ETHICON™

Johnson & Johnson SURGICAL TECHNOLOGIES

Family Group Artwork

Design Control Owner	Ethicon, Inc.
Product Covered	Ethizia in Non-CE Layout
Document Ref.	101123133 v1

SUMMARY OF CHANGES	
Revision No.	Description of Change
1	New product labeling specification created for Ethizia US Launch.

Scope

This document shows the information and layouts for ETHIZIA™ codes manufactured by GATT Technologies BV in the Netherlands, where Ethicon, Inc. is the design owner.

Definitions

Term	Description
Primary Packaging	Inner Package / Pouch is the level of packaging that forms the sterile barrier.
Secondary Packaging	The level of packaging normally considered to constitute the sales unit – contains one or more primary packs.
Barcodes	Barcodes are for placement location only.

Variable Information

Sterility Symbology

In this case the sterility is not variable. The sterility method is irradiation, and the symbol reflects R (irradiation).

Date Format

In this case the date format will be as follows:

Manufacturing Site	Packaging Level	Date Format
All Sites	All	YYYY-MM-DD

Translations

N/A – English Only

Country of Origin

The Country of Origin (COO) statement appearing on finished goods cartons will not vary.

Manufacturing Site	Country of Origin Statement
GATT Technologies BV Transistorweg 5 6534 AT Nijmegen The Netherlands	Made in Netherlands

Legal Manufacturer Statement

The legal manufacturer appearing on the packaging is:

Manufacturing Site	Legal Manufacturer (Primary and Secondary pack)
GATT Technologies BV Transistorweg 5 6534 AT Nijmegen The Netherlands	Ethicon, Inc. 1000 Route 202 Raritan, NJ 08869 USA 1-877-ETHICON +1-513-337-6928

EC Representative Address

The EC Representative address appearing on the packaging is:

EC Representative Address
N/A

Patent Information

Patent information will be referenced on the primary packaging (Pouch Label) only as follows:
pat. www.ethicon.com/patentmarking

Symbols Glossary

The link 'www.e-ifu.com/symbols-glossary' appears on the secondary packaging.

Packaging

The codes covered by this document use the following packaging types:

Pack Level	Packaging Name
Primary Packaging	Inner Package / Pouch Label
Secondary Packaging	Outer Package / Carton
Secondary Packaging	Barcode Label

