
ATRISORB[®]-D FreeFlow[™]

Bioabsorbable Guided Tissue Regeneration (GTR) Barrier with 4% Doxycycline

Manufactured by TOLMAR Inc.

Fort Collins, CO 80526

To Order Call: (877) 865-6271

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FreeFlow[™] is a trademark of TOLMAR Inc.

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INSTRUCTIONS FOR USE



See Instructions for Use



Expiration Date

Good through end of month
indicated



Do Not Reuse

LOT

Lot Number

REF

Catalog Number

30°C 86°F
15°C 59°F



Storage Temperature

STERILE

R

Radiation

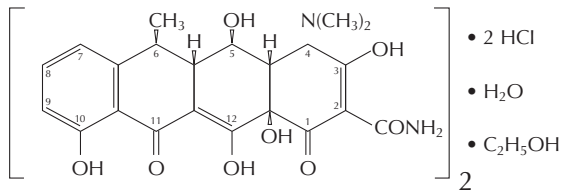
ATRISORB[®]-D FreeFlow[™] Bioabsorbable Guided Tissue Regeneration (GTR) Barrier with 4% Doxycycline

Formulation Description

The ATRISORB[®]-D FreeFlow[™] Bioabsorbable GTR Barrier with 4% Doxycycline (hereafter referred to as the ATRISORB[®]-D FreeFlow[™] Barrier) is formed after adding doxycycline hyclate to a flowable polymeric formulation composed of poly(DL-lactide) (PLA) dissolved in *N*-methyl-2-pyrrolidone (NMP).

Device Description

The ATRISORB[®]-D FreeFlow[™] Barrier contains foil pouches, each containing a single-patient use kit, and general use stainless steel cannulae for application of the formulation. Each pouched kit is comprised of one pouched capped syringe containing 715 mg of the ATRISORB[®] polymer formulation and one capped syringe containing 35 mg of doxycycline. Doxycycline is a synthetically derived broad-spectrum antibiotic in the tetracycline family.¹ The structural formula of doxycycline is:



Empirical Formula: (C₂₂H₂₄N₂O₈•HCl)₂•C₂H₆O•H₂O

¹ Stratton CW, Lorian V. Mechanisms for action for antimicrobial agents: general principles and mechanisms for selected classes of antibiotics. *Antibiotics in Laboratory Medicine, 4th edition, Williams and Wilkins, Baltimore MD, 1996.*

Mechanics

The ATRISORB[®]-D FreeFlow[™] Barrier functions as a guided tissue regeneration barrier by isolating the regenerative surgical site from the adjacent gingival connective tissue and epithelium. This facilitates population of the surgical site with cells from the periodontal ligament and adjacent alveolar bone that lead to regeneration. Additionally, it provides doxycycline at the surgical site that reduces bacterial colonization of the barrier.

Storage

15°-30°C (59°-86°F)

How Supplied

The ATRISORB[®]-D FreeFlow[™] Barrier is supplied as a sterile, single-patient use kit.

Clinical Study

A well-controlled, multi-center, single blind, randomized clinical study designed to evaluate bacterial growth on the barrier was carried out. Results of this study demonstrated that treatment of Class II furcations with the ATRISORB[®]-D FreeFlow[™] Barrier resulted in statistically superior reductions in total anaerobes and suspected periodontal pathogens at multiple time points in comparison to the ATRISORB[®] GTR Barrier.

Tables 1 through 7 below show the mean pathogen count and percent reductions at each timepoint for total anaerobes and six suspected periodontal pathogens.

TABLE 1:
 Mean and Percent Change in Total Anaerobes
 ATRISORB®-D FreeFlow™ Barrier with 4% Doxycycline -vs- ATRISORB® GTR Barrier

	ATRISORB®-D FreeFlow™ Barrier with 4% Doxycycline		ATRISORB® GTR Barrier	
	Mean Count	% Change	Mean Count	% Change
Baseline	4,128,096	–	5,302,817	–
Day 1	18,417	– 99.6	962,962	– 81.8
Day 7	213,840	– 94.8	53,220,536	+ 903.6
Day 21	1,743,512	– 57.8	2,152,119	– 59.4
Week 6	1,366,399	– 66.9	5,261,491	– 0.8

TABLE 2:
 Mean and Percent Change in *A. actinomycetemcomitans*
 ATRISORB®-D FreeFlow™ Barrier with 4% Doxycycline -vs- ATRISORB® GTR Barrier

