Indermil™ Tissue Adhesive

ENGLISH

⚠ **BEFORE USING PRODUCT, READ THE FOLLOWING INFORMATION THOROUGHLY.**

IMPORTANT!
This booklet is designed to assist in using the Indermil™ tissue adhesive. It is not a reference to surgical techniques.

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

DESCRIPTION:
Indermil™ is a sterile, liquid topical tissue adhesive composed of *n*-Butyl-2-Cyanoacrylate monomer. Indermil™ tissue adhesive is supplied in a 0.5g single patient use, plastic ampule. Each ampule is sealed within a foil packet so the exterior of the ampule is also sterile. Indermil™ remains liquid until exposed to water or water-containing substances/ tissue, after which it cures (polymerizes) and forms a film that bonds to the underlying surface.

INDICATIONS:
Indermil™ tissue adhesive is indicated for the closure of topical skin incisions including laparoscopic incisions, and trauma-induced lacerations in areas of low skin tension that are simple, thoroughly-cleansed, and have easily approximated skin edges. Indermil may be used in conjunction with, but not in place of, deep dermal stitches.

CONTRAINDICATIONS:
- Indermil™ tissue adhesive is not to be applied to subdermal layers of tissue. The polymerized adhesive is not absorbed by tissues and may elicit a foreign body reaction.
- The tissue adhesive is not to be applied to any internal organs, blood vessels, nerve tissue, mucosal surfaces or mucocutaneous junctions, areas with dense natural hair, or within the conjunctival sac of the eye.
- The tissue adhesive is not to be applied to the surface of the eye. If the eye is bonded closed, release eyelashes with warm water by covering with a wet pad. The adhesive will bond to eye protein and will cause periods of weeping which will help to debond the adhesive. Keep the eye covered until debonding is complete -- usually within 1 to 3 days. Do not force the eye open.
- The tissue adhesive is not to be applied to wounds subject to high skin tension, or on areas of increased skin tension such as the elbows, knees, or knuckles. The tissue adhesive is not to be used in areas of skin excision.
- The tissue adhesive is not to be applied to wounds that show evidence of infection or gangrene.
- The tissue adhesive is not to be used on patients with known preoperative systemic infections, uncontrolled diabetes, or diseases or conditions that are known to interfere with the wound healing process.
- The tissue adhesive is not to be used on patients with a known hypersensitivity to cyanoacrylate or formaldehyde.

WARNINGS:
- Indermil™ tissue adhesive should be used only on wounds that have been thoroughly cleaned and debrided.
- The tissue adhesive generates a small amount of heat during polymerization and should not to be applied to tissues that may be affected by such heat.
- The adhesive should always be applied very sparingly, either as minute drops or as a very thin film along the edges of the wound. Heavy application may cause thermal damage to tissues, and delayed healing may result.
- The tissue adhesive should not be applied to wet wounds. Excess moisture, such as water or alcohol, may accelerate polymerization, resulting in the generation of excess heat.
- Use of the tissue adhesive may result in localized sensitization or irritation reactions.

PRECAUTIONS:
- The tissue adhesive will readily adhere to most substrates. Care should be taken to avoid unwanted contact with the adhesive during polymerization. Polymerized adhesive can be removed from metal instruments with acetone. Accidental bonding of materials other than tissues may be reversed by peeling apart the adhered surfaces with the aid of warm soapy water, petroleum gel, saline solution, or 5% solution of sodium bicarbonate. Do not pull apart skin.
- Wounds should be kept dry following closure with the tissue adhesive. Do not apply topical medications following closure.
- In the event of spillage, Indermil™ tissue adhesive can be absorbed with talc. Flush area with water to solidify the adhesive.
- Indermil™ tissue adhesive has not been evaluated in patients with a history of hypertrophic scarring or keloid formation.