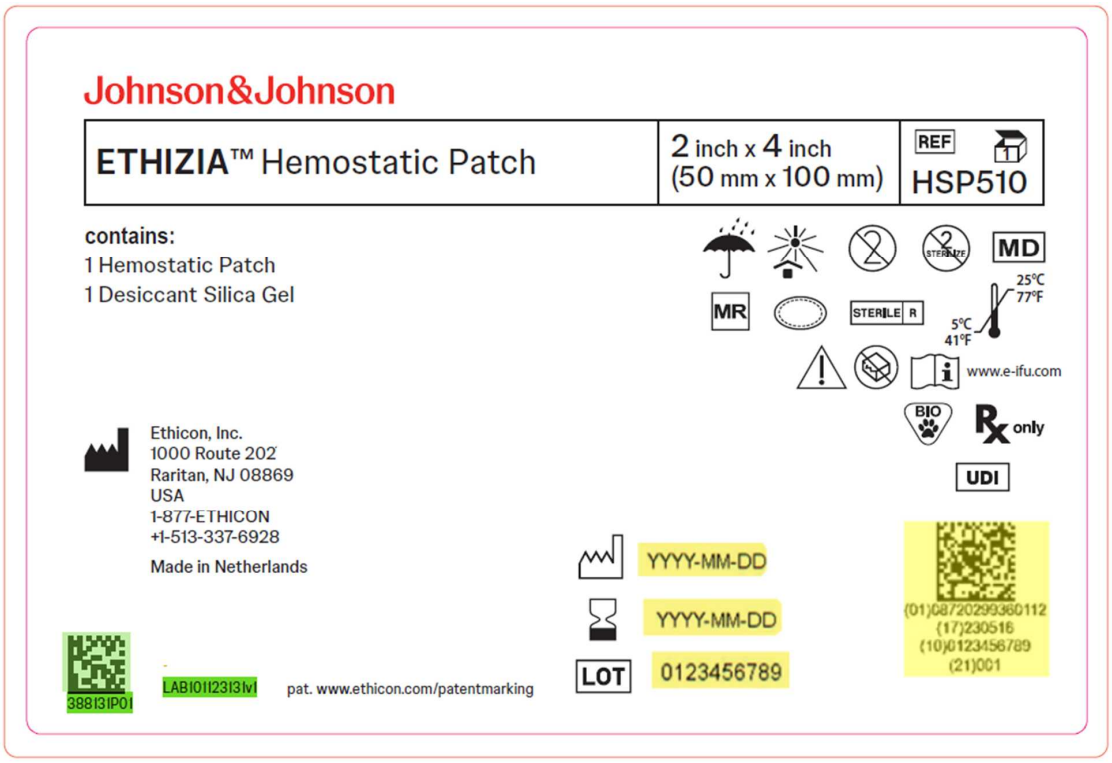
Sample Graphics

The following images are representative samples of all the packaging types covered by this document. Sample Graphics are *not* to scale.

- Variable content added during the manufacturing process is identified below with a yellow background.
- Pre-printed variable items are color coded with a green background.

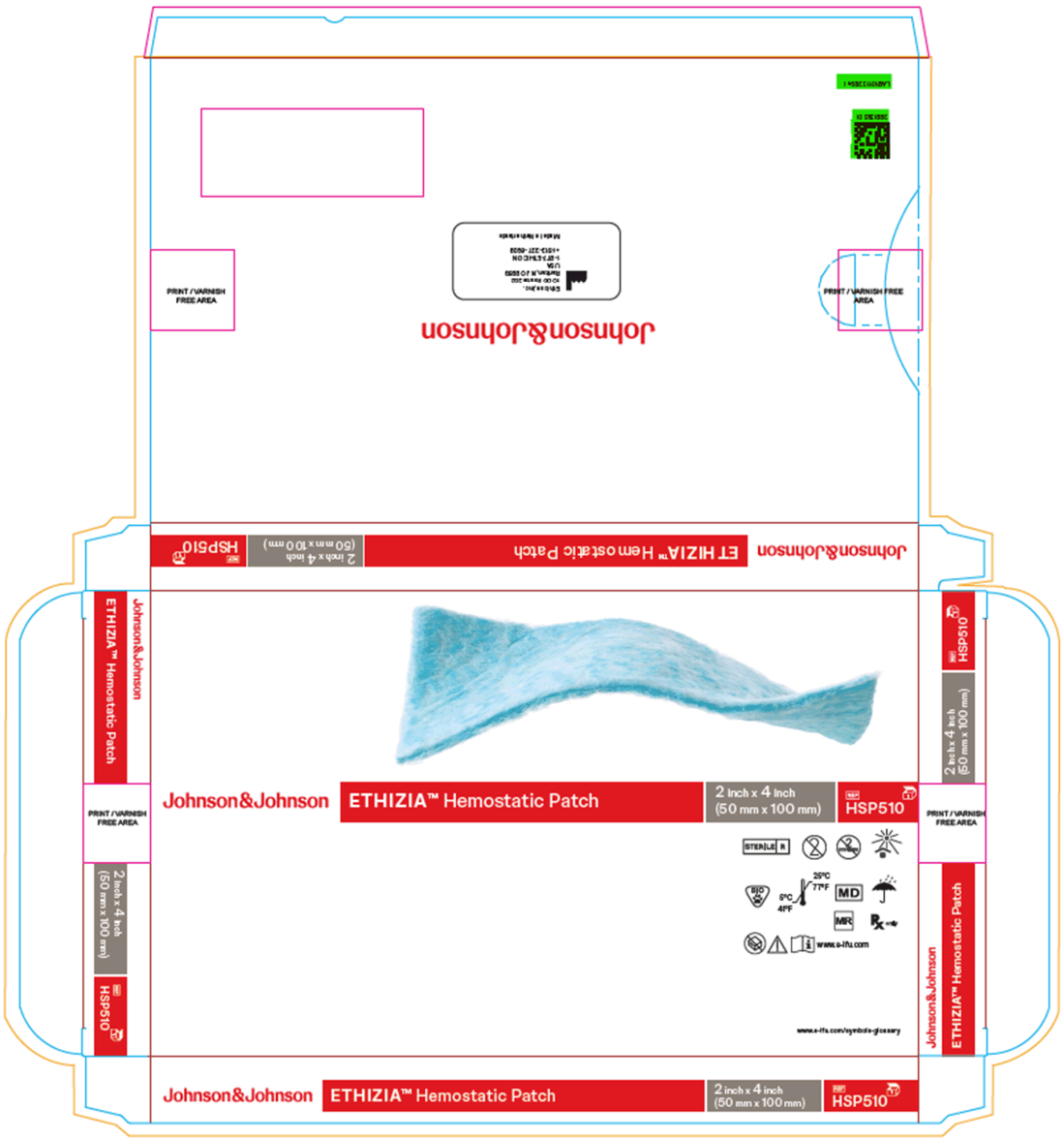
Primary Packaging (Pre-Printed)
For Reference Only