	ATRISORB®-D FreeFlow™ Barrier with 4% Doxycycline		ATRISORB® GTR Barrier	
	Mean Count	% Change	Mean Count	% Change
Baseline	589	–	8,154	–
Day 1	1	– 99.9	0	– 100.0
Day 7	0	– 100.0	103	– 98.7
Day 21	66	– 88.8	107	– 98.7
Week 6	42	– 92.9	1,266	– 84.5

TABLE 3:
 Mean and Percent Change in *P. gingivalis*
 ATRISORB®-D FreeFlow™ Barrier with 4% Doxycycline -vs- ATRISORB® GTR Barrier

	ATRISORB®-D FreeFlow™ Barrier with 4% Doxycycline		ATRISORB® GTR Barrier	
	Mean Count	% Change	Mean Count	% Change
Baseline	53,843	–	43	–
Day 1	1	– 100.0	4	– 89.7
Day 7	0	– 100.0	122	+ 181.6
Day 21	2	– 100.0	163	+ 275.9
Week 6	2	– 100.0	6,748	+ 15,415.2

TABLE 4:
 Mean and Percent Change in *P. intermedia/P. nigrescens*
 ATRISORB®-D FreeFlow™ Barrier with 4% Doxycycline -vs- ATRISORB® GTR Barrier

	ATRISORB®-D FreeFlow™ Barrier with 4% Doxycycline		ATRISORB® GTR Barrier	
	Mean Count	% Change	Mean Count	% Change
Baseline	574,823	–	577,651	–
Day 1	2,192	– 99.6	717	– 99.9
Day 7	193	– 100.0	23,965	– 95.9
Day 21	2,928	– 99.5	62,931	– 89.1
Week 6	26,842	– 95.3	432,463	– 25.1

TABLE 5:
 Mean and Percent Change in *B. forsythus*
 ATRISORB®-D FreeFlow™ Barrier with 4% Doxycycline -vs- ATRISORB® GTR Barrier

	ATRISORB®-D FreeFlow™ Barrier with 4% Doxycycline		ATRISORB® GTR Barrier	
	Mean Count	% Change	Mean Count	% Change
Baseline	5,660	–	66,967	–
Day 1	10	– 99.8	0	– 100.0
Day 7	0	– 100.0	81	– 99.9
Day 21	843	– 85.1	0	– 100.0
Week 6	1,362	– 75.9	98,215	+ 46.7

TABLE 6:
 Mean and Percent Change in *F. nucleatum*
 ATRISORB®-D FreeFlow™ Barrier with 4% Doxycycline -vs- ATRISORB® GTR Barrier

	ATRISORB®-D FreeFlow™ Barrier with 4% Doxycycline		ATRISORB® GTR Barrier	
	Mean Count	% Change	Mean Count	% Change
Baseline	10,058	–	16,567	–
Day 1	8	– 99.9	0	– 100.0
Day 7	44	– 99.6	806	– 95.1
Day 21	2,968	– 70.5	1,057	– 93.6
Week 6	966	– 90.4	1,147	– 93.1

TABLE 7:
 Mean and Percent Change in *C. rectus*
 ATRISORB®-D FreeFlow™ Barrier with 4% Doxycycline -vs- ATRISORB® GTR Barrier

	ATRISORB®-D FreeFlow™ Barrier with 4% Doxycycline		ATRISORB® GTR Barrier	
	Mean Count	% Change	Mean Count	% Change
Baseline	22,639	–	30,304	–
Day 1	26	– 99.9	51	– 99.8
Day 7	9	– 100.0	108	– 99.6
Day 21	28	– 99.9	1,703	– 94.4
Week 6	1,608	– 92.9	12,604	– 58.4

ATRISORB®-D FreeFlow™ Barrier - Indications

ATRISORB®-D FreeFlow™ Barrier is indicated for the surgical treatment of periodontal defects to aid in the regeneration and integration of tissue components in guided tissue regeneration procedures. ATRISORB®-D FreeFlow™ Barrier has been shown to reduce bacterial colonization of the barrier at the site of GTR surgery. ATRISORB®-D FreeFlow™ Barrier is not intended for use in defects outside the indications statement.

ATRISORB®-D FreeFlow™ Barrier - Contraindications

Patients who are allergic to NMP, PLA, or any drug in the tetracycline class should not be treated with this product. The ATRISORB®-D FreeFlow™ Barrier is contraindicated in those situations where general periodontal surgery should not be performed. There are currently no known additional contraindications to the use of the ATRISORB®-D FreeFlow™ Barrier.

