High viscosity
DERMABOND®
Topical Skin Adhesive
(2-Octyl Cyanoacrylate)

DESCRIPTION
High viscosity DERMABOND™ Topical Skin Adhesive is a sterile, liquid topical skin adhesive containing a monomeric (2-octyl cyanoacrylate) formulation and the colorant D & C Violet #2. It is provided in a single use applicator comprised in a blister pack. The applicator is comprised of a glass ampule containing a plastic vial with attached applicator tip. The product is also available with a pen applicator. As applied to skin, the liquid is syrups-like in viscosity and polymerizes within minutes. In vitro studies have shown that high viscosity DERMABOND adhesive acts as a barrier to microbial penetration as long as the adhesive film remains intact. Clinical studies were not conducted to demonstrate microbial barrier properties.

High viscosity DERMABOND adhesive is different from the regular, or low viscosity DERMABOND adhesive due to the increased viscosity of the liquid adhesive formulation. Low viscosity DERMABOND adhesive has a viscosity slightly greater than water, while high viscosity DERMABOND adhesive has a syrup-like viscosity. The increased viscosity of high viscosity DERMABOND adhesive is intended to reduce the risk of unintended placement of the adhesive during application due to migration of the liquid adhesive from the wound site.

INDICATIONS
High viscosity DERMABOND Topical Skin Adhesive is intended for topical application only to hold closed easily approximated skin edges of wounds from surgical incisions, including punctures from minimally invasive surgery, and simple, thoroughly cleansed, trauma-induced lacerations. High viscosity DERMABOND adhesive may be used in conjunction with, but not in place of, deep dermal stitches.

CONTRAINDICATIONS
• Do not use on any wound with evidence of active infection, gangrene, or wounds of decubitus etiology.
• Do not use on mucosal surfaces or across mucocutaneous junctions, such as oral cavity, lips, or skin which may be regularly exposed to body fluids or with dense natural hair, (e.g., scalp).
• Do not use on patients with known hypersensitivity to cyanoacrylate or formaldehyde.

WARNINGS
• High viscosity DERMABOND adhesive is a fast setting adhesive capable of adhering to most body tissue and many other materials, such as latex gloves and stainless steel. Inadvertent contact with any body tissue, and any surfaces or equipment that are not disposable or that cannot be readily cleaned with a solvent such as acetone should be avoided.
• Polymerization of high viscosity DERMABOND adhesive may be accelerated by water or fluids containing alcohol. High viscosity DERMABOND adhesive should not be applied to wet wounds.
• High viscosity DERMABOND adhesive should not be applied to the eye. If contact with the eye occurs, flush the eye copiously with saline or water. If residual adhesive remains, apply topical ophthalmic ointment to help loosen the bond and contact an ophthalmologist.

When closing facial wounds near the eye with high viscosity DERMABOND adhesive, position the patient in a horizontal position, with high viscosity DERMABOND adhesive applied from above, and (2) high viscosity DERMABOND adhesive should only be used after wounds have been cleaned, debrided and, if applicable, local anesthesia has been administered.

PRECAUTIONS
• High viscosity DERMABOND adhesive is packaged for single patient use. Discard remaining opened material after each wound closure procedure.
• Do not resterilize high viscosity DERMABOND adhesive.

High viscosity DERMABOND adhesive should not be used in high skin tension areas or across areas of increased skin tension, such as knuckles, elbows, or knees, unless the joint will be immobilized during the skin healing period or unless skin tension has been removed by application of another wound closure device (e.g., sutures or skin staples) prior to application of high viscosity DERMABOND adhesive.

Adverse reactions encountered during clinical study comparing low viscosity DERMABOND adhesive to sutures, staples, and adhesive strips are listed in the table below:

<table>
<thead>
<tr>
<th>Clinical Study Outcomes</th>
<th>No Subcuticular Sutures</th>
<th>With Subcuticular Sutures</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>DERMABOND</td>
<td>Control</td>
</tr>
<tr>
<td></td>
<td>DERMABOND</td>
<td>Control</td>
</tr>
<tr>
<td>N (%)</td>
<td>N (%)</td>
<td>N (%)</td>
</tr>
<tr>
<td>N, patients enrolled</td>
<td>240</td>
<td>243</td>
</tr>
<tr>
<td>N, patients treated</td>
<td>239</td>
<td>242</td>
</tr>
<tr>
<td>N, patients completed</td>
<td>228 (95%)</td>
<td>215 (88%)</td>
</tr>
<tr>
<td>Suspected infection*</td>
<td>8 (3.6%)</td>
<td>2 (0.9%)</td>
</tr>
<tr>
<td>Wound type</td>
<td></td>
<td></td>
</tr>
<tr>
<td># Lacerations</td>
<td>8</td>
<td>2</td>
</tr>
<tr>
<td># Incisions</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Dehiscence with Need for Retreatment

Acute Inflammation

Erythema
26 (11.5%) 74 (33.0%) 52 (31.3%) 75 (45.1%)
Edema
22 (9.7%) 28 (12.5%) 62 (37.3%) 71 (42.8%)
Pain
14 (6.1%) 13 (5.8%) 56 (33.7%) 57 (34.3%)
Warmth
3 (1.3%) 6 (2.6%) 3 (1.8%) 4 (2.4%)

*In the clinical study, presence of infection was to be identified by observation of redness more than 3–5 mm from the repaired wound, swelling, purulent discharge, pain, increased skin temperature, fever, or other systemic signs of infection. Confirmatory culture was not routinely obtained. Among cases of suspected infection for low viscosity DERMABOND adhesive, 71/14 (50%) were in patients less than 12 years old with traumatic lacerations; overall, 8 of the 14 (approximately 60%) low viscosity DERMABOND adhesive wounds with suspected infections were associated with sub-optimal cosmetic outcome.