Inner Package / Pouch

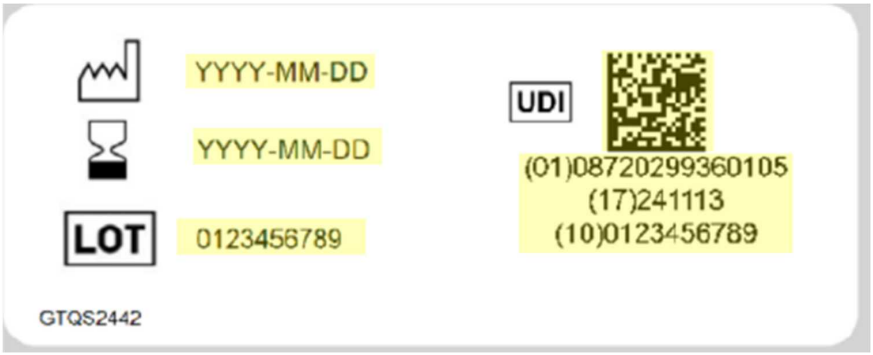


Secondary Packaging (Pre-Printed)
For Reference Only

Outer Package / Carton



Barcode Label (Printed In-Line)



DOCUMENT END

Instructions For Use

ETHIZIA™ Hemostatic Patch

Description

ETHIZIA™ Hemostatic Patch (ETHIZIA) is a sterile, resorbable hemostatic patch that should be applied on a visible bleeding site. It presents as a blue, soft, flexible, porcine gelatin (1 ± 0.2 grams per ETHIZIA) fiber-based gelatin carrier impregnated with NHS-POx / NU-POx granulate (1 ±0.2 grams per ETHIZIA). Blue color (202 – 686 µg per ETHIZIA) is an aid to visualize ETHIZIA when applied onto a bleeding location. ETHIZIA measures 10 by 5 cm and can be applied on both sides. As ETHIZIA is a homogenously impregnated fibrous material, it is also suited to being torn into smaller pieces for application on irregularly shaped structures and areas that are difficult to access.

The product is not removed at the end of surgery but is resorbed in 4-6 weeks.

Degradation of ETHIZIA depends upon several factors including the amount used, the anatomical location, and degree of saturation with blood or other fluids.

ETHIZIA Specifications	
Parameter	**Specification**
Appearance	Fibrous, coherent patch, homogeneously colored (blue)
Shape	Rectangular
Dimensions	Length: 100 ± 5 mm
	Width: 50 ± 5 mm
	Thickness: 5 ± 3 mm
Weight	1.6 – 2.5 g
Composition	Porcine gelatin (1 ± 0.2 grams per ETHIZIA)
	NHS POx/NU-POx granulate (1 ± 0.2 grams per ETHIZIA)
	FD&C Blue No. 1 (202 – 686 µg per ETHIZIA)
Ratio Blue NHS-POx/NU-POx	Blue NHS-POx/NU-POx (75:25 (w/w) to 85:15 (w/w)
Loading (% of granulates in final finished device)	36-61%
Sterility assurance level (SAL)	10^{-6}

Indications for Use

ETHIZIA is indicated for use in adult patients with a body weight of ≥25kg as an adjunct to hemostasis in open liver surgery for minimal, mild, or moderate bleeding sites when control of bleeding by standard surgical techniques (such as suture, ligature or cautery) is ineffective or impractical.

Contraindications

ETHIZIA is not indicated for use on severe (i.e. pulsatile) bleedings (defined by Surface Bleeding Severity Scale 4-5).

ETHIZIA is not intended for intravascular use. Do not attempt to force ETHIZIA into blood vessels, and only apply ETHIZIA after standard surgical techniques have been used to close the vessel. ETHIZIA should not be used in infected wounds.