ATRISORB®-D FreeFlow™ Barrier - Evaluation of Treatment Effects

The demonstrated microbial reductions have not been correlated to clinical significance. If after 12 months the treatment using the ATRISORB®-D FreeFlow™ Barrier has not been successful, retreatment may be considered.

ATRISORB®-D FreeFlow™ Barrier - Adverse Reactions

Possible complications with any periodontal surgery include thermal sensitivity, gingival recession, flap sloughing, resorption or ankylosis of the treated root, some loss of crestal bone height, perforations or abscess formation, infection, pain, gingival irregularities, and complications associated with the use of anesthesia.

ATRISORB®-D FreeFlow™ Barrier – Warnings

The use of tetracycline drugs during tooth development (last half of pregnancy) may cause permanent discoloration of the teeth. Tetracycline drugs should not be used in children up to the age of 8 years or pregnant women unless other treatment is not likely to be effective or if alternative therapy is contraindicated.

Tetracyclines as a class are associated with photosensitivity. Treatment should be discontinued at the first sign of cutaneous erythema.

Accumulations of tetracyclines have not been associated with renal failure.

ATRISORB®-D FreeFlow™ Barrier - Precautions

The ATRISORB®-D FreeFlow™ Barrier has not been tested in pregnant women.

The ATRISORB®-D FreeFlow™ Barrier has not been evaluated in patients with conditions involving extremely severe defects with very little remaining periodontium.

The ATRISORB®-D FreeFlow™ Barrier cannot be resterilized. Do not use if pouches have been previously opened or damaged, or if the canulae heat stakes are broken.

The ATRISORB®-D FreeFlow™ Barrier has not been tested in immunocompromised patients (such as patients immunocompromised by diabetes, chemotherapy, radiation therapy, or infection with HIV).

As with other antibiotic preparations, ATRISORB®-D FreeFlow™ Barrier therapy may result in overgrowth of nonsusceptible microorganisms, including fungi.

The ATRISORB®-D FreeFlow™ Barrier should be used with caution in patients with a history of or predisposition to oral candidiasis.

ATRISORB®-D FreeFlow™ Barrier – Information for Patients

Avoid excessive sunlight or artificial ultraviolet light while receiving doxycycline.

Doxycycline may decrease the effectiveness of birth control pills.

ATRISORB®-D FreeFlow™ Barrier – Carcinogenesis, Mutagenesis, Impairment of Fertility

Animal studies with the ATRISORB®-D FreeFlow™ Barrier have not been performed to evaluate carcinogenic potential, mutagenic potential, or effects on fertility.

ATRISORB®-D FreeFlow™ Barrier – Pregnancy Category C

Administration of tetracyclines during pregnancy may cause permanent discoloration of teeth of offspring. Animal studies indicate that tetracyclines can cause retardation of fetal skeletal development. Animal reproduction studies have not been conducted with the ATRISORB®-D FreeFlow™ Barrier. It is also not known whether the ATRISORB®-D FreeFlow™ Barrier can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. The ATRISORB®-D FreeFlow™ Barrier should only be used to treat a pregnant woman if clearly needed.

ATRISORB®-D FreeFlow™ Barrier - Nursing Mothers

Tetracyclines appear in breast milk following oral administration. It is not known whether doxycycline is excreted in human milk following use of the ATRISORB®-D FreeFlow™ Barrier. Because of the potential for serious adverse reactions in nursing

infants from doxycycline, a decision should be made whether to discontinue nursing or to postpone surgery, taking into account the mother's need for treatment.

Instructions for Use

Preparations for Application of the ATRISORB®-D FreeFlow™ Barrier

This guide provides detailed instructions for formation of the ATRISORB®-D FreeFlow™ Barrier using the direct application (in situ) method.

Patient Selection

Patients selected for GTR should be free from medical disorders that are general contraindications for periodontal surgical treatment. They should have established their willingness and ability to perform adequate oral hygiene. Smoking may affect outcomes following periodontal surgery. Treatment of patients who smoke is at the discretion of the clinician.

Defect Selection

The ATRISORB®-D FreeFlow™ Barrier application (in situ) technique requires the use of bone replacement graft material.

Regenerative therapy should only be performed in defects where a reasonable likelihood of success exists. When treating furcation defects, Class II furcation

defects are often considered good candidates for GTR treatment. However, size, defect morphology, and location of these defects vary considerably, and as a result, the predictability of success in these areas may be quite variable. When treating intrabony sites, defects deeper than 3 mm have greater potential for regeneration.

