. 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.

Primary Augmentation Patients: For primary augmentation patients, 396 (87%) 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 6% had no increase or decrease.

Allergan's 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, 317 (70%) provided a satisfaction rating at 7 years after implantation, with 300 (95%) of these patients indicating that they were satisfied with their breast implants.

Quality of life assessments were made at 1, 2, 4, and 6 years post-implant. Therefore, 6 year data is provided herein. 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 six scales after 6 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 6 years after receiving implants. Patient responses to questions on the Body Esteem Scale regarding overall body image showed no changes, but a decrease in weight concern and physical condition, and increase with regard to sexual attractiveness were shown.

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

Allergan's patient satisfaction was based on a 5-point scale of satisfaction with their implants at the time of the follow-up visits. Of the original 147 revision-augmentation patients, 91 (62%) provided a satisfaction rating at 7 years. Of these 91 patients, 81 (89%) indicated that they were satisfied with their breast implants.

Quality of life assessments were made at 1, 2, 4, and 6 years post-implant. Therefore, 6 year data is provided herein. For revision-augmentation patients, the SF-36, which measures mental and physical health, showed no significant changes in all but one scale (Vitality), which decreased after 6 years. Patient responses to questions on the Tennessee Self Concept Scale and Rosenberg Self Esteem Scale showed no changes 6 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.

Safety Outcomes

Tables 1 and 2 describe the complications experienced by primary augmentation and revision-augmentation patients in the Core Study. The rates reflect the number of patients out of 100 who experienced the listed complication at least once within the first 7 years after their implantation. Some complications occurred more than once for some patients.

Table 1

7-Year Complication Rates for Primary Augmentation Patients
N = 455 Patients

Key Complication[1]	% (95% CI)
Reoperation	30.1% (26.0%, 34.7%)
Capsular Contracture Baker Grade III/IV	15.5% (12.3%, 19.3%)
Implant Removal with Replacement	11.0% (8.4%, 14.4%)
Implant Rupture (MRI cohort)	8.6% (5.0%, 14.7%)
Implant Removal without Replacement	3.1% (1.8%, 5.5%)

Other Complications occurring in ≥ 1% of patients[2,3]	% (95% CI)
Breast Pain	11.4% (8.6%, 14.8%)
Swelling	9.2% (6.8%, 12.3%)
Nipple Complications	6.7% (4.7%, 9.5%)
Implant Malposition	5.2% (3.5%, 7.7%)
Scarring/Hypertrophic Scarring	3.7% (2.3%, 6.0%)
Asymmetry	3.3% (1.9%, 5.5%)
Ptosis	2.2% (1.2%, 4.2%)
Breast/Skin Sensation Changes	1.6% (0.8%, 3.3%)
Hematoma	1.6% (0.7%, 3.2%)
Implant Palpability/Visibility	1.6% (0.8%, 3.4%)
Seroma/Fluid Accumulation	1.6% (0.7%, 3.2%)
Wrinkling/Rippling	1.2% (0.5%, 2.9%)
Delayed Wound Healing	1.1% (0.5%, 2.7%)

[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.

[2] The following complications were reported at a rate less than 1%: bruising, infection, implant extrusion, lymphedema, other complications, redness, skin rash, and tissue/skin necrosis.

[3] The following complications were reported at a rate of 0%: capsule calcification, gel migration, irritation, lymphadenopathy, and pneumothorax.

Table 2
7-Year Complication Rates for Revision-Augmentation Patients
N = 147 Patients

Key Complications[1]	% (95% CI)
Reoperation	40.5% (32.8%, 49.3%)
Capsular Contracture Baker Grade III/IV	20.4% (14.4%, 28.4%)
Implant Removal with Replacement	20.9% (14.8%, 29.0%)
Implant Removal without Replacement	4.3% (1.8%, 10.1%)
Implant Rupture (MRI cohort)	0% (N/A)