ETHIZIA should not be used in patients with a known hypersensitivity to the component materials, including porcine proteins and FD&C Blue #1.

Warnings

ETHIZIA has not been studied in pediatric patients and pregnant or lactating women.

ETHIZIA has not been studied for use during cardiovascular, neurosurgical, ophthalmic, and urological (if the patch would come into contact with the urinary collection system) procedures.

ETHIZIA is not intended to be a substitute for standard surgical technique and/or the proper use of other conventional hemostatic techniques.

ETHIZIA must not be used if applying pressure on the entire surface of the patch would be difficult to achieve. This may result in incomplete hemostasis.

Care should be taken when using ETHIZIA in confined spaces. Product could swell around blood vessels or organs leading to compression or possible organ injury.

Use the smallest number of patches required to cover and extend the margins of the entire bleeding area by at least 1 cm. Maximum amount for ETHIZIA is 150 cm^2, calculating to approximately 3 ETHIZIA, based on a 70 kg patient or 2.1 cm^2/kg. The table below includes further information on the maximum amount of ETHIZIA when used in patients of different body weights. The safety of higher quantities has not been studied.

Patient body weight (kg)	**Maximum amount of ETHIZIA**
25-50kg	1 ETHIZIA
50-70kg	2 ETHIZIA

≥70kg	3 ETHIZIA

ETHIZIA must not be hydrated prior to application. Wetting a patch initiates the formation of a POx hydrogel. Initiating this process prior to application on tissue could lead to decreased hemostatic performance.

Do not reposition the patch after application with a saline wetted gauze. Once applied with a saline wetted gauze, instant polymer activation will adhere the patch to the tissue and repositioning will risk tearing the patch. Moreover, insufficient patch adhesion upon repositioning will compromise the creation of hemostasis.

Do not replace or peel off the patch when hemostasis has been achieved. Once hemostasis is achieved through adhesion of ETHIZIA to the surface of the tissue to create a physical barrier, attempts at patch manipulation could lead to tissue trauma or rebleeding.

ETHIZIA should be wetted homogeneously after application. Wetting a patch initiates the formation of a POx hydrogel. Implanted dry patch areas may lead to decreased hemostatic performance or adhesions.

After application of ETHIZIA, manipulation of the bleeding site and the patch should be minimized.

ETHIZIA may be present on imaging. The patch could potentially obscure underlying structures, present as a possible product encapsulation or mimic pathological conditions on imaging, possibly leading to the need for additional diagnostics or unwarranted intervention.

ETHIZIA is not indicated as a surgical sealant to prevent bile leakage and should not replace meticulous use of standard surgical techniques to prevent bile leakage. The use of surgical drains to mitigate potential complications as a result of bile leakage should be assessed in each specific procedure based on the surgeon’s knowledge and specific anatomical and physiologic considerations encountered in surgery.

Precautions

For single use only. Do not re-sterilize. Reuse of single-use devices creates a potential risk of patient infections.

The performance of ETHIZIA for sealing fluid leaks has not been tested.

The performance of ETHIZIA in anticoagulated patients has not been studied.

Do not use if the product sterile barrier system or its packaging is compromised.

ETHIZIA must be used within 1 hour after opening of the packaging.

Preparations

Circulating Nurse *(non-sterile):*

Open the outer non-sterile packaging and remove the inner pouch.

Visually inspect all packaging for damage including a careful inspection of all sterile barrier systems for breaches in package integrity immediately prior to use.

Do not use if the product sterile barrier system or its packaging is compromised.

Present the sterile contents (i.e. clamshell) to the sterile field using aseptic technique.

Scrub Nurse *(sterile field):*

ETHIZIA should be kept dry as it is presented to the surgical site. Contact with wet instruments or other wet materials may result in sticking to surfaces other than the intended target tissue.

Administration

ETHIZIA is intended to be used by physicians performing open surgical procedures when adequate pressure can be achieved upon application.

Dry gloves and surgical instruments (forceps, scissors) should be used to handle, cut and apply ETHIZIA. When applying ETHIZIA, minimize contact with wet or bloody surgical instruments or gloves as the device may adhere to other surfaces.

ETHIZIA may be used in combination with electrocautery devices used for general surgery.

ETHIZIA must not be hydrated prior to placement.

