BARRIGEL® INJECTABLE GEL
INSTRUCTIONS FOR USE

CAUTION: Federal law restricts this device to sale by or on the order of a physician.

COMPOSITION

Sodium hyaluronic acid (HA), stabilized	20 mg/ml
Phosphate buffered saline	q.s.

DEVICE DESCRIPTION

Barrigel is a sterile, transparent gel of stabilized sodium hyaluronate (HA) of non-animal origin at a concentration of 20 mg/ml in phosphate buffered saline.

Barrigel is supplied in a glass syringe sealed with a plunger and tip cap. The syringe is equipped with a plunger rod, finger grip, luer-lock connector, and rigid plastic tip cap shell. Each syringe contains 3 ml of Barrigel. The product is for single use only. Each syringe is terminally moist-heat sterilized in a sealed transparent pouch and packed in a cardboard carton.

Barrigel is recommended for use with a sterile, 18G x 20 cm applicator needle (e.g., Barrigel Applicator Needle).

Patient record labels are included in the product carton. These labels are to be attached to patient records to ensure traceability of the product.

ELECTRONIC IFU

A copy of this Barrigel Instructions for Use document in pdf format is available at www.barrigel.com.

In addition, paper copies of the Barrigel IFU may be requested by calling (844) 822-7744. A paper copy will be provided to the requestor within 72 hours.

INDICATIONS FOR USE

Barrigel is intended to temporarily position the anterior rectal wall away from the prostate during radiotherapy for prostate cancer and, in creating this space, it is the intent of Barrigel to reduce the radiation dose delivered to the anterior rectum. Barrigel is composed of biodegradable material and maintains space for the entire course of prostate radiotherapy treatment and is intended to be absorbed by the patient's body over time.

Barrigel should only be administered by qualified and properly trained physicians with experience in ultrasound guidance and injection techniques in the urogenital/pelvic area.

MODE OF ACTION

Barrigel acts by adding volume to the perirectal tissue, thereby mechanically creating an increased distance between the prostate and the anterior rectal wall. The product degrades over time.

CONTRAINDICATIONS

Barrigel is contraindicated in prostate cancer patients with clinical stage T4 disease.

WARNINGS

- Injection of air, fluid, or Barrigel intravascularly could potentially lead to arterial or venous embolism, vascular occlusion, ischemia, and necrosis. Physicians should aspirate to verify the needle tip is not in a blood vessel. If no blood is observed, injection of Barrigel may proceed. If any blood is observed, discontinue the procedure.
- Barrigel should be inserted under ultrasound guidance to maintain needle tip visibility and prevent rectal wall penetration.
- If the needle enters the rectal lumen at any time during the procedure, abandon the procedure to avoid infection.
- Do not use in patients with bleeding disorders, or in patients who are taking thrombolytics or anticoagulants such as Warfarin, before consulting a specialist in hematology.
- Do not inject if the patient is known to be allergic to hyaluronic acid-based products or has a history of hypersensitivity to streptococcal proteins, as the product may contain trace amounts of such material.
- Do not resterilize Barrigel as this will damage the product.
- Do not mix with other products.
- Do not use Barrigel if the expiration date or lot number is missing or illegible on the packaging.

PRECAUTIONS

- Injection procedures are associated with a risk of infection. Aseptic technique and standard practice to prevent perioperative injections are to be observed.
- Knowledge of the anatomy of the treatment site and special caution are required to avoid perforation or compression of vessels and other vulnerable structures and organs such as prostate, rectal wall, bladder, and urethra.
- Do not use where there is ongoing inflammation or infection, in or near the intended treatment site.
- Patients who are using substances that affect platelet function such as acetylsalicylic acid or non-steroidal anti-inflammatory drugs may experience, as with any injection, increased bruising, or bleeding at the injection sites.
- Patients with hemorrhoids should be evaluated for hemorrhoidal treatment prior to injection with Barrigel.
- For patients with an immunodeficiency disorder and/or undergoing immunosuppressive therapy, a specialist in infectious diseases should be consulted prior to injection with Barrigel.
- For patients with pre-existing anorectal constrictions such as anal fissures, stenosis or other malformation, a colorectal surgeon or proctologist should be consulted prior to treatment.
- Pre-existing scar tissue, strictures, stenosis, or adherences in the perirectal fat may affect the ability to inject Barrigel.
- There is no experience with injecting more than 12 ml of Barrigel.
- Do not inject into the anorectal region if another injectable implant [other than Barrigel] or non-injectable implant is present.
- Positioning the Barrigel implant may be more challenging in recurrent prostate cancer patients who have undergone previous local prostate cancer treatments.
- Injection should be stopped if excessive bleeding occurs.
- Care should be taken with the handling of the glass syringe and needle to avoid laceration or other injury.
- Positioning the needle may be more challenging when exchanging syringes.
- The device should be discarded if accidentally contaminated.
- Discard opened, unused Barrigel that has been accidentally contaminated.
- If placing fiducials, do so with a transperineal approach prior to Barrigel injection.
- Barrigel is provided sterile. Do not use if the packaging or seal has been damaged or opened.
- Barrigel has not been tested in children.