ADVERSE REACTIONS:

In a study with 1,092 patients and 2,304 wounds, the following adverse reactions were reported:

Adverse Reactions observed at 10-14 days, per wound evaluated	*No Subcuticular Sutures (NSS)*		*With Subcuticular Sutures (WSS)*	
	Indermil™	Control	Indermil™	Control
N, patients treated	346	326	210	210
N, wounds treated	925	820	281	278
*Dehiscence***	30/853 (3.5%)*	9/709 (1.3%)	4/253 (1.6%)	2/257 (0.8%)
Not requiring treatment	28/853 (3.2%)*	6/709 (0.9%)	3/253 (1.2%)	1/257 (0.4%)
Requiring treatment	2/853 (0.2%)	3/709 (0.4%)	1/253 (0.4%)	1/257 (0.4%)
With infection	2/853 (0.2%)	1/709 (0.1%)	0/253 (0.0%)	0/257 (0.0%)
By wound class:				
Clean	23/564 (4.1%)	4/436 (0.9%)	4/222 (1.8%)	2/226 (0.9%)
Clean-contaminated	7/273 (2.6%)	3/261 (1.1%)	0/31 (0.0%)	0/29 (0.0%)
Contaminated	0/16 (0.0%)	2/10 (20.0%)	none	0/2 (0.0%)
Dirty	none	0/2 (0.0%)	none	none
*Infection****	5/853 (0.6%)	4/709 (0.6%)	1/253 (0.4%)	3/257 (1.2%)
Acute Inflammation				
Erythema	102/852 (12.0%)	85/709 (12.0%)	19/254 (7.5%)	17/256 (6.6%)
Edema	23/853 (2.7%)*	18/707 (2.5%)	6/253 (2.4%)	15/256 (5.9%)
Hypersensitivity	6/853 (0.7%)	1/706 (0.1%)	0/254 (0.0%)	2/256 (0.8%)
Drainage	39/853 (4.6%)*	14/709 (2.0%)	7/254 (2.8%)	6/257 (2.3%)
Sinus Tracts	4/850 (0.5%)	0/705 (0.0%)	2/253 (0.8%)	1/256 (0.4%)

* Differences between Indermil and Control were statistically significant (p< 05).

** Dehiscence was defined as "any disruption in which the edge of the skin wound separates sufficiently to expose subcutaneous tissues".

*** Infection was defined as "a purulent discharge from the wound, a positive culture or microbial count for pathogen that can be documented". Only two wounds met this criteria, all other "suspected infections" were based solely on clinical observation.

CLINICAL STUDY:

A prospective, randomized, multicenter, controlled, study was conducted to evaluate the safety and effectiveness of closing the approximated skin edges of surgical incisions, including punctures from minimally invasive surgery, and trauma-induced lacerations using Indermil™ in comparison to suture, staples or adhesive strips.

The study population included patients who presented for simple skin closure of wounds equal to or less than 8 cm. Patients or their legal representative had to sign informed consent and agree to return for follow-up visits. Patients were excluded if the tissue adhesive might come into contact with blood vessels, had wounds under tension or over joints, had known preoperative systemic infections or infections of the site, had uncontrolled diabetes, or had diseases or conditions that are known to interfere with the wound healing process.

Follow-up was at 24 hrs (or time of discharge), 1 to 2 weeks and at 3 months. All wound closure times were obtained at time of treatment, complications were assessed at the 1-2 week interval. Cosmesis was evaluated at the 3-month follow-up visit by means of a masked evaluation.

Summary of Patient Accounting, Demographics, and Wound Characteristics

	No Subcuticular Sutures (NSS)		*With Subcuticular Sutures (WSS)*	
	Indermil™	Control	Indermil™	Control
Accounting				
N, patients enrolled	346	326	210	210
N, patients treated	346	326	210	210
N, wounds treated	925	820	281	278
N, patients, control device: suture/strips/staples **		294 / 32 / 18		126 / 20 / 83
N, wounds, control device: suture/strips/staples**		741 / 107 / 40		185 / 24 / 90
Patients completed:				
24 hour	98.6%	98.5%	99.5%	99.0%
7-14 days	92.5%	87.7%	94.3%	93.8%
80 – 120 days	83.2%	79.4%	91.4%	88.5%
Patient Demographics				
Age 0 - 4y	3.5%	4.6%	0.0%	1.9%
5 - 18y	9.5%	6.4%	2.4%	0.5%
19 – 60y	64.7%	67.8%	54.1%	52.9%
>60y	22.3%	21.2%	43.5%	44.7%
Race White	80.1%	81.3%	85.2%	88.6%
Black	8.4%	8.9%	5.2%	6.7%
Asian	1.2%	0.6%	0.0%	0.0%
Hispanic	8.7%	5.8%	7.6%	3.3%
Other	1.7%	3.4%	1.9%	1.4%
Wound Characteristics				
Length in cm mean	1.5*	1.7	4.3	4.5
Depth in cm mean	1.5	1.5	1.5	1.4
Width in cm mean	0.5	0.5	0.6	0.6
Class Clean	66.8%	64.7%	87.9%	88.5%
Clean-contaminated	31.4%	33.9%	11.7%	10.4%
Contaminated	1.8%	1.2%	0.4%	0.7%
Dirty	0.0%	0.2%	0.0%	0.4%
Incisions	88.2%	87.9%	96.4%	95.7%
Lacerations	11.8%	12.1%	3.6%	4.3%
Use of Anesthesia				
General	137 (40%)	121 (37%)		
Local only	121 (35%)*	196 (60%)		
None	88 (25%)	9 (3%)		