ETHIZIA may be cut to the desired size and shape. Select the appropriate size of ETHIZIA so that it overlaps the margins of the bleeding surface by at least 1 cm.

Multiple (pieces of) patches may be used, up to the maximum of 2.1 cm^2/kg body weight, calculating to 1 full ETHIZIA for patients of 25-50 kg, 2 full ETHIZIA for patients 50-70 kg, and 3 full ETHIZIA for patients ≥70 kg. ETHIZIA may be applied to, or (partially) overlap, a previously applied (piece of) patch (“patch on patch”).

It is recommended that dry parts of ETHIZIA after application are wetted.

Leave ETHIZIA in situ after hemostasis has been achieved. Do not try to forcefully remove the patch.

Do not remove ETHIZIA at the end of the surgery. Excess ETHIZIA material may be removed carefully, at the discretion of the surgeon.

Method of Application

Apply ETHIZIA dry to the bleeding site with at least 1cm margins, and immediately hold in place with a saline wetted gauze and uniform pressure over the entire patch surface for 30 seconds. Gently remove the wet gauze from the patch. If complete hemostasis has not been achieved in 30 seconds, re-apply pressure with a saline wetted gauze or surgical sponge for an additional 30 seconds.

- If hemostasis is not complete with a single patch and blood comes through the patch, apply a new (piece of) ETHIZIA on the bleeding site with a 1 cm overlap with tissue or previously placed ETHIZIA on all sides ("patch-on-patch"). Apply according to the steps above.
- If hemostasis is not complete because ETHIZIA is not adherent to the underlying tissue, with or without hematoma formation underneath, remove the non-adherent part and apply a new (piece of) ETHIZIA on the bleeding site with a 1 cm overlap with tissue or previously placed ETHIZIA on all sides ("patch-on-patch"). Apply according to the steps above.
- Repeat the above steps as necessary, with a maximum of 2.1 cm^2 / kg of patient body weight covered by ETHIZIA and remaining in-situ at the end of the operation (approximately 3 patches in an adult patient of 70kg).

Shelf Life, Storage and Disposal

ETHIZIA must be stored in the provided packaging which includes the drying agent and at specified environmental conditions, including storage at acceptable room temperature of 5-25°C (41-77°F).

Observe the expiration date indicated on the outer packaging. Do not use after expiration.

ETHIZIA and packaging may be disposed of as general surgical waste in accordance with local regulations.

Clinical Experience

A Prospective, Multicenter, Single-arm, Clinical Investigation Evaluating the Safety and Performance of ETHIZIA for Hemostasis during Open Liver Surgery (NCT04819945)

Patients: 47 patients undergoing elective open liver surgery were treated with ETHIZIA for minimal, mild, or moderate bleeding (i.e. Surface Bleeding Severity Scale 1-3).

Effectiveness: Among 47 patients and 63 target bleeding sites, hemostasis was achieved in 30 seconds in 82.7% (N=52/63), in 60 seconds in 93.7% (N=59/63), and in 3 minutes in 96.8% (N=61/63) of bleeding sites. As compared with a literature-derived performance goal of 65.4%,

ETHIZIA demonstrated to be non-inferior to a range of approved hemostatic agents in achieving hemostasis within 3 minutes.

Safety: There were 44 adverse events in total in the 28 of 47 (59.6%) subjects with adverse events. Most patients experienced gastrointestinal disorders (N=5/47; 10.6%), hepatobiliary disorders (N=15/47; 31.9%), infections and infestations (N=8/47, 17.0%), and/or events related to injury and procedural complications (N=4/47; 8.5%). There were 3/44 (6.8%) severe adverse events, which were ascites, hepatic failure, and an abdominal abscess. The majority of events, 36/44 (81.8%) in total, were related to the procedure. Three of the 44 events (6.8%) were also related to the device and were a biloma, an abdominal abscess, and a post-procedural hematoma. All of these events were considered to be possibly related to the device; there were no events that were probably related to the device or with a causal relationship with the device.