Other Complications occurring in ≥ 1% of patients[2,3]	% (95% CI)
Breast Pain	10.6% (6.4%, 17.4%)
Swelling	8.4% (4.7%, 14.8%)
Implant Palpability/Visibility	6.8% (3.6%, 12.6%)
Implant Malposition	6.1% (3.1%, 11.9%)
Seroma/Fluid Accumulation	6.1% (3.1%, 12.0%)
Scarring/Hypertrophic Scarring	6.0% (3.0%, 11.6%)
Ptosis	4.8% (2.2%, 10.5%)
Wrinkling/Rippling	4.6% (2.1%, 10.0%)
Asymmetry	3.7% (1.5%, 8.6%)
Bruising	3.0% (1.1%, 7.9%)
Breast/Skin Sensation Changes	2.2% (0.7%, 6.8%)
Hematoma	2.1% (0.7%, 6.3%)
Infection	1.4% (0.4%, 5.5%)

[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.

[2] The following complications were reported at a rate less than 1%: delayed wound healing, irritation, nipple complications, other complications, redness, and skin rash.

[3] The following complications were reported at a rate of 0%: capsule calcification, gel migration, implant extrusion, lymphadenopathy, lymphedema, pneumothorax, and tissue/skin necrosis.

Reasons for Reoperation

There were 455 additional surgical procedures performed during 177 reoperations involving 130 primary augmentation patients. The most common reason for reoperation through 7 years in primary augmentation patients was because of capsular contracture (27% of 177 reoperations). The most common type of surgical procedure through 7 years was capsule procedure (34% of 455 procedures).

There were 267 additional surgical procedures performed during 97 reoperations involving 56 revision-augmentation patients. The most common reason for reoperation through 7 years in revision-augmentation patients was also because of capsular contracture (21% of 97 reoperations). The most common type of surgical procedure through 7 years was capsule procedure (30% of 267 procedures).

Tables 3 and 4 provide the main reason for each reoperation performed through 7 years in primary augmentation and revision-augmentation patients.

Table 3

Main Reasons for Reoperation in Primary Augmentation Patients through 7 Years

Reason for Reoperation	n (%)
Capsular Contracture	47 (26.6%)
Implant Malposition	24 (13.6%)
Ptosis	21 (11.9%)
Need for Biopsy	19 (10.7%)
Suspected Rupture	13 (7.3%)
Hematoma/Seroma	12 (6.8%)
Patient Request for Size/Style Change	9 (5.1%)
Scarring/Hypertrophic Scarring	8 (4.5%)
Asymmetry	6 (3.4%)
Breast Cancer	3 (1.7%)
Breast Pain	3 (1.7%)
Delayed Wound Healing	3 (1.7%)
Implant Palpability/Visibility	2 (1.1%)
Infection	2 (1.1%)
Wrinkling	2 (1.1%)
Implant Extrusion	1 (0.6%)
Necrosis	1 (0.6%)
Nipple Complications	1 (0.6%)
Total	**177 (100%)**

Table 4

Main Reasons for Reoperation in Revision-Augmentation Patients through 7 Years

Reason for Reoperation	n (%)
Capsular Contracture	20 (20.6%)
Hematoma/Seroma	13 (13.4%)
Implant Malposition	11 (11.3%)
Ptosis	9 (9.3%)
Need for Biopsy	8 (8.2%)
Scarring/Hypertrophic Scarring	7 (7.2%)
Suspected Rupture	5 (5.2%)
Asymmetry	3 (3.1%)
Breast Cancer	3 (3.1%)
Infection	3 (3.1%)
Patient Request for Style/Size Change	3 (3.1%)
Nipple Complications	3 (3.1%)
Delayed Wound Healing	2 (2.1%)
Wrinkling	2 (2.1%)
Breast Pain, Breast Tissue Contour Deformity, Device Injury, Implant Palpability/Visibility, Implant Extrusion	1 each (1.0%)
Total	**97 (100%)**

Reasons for Implant Removal

For women receiving primary augmentation implants in Allergan's Core Study, 58 patients had 107 implants removed through 7 years. Of these 107 implants, 85 (79%) were replaced. Capsular contracture and patient request for style/size change were the most common reasons for implant removal.

For women receiving revision-augmentation implants in Allergan's Core Study, 32 patients had 59 implants removed through 7 years. Of these 59 implants, 51 (86%) were replaced. The most common reasons for implant removal were capsular contracture, patient request for style/size change, and implant malposition.