Presurgical Treatment

Oral Hygiene Instructions

Before undergoing GTR surgery, patients should receive oral hygiene instruction and demonstrate a willingness and ability to perform adequate plaque control.

Scaling and Root Planing

Scaling and root planing are generally recommended prior to surgery. The resulting improvement in tissue health will aid flap reflection and manipulation.

Presurgical Medication

Antimicrobial oral rinses such as chlorhexidine should begin the day before the planned surgery.

ATRISORB®-D FreeFlow™ Barrier Site and Barrier Preparation

1. Use proper aseptic technique throughout the procedure.
2. Perform standard full-thickness flap surgery including debridement of soft

tissue, and scaling and planing of the root surface (including the furcation region, if involved). Assure that flap reflection is adequate to provide sufficient access for placement of the barrier.

3. Fill the defect with bone replacement graft material as per manufacturer's instructions.
4. Remove the contents of the kit. Open the pouches containing the syringes and remove the caps from both syringes. Couple Syringe A (liquid delivery system) and Syringe B (doxycycline powder).
5. Inject the liquid contents of Syringe A into Syringe B and then push the contents back into Syringe A. This entire operation is one mixing cycle.
6. Complete 100 mixing cycles at a pace of one cycle per second using brisk strokes.
7. The contents will be in Syringe A. Hold the coupled syringes vertically with Syringe A at the bottom. Pull back on the Syringe A plunger and allow the contents to flow down the barrel for several seconds.
8. Uncouple the two syringes and attach the blunt cannula to Syringe A.

Product is now ready for application.

Barrier Placement

1. Tilt the patient's head to facilitate barrier placement. Appropriate head position is one that takes advantage of gravity in placing the barrier.
2. Assure through evacuation that the surgical field remains as saliva-free and hemorrhage-free as possible taking care not to disturb the bone replacement graft.
3. Hold the cannula tip 1-2 mm away from the graft and apply the fluid polymer from the syringe so there is a continuous flow of polymer.
4. Express the polymer from the syringe to cover the graft and defect site. The polymer should cover the graft, be in intimate contact with the tooth surface, and extend slightly over the adjacent alveolar bone.
5. Mist the barrier with a fine spray of sterile water or saline (i.e. from the high-speed or ultrasonic handpiece) for approximately 10 - 20 seconds to facilitate the initial "set" of the barrier.
6. Inspect the precipitating barrier. If additional polymer is required it can be added from the syringe in the manner previously described. The newly added polymer is then "set" with the sterile water or saline spray.
7. Do not disturb the barrier after it has been placed and formed. Close the surgical wound with sutures.
8. Place periodontal dressing at the surgical site, if desired.

Barrier Exposure

Some barrier exposure may occur during the initial healing. The exposed material should not be trimmed because of the possibility of disrupting the healing tissue and/or site. Instruct the patient to keep the exposed material clean by applying chlorhexidine directly to the site twice daily with a cotton tip applicator. Generally, this material will disappear by 6 to 8 weeks following surgery due to absorption or attrition.

The granulation tissue that forms at the surgical site under the barrier may cause barrier displacement. In these cases, if necessary, a periodontal dressing such as Coe-Pak™ periodontal dressing can be replaced weekly to assure that the barrier remains in place through the first 4 weeks.

Postoperative Considerations

Postsurgical Care

It is imperative that regenerative sites be kept free of plaque accumulation. Also, mechanical disruption of the healing site should be avoided. The following recommendations are made:

1. For 8 weeks following surgery, the patient should not clean the treated area by brushing, flossing, using a toothpick, or other interdental cleaning techniques.
2. During this period, rinsing or direct application with an anti-infective agent such as chlorhexidine is strongly recommended. After this 8-week period, mechanical tooth cleaning can resume.

3. Professional removal of supragingival plaque should be performed every week for 4 weeks, then bi-weekly through 8 weeks.

4. Probing the surgical site for treatment evaluation and subgingival scaling should not be done until at least 6 months following surgery.

ATRISORB®-D FreeFlow™ Barrier - Use of Antibiotics

Antibiotic therapy following regenerative surgeries as part of postoperative care has not been evaluated with the use of the ATRISORB®-D FreeFlow™ Barrier and use is at the discretion of the clinician. In cases of postsurgical infection or abscess that do not resolve with palliative treatment, it may be necessary to remove the ATRISORB®-D FreeFlow™ Barrier depending on the severity of the complication.