A Prospective, Multicenter, Randomized Clinical Investigation Evaluating the Safety and Performance of ETHIZIA versus TachoSil for Hemostasis during Open Liver Surgery (NCT 05385952)

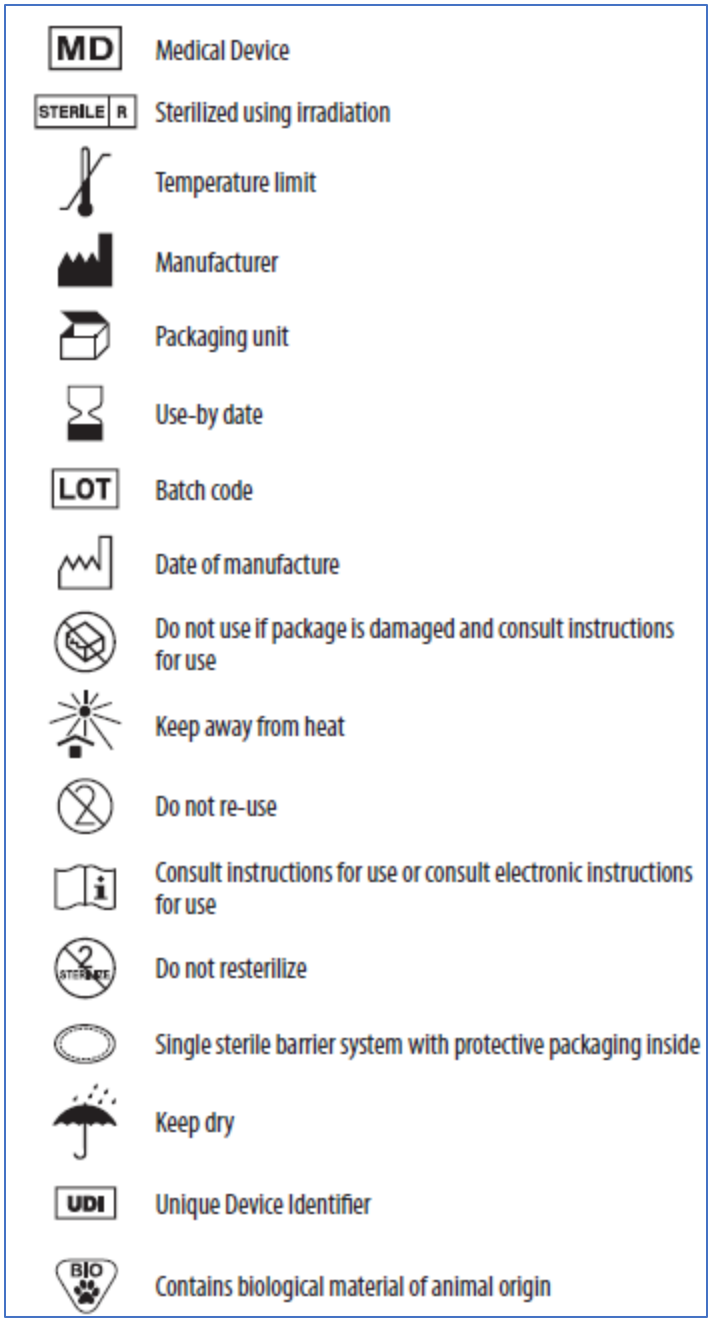
Patients: 131 patients undergoing elective open liver surgery were randomized 2:1 to either ETHIZIA or to the control group (TachoSil). In total, 87 patients were treated with ETHIZIA for minimal, mild, or moderate bleeding (i.e. Surface Bleeding Severity Scale 1-3). There were 44 patients randomized to TachoSil and 43 received the treatment.

Effectiveness: The primary endpoint of hemostasis at 3 minutes without rebleeding at the 10-minute time point was 93.1% (N=81/87) for ETHIZIA and 76.7% (N=33/43) for TachoSil. This data demonstrates that ETHIZIA is non-inferior to the control group TachoSil ($p<0.0001$). Upon achieving non-inferiority, sequential hypothesis testing demonstrates that ETHIZIA is superior to the control group, TachoSil ($p=0.0038$). Among the 87 patients there were 139 target bleeding sites treated with ETHIZIA and hemostasis was achieved in 30 seconds in 81.3% (N=113/139), in 60 seconds in 92.1% (N=128/139), and in 3 minutes in 95.7% (N=133/139) of bleeding sites, with the median time to hemostasis being significantly shorter for ETHIZIA (30 seconds) versus TachoSil (180 seconds) ($p<0.0001$).