The main reasons for implant removal among primary augmentation and revision-augmentation patients in Allergan's Core Study over the 7 years are shown in Tables 5 and 6 below.

Table 5

Main Reason for Implant Removal for Primary Augmentation Patients through 7 Years

Reason for Removal	n (%)
Capsular Contracture	35 (32.7%)
Patient Request for Style/Size Change	22 (20.6%)
Implant Malposition	11 (10.3%)
Suspected Rupture	11 (10.3%)
Asymmetry	8 (7.5%)
Ptosis	5 (4.7%)
Breast Pain	4 (3.7%)
Wrinkling	4 (3.7%)
Breast Cancer	2 (1.9%)
Infection	2 (1.9%)
Breast Tissue Contour Deformity, Implant Extrusion, Need for Biopsy	1 each (0.9%)
Total	**107 (100%)**

Table 6

Main Reason for Implant Removal for Revision-Augmentation Patients through 7 Years

Reason for Removal	n (%)
Capsular Contracture	18 (30.5%)
Patient Request for Style/Size Change	10 (17.0%)
Implant Malposition	10 (17.0%)
Ptosis	6 (10.2%)
Suspected Rupture	4 (6.8%)
Scarring/Hypertrophic Scarring	3 (5.1%)
Breast Cancer	2 (3.4%)
Infection	2 (3.4%)
Wrinkling	2 (3.4%)
Asymmetry	1 (1.7%)
Breast Pain	1 (1.7%)
Total	**59 (100%)**

Other Clinical Data Findings

Below is a summary of clinical findings from Allergan's Core Study with regard to connective tissue disease (CTD), CTD signs and symptoms, cancer, lactation complications, reproduction complications, and suicide for primary augmentation and revision-augmentation patients. These issues, along with others, are being further evaluated as part of an Allergan postapproval study of a large number of patients followed through 10 years (BIFS).

CTD Diagnoses

Four primary augmentation patients (0.9%) were reported to have a new diagnosis of CTD; 2 with rheumatoid arthritis at 7 months and at 3 years after implantation in the Core Study and 2 patients with fibromyalgia at 4.5 years after implantation for both. One revision-augmentation patient (0.7%) was reported to have a new diagnosis of fibromyalgia at 10 months after implantation. It

cannot be concluded that these CTD diagnoses were caused by the implants because there was no comparison group of similar women without implants.

CTD Signs and Symptoms

In Allergan's Core Study, numerous signs and symptoms were collected. For primary augmentation patients at 6 years after implantation, statistically significant increases were found for the symptom category of Joint (includes joint pain, stiff in morning, swelling in other joints, and swelling of hands), Muscular (includes back pain, muscle pain, aches, or cramps, muscle weakness, neck pain, paralysis of arms or legs), Gastrointestinal (includes constipation, diarrhea, gastrointestinal pain, heartburn, loss of appetite, stomach pain or cramps, and vomiting), Neurological (includes headaches, loss of balance, numbness/tingle of arms or legs, problems with memory, problems with thinking, and ringing in ears), Urinary (includes problems with urination and urinating too often), and Fibromyalgia (includes back pain, fatigue, neck pain, pain, and pain in the chest). No significant increases were found in the categories of General, Global, Pain, Skin, Fatigue, and Other. For revision-augmentation patients at 7 years after implantation, no statistically significant increases were found in any of the symptom categories.

The Core Study was not designed to evaluate cause-and-effect associations because there is no comparison group of women without implants, and because other contributing factors, such as medications and lifestyle/exercise, were not studied. Therefore, it cannot be determined whether this increase was due to the implants or not, based on Allergan's Core Study. However, your patient should be aware that she may experience an increase in these symptoms after receiving breast implants.

Cancer

There was 1 primary augmentation patient with a new diagnosis of breast cancer through 7 years in the Core Study. There was a 13% benign breast disease rate and a 1% malignant breast disease rate. For revision-augmentation patients, there was 1 patient with a new diagnosis of breast cancer. There was a 15% benign breast disease rate and a 1% malignant breast disease rate through 7 years. In primary augmentation patients there was 1 report of thyroid cancer and 1 report of brain cancer. There were no reports of other cancers, such as respiratory or cervical/vulvar, in revision-augmentation patients.