- As only a limited number (6% = 6/98) of patients were followed to complete resorption at 18 months, it is unknown if there are potential late complications or side effects of incompletely absorbed gel. The table below represents resorption data available for 96 patients at the 3-month visit, 55 patients at the 12-month visit, and 20 patients at the 18-month visit. There is currently no evidence to reflect potential late complications or side effects on incompletely resorbed gel.

Table 1. Resorption of Barrigel over Time (as reflected by patient visit)

VISIT	STATISTIC	PERCENT RESORPTION
IMMEDIATE POST-INJECTION	N (Patients)	**98**
	Min	0%
	Max	0%
	Mean	0%
	Standard Deviation	0
3-MONTH VISIT	N (Patients)	**96**
	Min	-11.4%*
	Max	66.8%
	Mean	18.4%
	Standard Deviation	15.4
12-MONTH VISIT	N (Patients)	**55**
	Min	20.4%
	Max	90.3%
	Mean	57.2%
	Standard Deviation	16.8
18-MONTH VISIT	N (Patients)	**20**
	Min	35.0%
	Max	93.9%
	Mean	73.6%
	Standard Deviation	15.5

* Negative resorption in some subjects due to the hydrophilic nature of Barrigel and the temporary increase in water present at the point of injection.

COMPLICATIONS

Anticipated procedure-related side effects may include pain at the injection site and short transient injection site bleeding from the needle stick. Post treatment anticipated side effects include mild to moderate sensation of rectal filling which may lead to attempts to force defecation. In the Barrigel Prostate Trial, providing information to the patient that this symptom may be expected after Barrigel treatment showed that the symptom was accepted by the patient without any attempt to force defecation.

Other adverse events that may occur after injection of Barrigel include injection site discomfort, injection site irritation, injection site bleeding or hematoma, injection site inflammation, infection, dysuria, or a weak urine

stream. Injection of an excessive volume of Barrigel may cause rectal tissue tension possibly with rectal pain or discomfort and painful and/or difficult defecation, or constipation due to pressure effect. Unintentional injection leading to perforation or compression of vulnerable structures and organs such as vessels, nerves, prostate, rectal wall, rectal lumen, bladder, urethra, and urethral sphincter may cause bleeding, hematoma, prostatitis, focal rectal mucosal necrosis, urinary retention, or erectile dysfunction.

Inadvertent injection in vessels may cause vascular occlusion or distal embolization. To secure correct placement of Barrigel, ultrasound guidance should be used when performing the injection.

Isolated cases of transient rectal hemorrhage in the presence of concomitant hemorrhoids [onset 3 days post injection], fever [onset 5 days post injection], acute prostatitis [onset 10 days post injection] and urinary incontinence [onset 60 days post injection] have been reported.

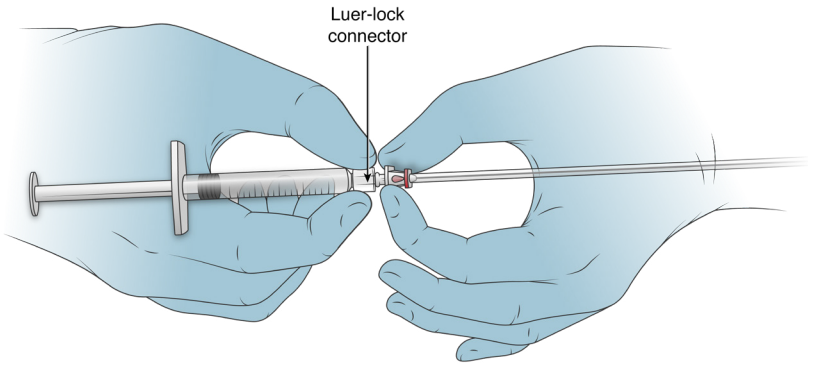
INJECTION PROCEDURE

- The injection procedure should be performed under local anesthesia. Further anesthesia can be provided at the discretion of the physician.
- For the safe use of Barrigel, it is important to use a sterile needle with a hub that fits the luer lock of the syringe. It is recommended to use an 18G or wider needle with a length of up to 20 cm (e.g., Barrigel Applicator Needle). Use of needles other than those recommended should be avoided.