Safety: There were 326 total adverse events in 97 of the 130 (74.6%) subjects. During the study 75.9% (N=66/87) of patients in the ETHIZIA group experienced an adverse event and 72.1% (N=31/43) in the TachoSil group. There were 47 patients with serious adverse events in total, 42.5% (N=37/87) of patients in the ETHIZIA group experienced a serious adverse event and 23.3% (N=10/43) in the TachoSil group. Most patients with serious adverse events in both groups experienced gastrointestinal disorders (N=20/130; 15.4%), events related to injury and procedural complications (N=17/130; 13.1%), infections and infestations (N=9/130; 6.9%), and cardiac disorders (N=6/130; 4.6%). Of the 326 total adverse events, 8/87 (9.2%) of patients experienced events related to ETHIZIA and these were intra-abdominal fluid collection in 4/87

(4.6%) followed by post procedural bile leak in 2/87 (2.3%) and abdominal pain, intraoperative hepatic hemorrhage, hematoma, and pyrexia in 1/87 each (1.1% of subjects each) and 9/43 (20.9%) of patients experienced events related to TachoSil and these were intraoperative hepatic hemorrhage in 6/43 (14.0%) followed by abdominal pain, post procedural bile leak, hematoma, and bacteremia in 1/43 each (2.3% of subjects each). All of these events were considered to be possibly related to the device per investigator; there were no events that had a causal relationship with the device.

Long-term Observational Follow-up: A 5-year observational follow-up for patients who underwent liver resection for cancer is ongoing. The clinical data from this follow-up will include cancer recurrence, cancer-free survival and overall cancer survival.



Rx only Caution: Federal law restricts this device to sale by or on the order of a licensed healthcare practitioner.

REF Catalogue number

Caution

MR MR Safe

Ethicon, Inc.
1000 Route 202
Raritan, NJ 08869USA
1-877-ETHICON
1-513-337-6928

2024-09

398211E01
LAB101141211v1
(Time/Date Stamp will be included per eIFU Template in PS-0000695.)

ETHIZIA ™ Hemostatic Patch

Optimized Device Performance Quick Guide

Product Overview

Key Features

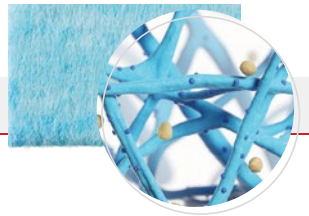
Sterile, flexible, resorbable hemostatic patch[1]

- Bleeding controlled in 30 seconds[2*]
- Approved for use in open liver procedures[1]
- First and only hemostatic matrix designed to be equally active and effective on both sides[3†]
- Gelatin-based carrier impregnated patch with POx polymer-based technology[2,3]

ETHIZIA™ is indicated for use in adult patients with a body weight of ≥25kg as an adjunct to hemostasis in open liver surgery for minimal, mild, or moderate bleeding sites when control of bleeding by standard surgical techniques (such as suture, ligature or cautery) is ineffective or impractical.

Mechanism of Action [2,4]

ETHIZIA is composed of a flexible fibrous gelatin matrix containing a granulate (homogeneous powder) of two synthetic biocompatible polyoxazoline (POx) polymers that, in the presence of water (in an aqueous environment) rapidly link into a hydrogel. The polyoxazoline polymers consist of a POx-ester and a POx-amine that result in a hydrogel entrapped within the gelatin matrix adhering to tissue, independent of the coagulation cascade. Upon application and tamponade, the combination of the blood absorbing gelatin fibers and the water soluble polyoxazoline polymers creates a hemostatic mechanical barrier.



Scan here to watch the in-service video

FPO

Application

Open Surgery1

1: **Use dry gloves** to open outer packaging and present inner, sterile pouch to the sterile eld using aseptic technique.

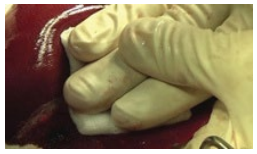
2: If bleeding site is small, patch may be **cut to size** . Ensure scissors are **dry** .

3: **Apply** dry patch to bleeding site with at least **1-cm margins** .

4: Hold in place with **saline -wetted woven gauze** , squeezed of excess moisture.

5: **Immediately apply uniform pressure for 30 seconds** Entire surface of the patch; gently remove saline-wetted woven gauze.

6: If complete hemostasis has not been achieved in 30 seconds, **reapply pressure** with saline-wetted woven gauze or saline-wetted surgical sponge for additional 30 seconds. Additional patches or pieces of patch may be applied.