Lactation Complications

16 (21%) of the 75 primary augmentation patients who attempted to breastfeed following breast implantation in the Core Study through 7 years experienced difficulty with breastfeeding. The most common difficulty was inadequate milk production. For the 19 revision-augmentation patients who attempted to breastfeed after receiving breast implants, 6 (32%) had difficulty breastfeeding, 5 due to inadequate milk production and 1 due to pain.

Reproduction Complications

29 (6%) of the primary augmentation patients in the Core Study reported a reproduction problem through 7 years, most commonly miscarriage. For the 5 (3.4%) revision-augmentation patients who experienced a reproduction problem through 7 years, the most common problem was infertility.

Suicide

There was 1 report of suicide in the primary augmentation patients and 2 reports of suicide in the revision-augmentation patients in the Core Study through 7 years.

PRIMARY RECONSTRUCTION AND REVISION-RECONSTRUCTION PATIENTS

Patient Accounting (Follow-Up Rates)

Allergan's Core Study enrolled 98 reconstruction patients. Of the women expected to be seen at the 7-year follow-up visit, 87% were seen.

Allergan's Core Study enrolled 15 revision-reconstruction patients. Of the women expected to be seen at the 7-year follow-up visit, 83% were seen.

Effectiveness Outcomes

The benefits of silicone gel-filled 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 for those patients who still had their original implants and who came back for these visits.

Primary Reconstruction Patients: 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 98 patients, 63 (64%) provided a satisfaction rating at 7 years after implantation, with 57 (90%) of these patients indicating that they were satisfied with their breast implants.

Quality of life assessments were made at 1, 2, 4, and 6 years post-implant. Therefore, 6 year data is provided herein. For primary reconstruction patients, the SF-36, which measures mental and physical health, showed no changes after 6 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 6 years after receiving implants. Patient responses to questions on the Body Esteem Scale regarding overall body image also did not show a change 6 years after receiving implants.

Revision-Reconstruction Patients: Allergan's 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, 10 (67%) provided a satisfaction rating at 7 years. Of these 10 patients, 9 (90%) 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.

Safety Outcomes

Tables 7 and 8 describe the complications experienced by primary reconstruction and revision-reconstruction patients in Allergan's Core Study. The rates reflect the number of patients out of 100 who experienced the listed complication at least once within the first 7 years after their implantation. Some complications occurred more than once for some patients.

Table 7
7-Year Complication Rates for Primary Reconstruction Patients
N = 98 Patients

Key Complications[1]	% (95% CI)
Reoperation	53.3% (43.3%, 63.9%)
Implant Removal with Replacement	23.7% (16.1%, 34.2%)
Capsular Contracture Baker Grade III/IV	17.1% (10.6%, 26.8%)
Implant Rupture (MRI cohort)[2]	11.4% (4.9%, 25.3%)
Implant Removal without Replacement	7.7% (3.5%, 16.4%)

Other Complications occurring in ≥ 1% of patients[3]	% (95% CI)
Asymmetry	22.8% (15.3%, 33.3%)
Wrinkling/Rippling	9.1% (4.4%, 18.4%)
Swelling	7.1% (3.5%, 14.4%)
Breast Pain	4.8% (1.8%, 12.6%)
Scarring/Hypertrophic Scarring	4.5% (1.7%, 11.5%)
Implant Palpability/Visibility	4.1% (1.3%, 12.1%)
Implant Malposition	3.9% (1.3%, 11.9%)
Nipple Complications	3.3% (1.1%, 9.8%)
Infection	3.2% (1.0%, 9.5%)
Tissue/Skin Necrosis	2.3% (0.6%, 8.8%)
Redness	2.1% (0.5%, 8.3%)
Skin Rash	2.0% (0.5%, 7.9%)
Hematoma	1.5% (0.2%, 10.4%)
Bruising, Delayed Wound Healing, Implant Extrusion, Other Complications	1.0% each (0.1%, 7.1%)

[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.

[2] MRI cohort sample size for Reconstruction equals 51 patients. No ruptures were reported in the non-MRI cohort, which had a sample size of 47 patients.