ASSEMBLY OF NEEDLE TO SYRINGE

Remove stylet from the needle. Use the thumb and forefinger to grasp the needle by the hub. With the other hand, hold the syringe by the luer-lock connector. Important: DO NOT hold the glass syringe body. Connect and twist while holding the luer lock and hub. Create a firm connection (DO NOT overtighten). See the figure below.

Strict aseptic technique must be followed. Improper assembly may result in separation of the needle and syringe at injection.



To avoid an interruption in patient treatment or the need to repeat the procedure because of leakage, or accidental contamination or damage of a syringe or needle, it is recommended that extra syringes and needles be kept in inventory.

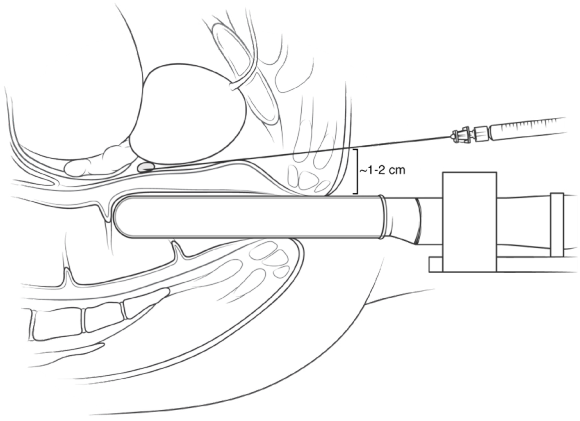
TREATMENT PREPARATION

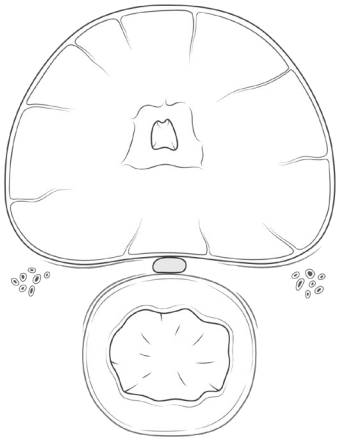
- The patient should be informed about the indications, precautions, and potential adverse events prior to treatment.
- The injection procedure should be performed under local anesthesia. Further anesthesia can be provided at the discretion of the physician.
- The rectum should be made as empty as possible as per institutional standard (e.g., fleet enema).

- Antibiotic prophylaxis should be administered before injection of Barrigel.
- Aseptic technique is to be observed.
- The patient should be suitably positioned for transperineal injection.
- Prepare the biplane probe with a standoff (endocavity balloon) or condom probe cover with ultrasound gel, avoiding air bubbles.
- Insert probe and advance to the base of the prostate. Ensure contact with the probe is optimal for image clarity. Check axial and sagittal views for quality imaging of critical anatomical structures.
  - If critical anatomical structures cannot be identified, check for rectal prep and gas, probe position and ultrasound settings.
- Identify perirectal fat and target zone. Target zone should be at the thickest portion of the perirectal fat, typically in the seminal vesicle/base area, where the needle tip can be furthest from the rectum as possible.
  - Be aware of the 5 and 7 o'clock positions on axial view where vascular bundles are typically present.