℞ only

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

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*Based on clinical trial data. The Full Analysis Set showed 32/39 patients (82%) achieved hemostasis in 30 seconds.
†Pre-clinical test data are not necessarily indicative of clinical performance.

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ETHIZIA ™ Hemostatic Patch

Optimized Device Performance Quick Guide

Easy to handle in open surgery*

ETHIZIA™ Hemostatic Patch is flexible and pliable to be shaped for use in a variety of clinical situations, and on irregular tissue surfaces and cavities. ETHIZIA™ Hemostatic Patch can be stuffed, rolled, pulled apart and trimmed. 2,6-9*

ETHIZIA™ Hemostatic Patch can be applied using the “tuft and stuff ” technique in open procedures. Part of one patch or a whole patch is inserted or stuffed into a small cavity, and the remainder of the patch or another patch is laid at over top[10**]

Quick Tips for Optimized Device Performance

Do[1,2]:

- Store in the provided packaging which includes the drying agent at specified environmental conditions, including storage at acceptable room temperature 5-25°C (41-77°F).
- Observe the expiration date indicated on the outer packaging. Do not use after expiration.
- Use within one hour of opening inner package
- Use dry gloves and surgical instruments (forceps, scissors, trocars) to handle, cut, and apply
- Cut or tear to desired size and shape as needed
- If using tuft and stuff technique, ensure one patch or piece of patch is applied at over top of the stuffed piece/patch.**
- Leave the patch in situ after hemostasis has been achieved
- If complete hemostasis has not been achieved in 30 seconds, reapply pressure with a saline-wetted woven gauze or saline-wetted surgical sponge for an additional 30 seconds
- Use multiple patches if needed (a maximum of 2.1cm2/kg of patient body weight remaining in situ at the end of the operation, or approximately 3 patches in an adult patient of 70kg)

Do Not[1]:

- Use for severe (ie, pulsatile) bleeding
- Use in cardiovascular, neurosurgical, ophthalmic, and urological (if the patch would come in contact with the urinary collection system) procedures because ETHIZIA™ has not been studied in these.
- Hydrate prior to placement
- Replace, reposition, or peel off the patch after application with saline-wetted woven gauze
- Remove the patch at the end of surgery; patch fully resorbed within 4-6 weeks
- Reuse or resterilize

Please refer always to the Instructions for Use / Package Insert that come with the device for the most current and complete instructions.

*Pre-clinical test data are not necessarily indicative of clinical performance. The performance of ETHIZIA™ in anticoagulated patients has not been studied.

** This method was only qualified for bleeding sites which can be easily visualized. The performance of ETHIZIA™ in anticoagulated patients has not been studied.

References: 1. ETHIZIA™ Hemostatic Patch Instructions for Use. Ethicon, Inc. **2.** GATT Technologies BV, DHF-01-QR-021 Clinical Investigation Report, Feb 2022, Data on file. **3.** Roozen EA, Lomme RMLM, Calon NUB, Ten Broek RPG, van Goor H. Efficacy of a novel polyoxazoline-based hemostatic patch in liver and spleen surgery. ***World J Emerg Surg*** . 2023;18(1):19. doi:10.1186/s13017-023-00483-x **4.** Boerman MA, Roozen E, Sánchez-Fernández MJ, et al. Next generation hemostatic materials based on NHS-ester functionalized poly(2-oxazoline)s. ***Biomacromolecules*** . 2017;18(8):2529-2538. doi:10.1021/acs.biomac.7b00683 **5.** GATT Technologies BV, DHF-01-SFT-200 GATT-Patch Summative Usability Report, Jan 2023, Data on file. **6.** GATT Technologies BV, DHF-SR-120 Partly heparinized in vivo porcine model ORSI, Nov 2021, Data on file. **7.** GATT Technologies BV, DHF-SR-142 Partly heparinized in vivo porcine model Radboudumc, Jan 2023, Data on file. **8.** GATT Technologies BV, DHF-01-SR-152 - GATT-Patch vs Floseal in porcine kidney cavity bleeding, Jan 2022, Data on file. **9.** Orsi Academy, DHF-01-SR-154 GATT-Patch vs Suturing in a robotic porcine partial nephrectomy model, Feb 22, Data on file. **10.** Orsi Academy, DHF-01-SR-120 GATT-Patch; partly heparinized in vivo porcine model, April 2021, Data on file.

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