[3] The following complications were reported at a rate of 0%: breast/skin sensation changes, capsule calcification, gel migration, irritation, lymphadenopathy, lymphedema, pneumothorax, ptosis, and seroma/fluid accumulation.

Table 8
7-Year Complication Rates for Revision-Reconstruction Patients
N = 15 Patients

Key Complications[1]	% (95% CI)[2]
Reoperation	40.0% (16.3%, 67.7%)
Implant Removal with Replacement	6.7% (0.2%, 31.9%)
Capsular Contracture Baker Grade III/IV	6.7% (0.2%, 31.9%)
Implant Removal without Replacement	0% (N/A)
Implant Rupture (MRI cohort)[3]	0% (N/A)

Other Complications occurring in ≥ 1% of patients[4]	% (95% CI)
Asymmetry	13.3% (1.7%, 40.5%)
Implant Malposition	13.3% (1.7%, 40.5%)
Breast Pain	6.7% (0.2%, 31.9%)
Bruising	6.7% (0.2%, 31.9%)
Lymphedema	6.7% (0.2%, 31.9%)
Implant Palpability/Visibility	6.7% (0.2%, 31.9%)
Seroma/Fluid Accumulation	6.7% (0.2%, 31.9%)
Wrinkling/Rippling	6.7% (0.2%, 31.9%)
Skin Rash	6.7% (0.2%, 31.9%)

[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.

[2] Calculated as a percentage of enrolled with binomial confidence interval.

[3] MRI cohort sample size for Revision-Reconstruction equals 5 patients. No ruptures were reported in the non-MRI cohort, which had a sample size of 10 patients.

[4] The following complications were reported at a rate of 0%: breast/skin sensation changes, capsule calcification, delayed wound healing, gel migration, hematoma, implant extrusion, infection, irritation, lymphadenopathy, nipple complications, other complications, pneumothorax, ptosis, redness, scarring/hypertrophic scarring, swelling, and tissue/skin necrosis.

Reasons for Reoperation

There were 155 additional surgical procedures performed during 73 reoperations involving 49 primary reconstruction patients. The most common reason for reoperation through 7 years in primary reconstruction patients was because of implant malposition (19% of 73 reoperations). The most common type of surgical procedure through 7 years was capsule procedure (28% of 155 procedures).

There were 11 additional surgical procedures performed during 9 reoperations involving 6 revision-reconstruction patients. The most common reason for reoperation through 7 years in revision-reconstruction patients was because of nipple complications (5 out of 9 reoperations). The most common type of surgical procedure through 7 years was revision of nipple reconstruction/tattoo (6 out of 11 procedures).

Tables 9 and 10 provides the main reason for each reoperation performed through 7 years in primary reconstruction and revision-reconstruction patients.

Table 9
Main Reasons for Reoperation For Primary Reconstruction Patients Through 7 Years

Reason for Reoperation	n (%)
Implant Malposition	14 (19.2%)
Asymmetry	12 (16.4%)
Capsular Contracture	10 (13.7%)
Need for Biopsy	8 (11.0%)
Hematoma/Seroma	6 (8.2%)
Ptosis	4 (5.5%)
Patient Request for Style/Size Change	3 (4.1%)
Scarring/Hypertrophic Scarring	3 (4.1%)
Suspected Rupture	3 (4.1%)
Breast Cancer, Breast Tissue Contour Deformity, Implant Extrusion	2 each (2.7%)
Delayed Wound Healing, Necrosis, Nipple Complications, Wrinkling	1 each (1.4%)
Total	**73 (100%)**

Table 10
Main Reasons for Reoperation For Revision-Reconstruction Patients Through 7 Years

Reason for Reoperation	n (%)
Nipple Complications	5 (55.6%)
Asymmetry	1 (11.1%)
Capsular Contracture	1 (11.1%)
Ptosis	1 (11.1%)
Scarring/Hypertrophic Scarring	1 (11.1%)
Total	**9 (100%)**

Reasons for Implant Removal

For women receiving primary reconstruction implants in Allergan's Core Study, 27 patients had 34 implants removed through 7 years. Of these 34 implants, 27 (79%) were replaced. For women receiving revision-reconstruction implants in Allergan's Core Study, 1 patient had 1 implant removed due to asymmetry through 7 years. This implant was replaced. The main reasons for implant removal among primary reconstruction patients in the Allergan Core Study over the 7 years are shown in Table 11 below.