* Differences between Indermil and Control were statistically significant (p< 05).
** Several patients/ wounds were treated with more than one control device.

Summary of Effectiveness Results
All Treated Wounds

Clinical Study Outcomes	*NSS*		*WSS*	
	Indermil™	Control	Indermil™	Control
Wound Closure Assessment:				
Dermal Apposition	823/853 (96.5%)*	700/709 (98.7%)	249/253 (98.4%)	255/257 (99.2%)
Immediate: Additional Device (Adhesive strips)	1/925 (0.1%)*	340/820 (41.5%)	2/281(0.7%)*	88/278 (31.6%)
*Cosmesis @ 3 months*** VAS Score, 100= (optimal)				
Mean Score				
All wounds	88.0*	92.2	89.3	89.9
Dehisced wounds	82.9	91.4	87.3	96.5
*Median Time to Close (minutes)****	0.6*	1.0	1.1*	2.2

* Differences between Indermil and Control were statistically significant (p< 05).

** Cosmesis: Visual Analog Scale (VAS); 3-month actual time range = 80 – 120 days
*** Time to Close was measured from the initial apposition of wound edges to the time of closure.

HOW SUPPLIED:
Indermil™ tissue adhesive is supplied in a 0.5g single patient use, plastic ampule. The ampule has been sealed in a foil pouch before being terminally sterilized by gamma radiation. Indermil™ tissue adhesive is supplied in boxes containing 5 unit doses or 20 unit doses.

INSTRUCTIONS FOR USE:
1. Clean and dry the wound prior to the application of the tissue adhesive. When necessary, debride the wound and remove excessive blood.

2. Peel open the foil pouch to expose the sterile, single patient use ampule.

3. Before opening the ampule, hold it in one hand with the tip pointed upward. Sharply flick the tip with the forefinger of the other hand to remove any adhesive trapped in the tip during transit. While still holding the ampule in the vertical position, twist and snap off the winged cap. Retain the cap for resealing the tip after use and prior to disposal.

4. On application of light pressure on the ampule, Indermil™ is expressed from the ampule tip.

5. Tissue edges should be approximated and maintained in apposition during application.

6. Apply Indermil™ tissue adhesive very sparingly, either as minute drops or as a very thin film along the edges of the wound. Avoid heavy application.

7. Light pressure should be applied to the wound line apposition for approximately 30 seconds to allow the tissue adhesive to cure. Wounds that are subject to tension can be secured by subcuticular sutures prior to the topical application of the tissue adhesive.

8. Following application, the retained cap should be reversed and used to reseal the tip of the ampule. The resealed ampule, with any remaining adhesive, should be discarded.

PATIENT INSTRUCTIONS:
No additional or special care is needed for wounds closed using Indermil™ Tissue Adhesive, however it is recommended that the following information be shared with the patient as necessary.

- Do not shower, bathe or swim for 48 hours following wound closure.
- Do not scrub or soak the wound in water for 7-10 days.
- Do not apply any medications or cream to the wound.
- Keep the wound dry with a non-stick, non medicinal and water resistant bandage, per your doctor's instructions.
- Do not pull or pick at the wound or bandage
- Report any discomfort or other concerns regarding your wound to your doctor.

STORAGE:
Indermil™ tissue adhesive should always be stored in its original sealed foil pouch. During prolonged periods, Indermil™ tissue adhesive should be kept refrigerated at a temperature from 2°C to 5°C. Shorter storage periods at ambient conditions of 20°C will not adversely affect product performance. Do not expose to temperatures in excess of 25°C. Indermil™ tissue adhesive should not be used after the expiration date shown on the foil pouch, preceded by the expiration symbol.

STERILITY:
Indermil™ tissue adhesive is packaged for single patient use. Do not resterilize. Do not use if package is opened or damaged.

Distributed by:

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