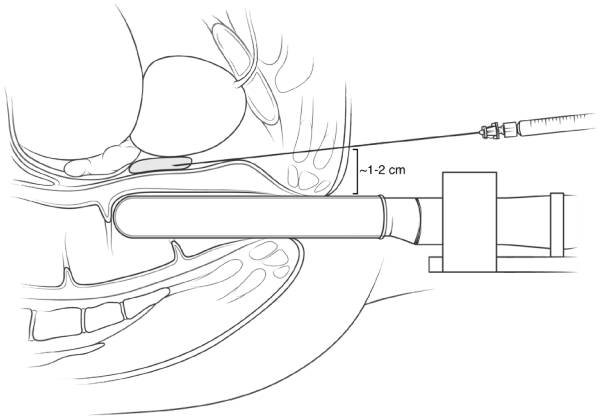
PROCEDURE

- Prime the needle with Barrigel to remove any air in the needle by pressing the plunger rod carefully until a small droplet of product is visible at the tip of the needle.
- To secure correct placement of Barrigel, ultrasound guidance should be used when performing the injection.
- Insert needle ~ 1-2 cm above the ultrasound probe. Angle the needle tip, bevel down, over the rectal hump, through the perirectal fat, under the Denonvilliers' fascia.
- Further advance the needle to the target zone, keeping the needle orthogonal to probe to ensure visualization of needle tip.
  - Care should be taken to avoid perforation of the prostate capsule with the needle tip and to keep the tip as far as possible from the capsule without perforating the rectum. To avoid breakage, do not attempt to bend the needle.
  - Do not apply excessive pressure to the syringe at any time. Presence of pre-existing scar tissues, strictures, stenosis, or adherences in the perirectal fat may impede advancement of the needle. If resistance is encountered, the needle should be partially withdrawn and checked for function.
- Using ultrasound guidance, and in both sagittal and axial views, verify the needle tip is in target zone then begin dissection by injecting a small bolus (0.5cc) of Barrigel. Confirm placement at midline in axial and sagittal views.
  - If needle is not midline, reposition the needle and repeat first steps.
  - Be aware of the 5 and 7 o'clock positions on axial view where vascular bundles are typically present.

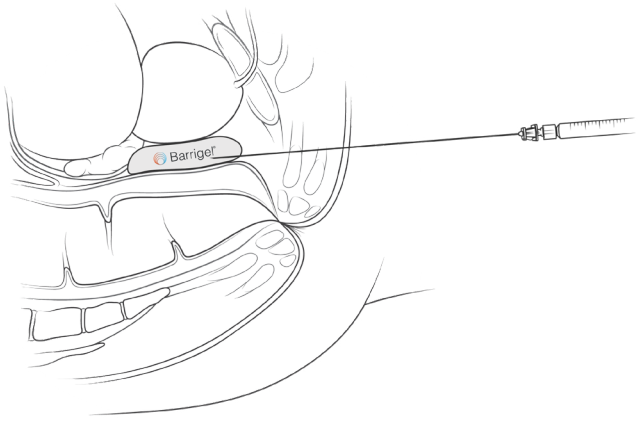




- After the insertion of the needle and prior to injection of Barrigel, the user should aspirate by pulling back on the syringe plunger to ensure that the needle tip has not accidently punctured a blood vessel. If any blood is observed, discontinue the procedure.
- Inject Barrigel slowly into the anterior perirectal fat, while pulling the syringe backwards, under continuous ultrasound guidance in order to view and verify the new space created by the injection.



- After injecting the first syringe, check implant placement on axial view and attach the second syringe to slowly continue Barrigel deployment.
  - After attaching and prior to injecting the second and third syringes, reverify needle tip location.
- Maintain visualization throughout the entire procedure.
  - If visualization of needle tip is lost during the procedure, stop and follow needle tip verification steps to re-verify needle tip location.
- A volume of 9 ml of Barrigel is adequate to create a space of 1 cm. Based on individual patient anatomy, a larger volume of Barrigel may be used. Use of up to 12 ml has been documented with no adverse issues.



- Stop the injection procedure if the patient experiences excessive bleeding or pain.
- Do not re-shield used needles. The syringe, disposable needle and any unused material must be discarded immediately after the treatment session and must not be reused due to risk of contamination of the unused material and associated risks, including infections. Disposal should be in accordance with accepted medical practice and applicable national, local, or institutional guidelines.

POST-TREATMENT CARE

- The patient should be informed about the risk of infection and potential mild to moderate sensation of rectal filling and to contact the treating physician if they experience rectal bleeding, bloody diarrhea, fever, tenesmus, or problems with urinating.
- The patient should be made aware that the implant might be detected by anorectal examinations and radiographic imaging of the pelvis and that future physicians should be informed that the patient had a treatment with Barrigel.

SHELF-LIFE AND STORAGE

The expiration date is indicated on the package. Store up to 25° C (77° F). Protect from freezing and sunlight.

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