Table 11
Main Reasons for Implant Removal For Primary Reconstruction Patients Through 7 Years

Reason for Removal	n (%)
Implant Malposition	9 (26.5%)
Asymmetry	7 (20.6%)
Capsular Contracture	7 (20.6%)
Patient Request for Style/Size Change	4 (11.8%)
Suspected Rupture	3 (8.8%)
Hematoma/Seroma, Implant Extrusion, Necrosis, Wrinkling	1 each (2.9%)
Total	**34 (100%)**

Other Clinical Data Findings

Below is a summary of clinical findings from the Allergan Core Study with regard to connective tissue disease (CTD), CTD signs and symptoms, cancer, lactation complications, reproduction complications, and suicide for primary reconstruction and revision-reconstruction patients. These issues, along with others, are being evaluated as part of an Allergan postapproval study (BIFS) of a large number of patients followed through 10 years.

CTD Diagnoses

There was 1 primary reconstruction patient (1%) in the Core Study who was reported to have a new diagnosis of an undifferentiated CTD at 3 months after implantation and 1 patient (1%) with

a new diagnosis of rheumatoid arthritis at 5.5 years after implantation. No revision-reconstruction patients had new diagnoses of a CTD through 7 years. These data should be interpreted with caution because there was no comparison group of similar women without implants.

CTD Signs and Symptoms

In Allergan's Core Study, numerous signs and symptoms were collected at 2, 4, and 6 years post-implant. For primary reconstruction patients at 6 years after implantation, a statistically significant increase was found for the symptom category of Joint (includes joint pain, stiffness in the morning, and swelling in other joints or hands). No significant increases were found in the categories of General, Skin, Muscular, Neurological, Urinary, Fatigue, Pain, Fibromyalgia, Global, and Other. For revision-reconstruction patients at 6 years after implantation, no statistically significant increases were found in any domain category.

The Core Study was not designed to evaluate cause and effect associations because there is no comparison group of women without implants, and because other contributing factors, such as medications and lifestyle/exercise, were not studied. Therefore, it cannot be determined whether this increase was due to the implants or not, based on the Allergan Core Study. However, your patient should be aware that she may experience an increase in these symptoms after receiving breast implants.

Cancer

There were 8 primary reconstruction patients (8%) with new reports of breast cancer through 7 years in the Core Study. There was a 17% benign breast disease rate and a 10% malignant breast disease rate through 7 years. For revision-reconstruction patients, there were no reports of new diagnoses or reoccurrence of breast cancer. There was a 7% benign breast disease rate through 7 years. There were no reports of other cancers, such as brain, respiratory, or cervical/vulvar in primary reconstruction or revision-reconstruction patients.

Lactation Complications

One of the 98 primary reconstruction patients attempted to breastfeed following breast implantation in the Core Study through 7 years and did not experience any difficulties. No revision-reconstruction patients attempted to breastfeed after receiving breast implants.

Reproduction Complications

Two (2%) of the primary reconstruction patients in the Core Study reported a reproduction problem through 7 years. No revision-reconstruction patients experienced a post-implantation reproduction problem.

Suicide

There were no reports of suicide in the primary reconstruction and revision-reconstruction patients in the Core Study through 7 years.

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. Stickers are also included for the Device Tracking Form and the patient's Device Identification Card.

Surgical Planning

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

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, 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 Gel-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 gel-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 and accessories from their packages in an aseptic environment and using talc-free gloved hands.

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

DO NOT resterilize the product.

Avoid unnecessary exposure of the breast implant to lint, talc, sponges, towels, skin oils, and other contaminants.

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

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 Product Support Department at 800.624.4261.

Surgical Placement Procedure

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.

A sterile BIOCELL® Delivery Assistance Sleeve is available separately and can be used to assist with placement of the breast implant. Use of this sleeve for insertion of BIOCELL® textured breast implants provides a shell/tissue interface with less friction. Insert the implant into one end of the sleeve. Insert the proximal end of the sleeve into the surgically prepared pocket. With the tissue retracted, the sleeve can be twisted at its distal end to gently guide the breast implant into the pocket. Once the breast implant is inserted, gently remove the sleeve.

DO NOT use lubricants to facilitate placement. Their use creates the risk of pocket contamination and may also affect the tissue-capsule interface.

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 gel-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.

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.

ALLERGAN ACADEMY™ Educational Materials are available through www.allerganacademy.com to supplement surgical knowledge of the dimensional techniques recommended for use with *NATRELLE*® breast implants.

Documentation the Physician Should Provide to the Patient

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

- *Patient Planner*

Designed specifically for Augmentation and for Reconstruction patients, the Patient Planner contains ***Breast Augmentation/Reconstruction with NATRELLE® Silicone-Filled Breast Implants (the patient labeling)*** and should be used to facilitate patient education on the risks and benefits of silicone gel-filled breast implant surgery. The patient labeling 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 form and using this as a foundation for subsequent preoperative discussion.

- *Device Identification Card*

Enclosed with each silicone gel-filled breast implant is Allergan's Device Identification Card. To complete Allergan's Device Identification Card, place one device identification sticker for each implant on the back of the card. Stickers are located on the internal product packaging attached to the label. If a sticker is unavailable, the lot number, catalog number and description of the device may be copied by hand from the device label. Patients should be provided with these cards for personal reference. They should record their device identification information on the Patient Surgery Record form in their Patient Planner and place the Device Identification Card in the pocket provided inside the front cover of their Patient Planner.

ADDITIONAL SPECIFIC PRODUCT INFORMATION

BIOCELL® Delivery Assistance Sleeve

Sterile BIOCELL® Delivery Assistance Sleeves are available from your Allergan Breast Aesthetics Business Development Manager or Customer Care Department at 800.766.0171.

Returned Goods Policy

Product returns should be handled through an Allergan Breast Aesthetics Business Development Manager or through the Customer Care Department at 800.766.0171. 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 800.624.4261 for an Explant Kit and explant return instructions.

ConfidencePlus® Limited Warranties
The *ConfidencePlus®* Limited Warranties provide lifetime replacement and limited financial reimbursement in the event of shell leakage or breakage resulting in implant rupture, subject to certain conditions as fully discussed in the *ConfidencePlus®* literature. Allergan offers two levels of coverage under its warranty program. Our standard *ConfidencePlus®* Limited Warranty program applies automatically to every *NATRELLE®* breast implant recipient subject to the conditions discussed in the *ConfidencePlus®* literature. The optional *ConfidencePlus®* Premier Limited Warranty program is available for a low enrollment fee and increases the financial benefit in the event of implant rupture, subject to the conditions discussed in the *ConfidencePlus®* literature. For more information, please contact Allergan's Product Support Department at 800.624.4261.

Product Ordering
To order directly in the U.S.A or for product information, please contact your local Allergan Breast Aesthetics Business Development Manager or the Allergan Customer Care Department at 800.766.0171.

Reporting Problems
The Food and Drug Administration (FDA) requires that serious injuries (defined as those that need medical or surgical intervention to prevent permanent damage) be reported by hospitals if they are aware of the serious injuries. In addition, injuries or complications can be voluntarily reported directly by the patient to FDA's MedWatch.

If you have a patient who has experienced one or more serious problems related to her breast implants, you are encouraged to report the serious problem(s) to the FDA through the MedWatch voluntary reporting system. Examples of serious problems include disability, hospitalization, harm to offspring, and medical or surgical intervention to prevent lasting damage.

You are also required to report any product problem or serious adverse event to Allergan. Deaths must be reported to Allergan and FDA. You can report by telephone to 1-800-FDA-1088; by FAX, use Form 3500 to 1-800-FDA-0178; electronically at **http://www.fda.gov/medwatch/index.html**; or by mail to MedWatch Food and Drug Administration, HF-2, 5600 Fishers Lane Rockville, MD 20857-9787. **Keep a copy of the completed MedWatch form for your records.**

This information reported to MedWatch is entered into databases to be used to follow safety trends (patterns) of a device and to determine whether further follow-up of any potential safety issues related to the device is needed.

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