High viscosity DERMABOND adhesive permeability by fluids is not known and has not been studied.

High viscosity DERMABOND adhesive, as a liquid, is syrup-like in viscosity. To prevent inadvertent flow of liquid high viscosity DERMABOND adhesive to unintended areas: (1) the wound should be held in a horizontal position, with high viscosity DERMABOND adhesive applied from above, and (2) high viscosity DERMABOND adhesive should be applied in multiple (at least two), thin layers rather than in a few large droplets.

Hold applicator away from yourself and the patient and break ampule close to its center one time only. Do not crush the contents of the applicator tube repeatedly as further manipulation of the applicator may cause glass shard penetration of the outer tube.

High viscosity DERMABOND adhesive should be used immediately after crushing the glass ampule as the liquid adhesive will not flow freely from the applicator tip after a few minutes.

If unintended bonding of intact skin occurs, peel, but do not pull the skin apart. Petroleum jelly or acetone should be avoided. If the bond cannot be loosened, the patient should be referred to a surgeon.

High viscosity DERMABOND adhesive should only be used after wounds have been cleaned, debrided and, if applicable, local anesthesia has been administered.

High viscosity DERMABOND adhesive should not be used in high skin tension areas or across areas of increased skin tension, such as knuckles, elbows, or knees, unless the joint will be immobilized during the skin healing period or unless skin tension has been removed by application of another wound closure device (e.g., sutures or skin staples) prior to application of high viscosity DERMABOND adhesive.

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Reactions may occur in patients who are hypersensitive to cyanoacrylate or formaldehyde. See CONTRAINDICATIONS.

Adverse reactions may be experienced following high viscosity DERMABOND adhesive contact with the eye.

CLINICAL STUDIES

Clinical Study Comparing High Viscosity DERMABOND Adhesive and Low Viscosity DERMABOND Adhesive for Closure of Trauma-Induced Lacerations

Description: A prospective, randomized, controlled, unmasked study was conducted to evaluate the safety and effectiveness of closing the approximated skin edges of trauma-induced lacerations using high viscosity DERMABOND adhesive in comparison to the currently marketed low viscosity DERMABOND adhesive, with or without stitches placed below the skin surface according to investigator judgment.

The study population included patients at least one year of age, in good general health, who signed informed consent and agreed to follow-up visits. Patients were excluded if presenting with: significant multiple trauma, peripheral vascular disease, insulin dependent diabetes mellitus, blood clotting disorder, keloid formation or hypertrophy history (patient or family), cyanoacrylate or formaldehyde allergy, burst or stellate lacerations due to crush or hard blow, animal or human bite, and decubitus ulcer. One unit of either the high viscosity or low viscosity DERMABOND product was used to close the wound. Wound length and width were measured in millimeters; wound depth was not measured. Most wounds in the study were clean, small, superficial lacerations which did not penetrate the dermis completely nor sufficiently to require dermal suture placement (average wound length=18.7mm).

Follow-up was at 14 days (± 2 days) and at 30 days (± 2 days). The Modified Hollander Cosmesis Scale (MHCS), a validated scale, was used to evaluate cosmesis at the 30-day (± 2 days) follow-up visit. This scale evaluates step-off borders, edge inversion, contour irregularities, excess inflammation, wound margin separation, and overall wound appearance.

Results: The primary measure of device effectiveness in the study was wound closure at day 14, defined as continuous approximation of wound margins from the time of wound closure until the day of evaluation. Results indicate that high viscosity DERMABOND adhesive was equivalent to the low viscosity DERMABOND adhesive control for effectiveness of wound closure at day 14. Secondary effectiveness measures included an assessment of migration of the liquid adhesive from the wound site during application and an assessment of the presence of the polymer film on the wound at the time of the 14 day follow-up. Results show a significant reduction in the occurrence of migration of the liquid adhesive from the wound site during application for the high viscosity DERMABOND adhesive compared to the low viscosity DERMABOND adhesive control. No significant difference was observed between the two treatment groups for the presence of the polymer film at day 14.

Clinical Study Comparing Low Viscosity DERMABOND Adhesive to Sutures, Staples, and Adhesive Strips

Description: A prospective, randomized, controlled, unmasked 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 low viscosity DERMABOND adhesive in comparison to U.S.P. size 5-0 or smaller sutures, adhesive strips or staples, with or without dermal closure (subcuticular stitch) as per investigator judgment.
Summary of Effectiveness Results Comparing Low Viscosity DERMABOND Adhesive to Sutures (U.S.P. size 5-0 and smaller diameter), Staples, and Adhesive Strips

<table>
<thead>
<tr>
<th>Clinical Study Outcomes</th>
<th>NSS DERMABOND N (%)</th>
<th>Control N (%)</th>
<th>WSS DERMABOND N (%)</th>
<th>Control N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Accounting</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N. patients enrolled</td>
<td>240</td>
<td>243</td>
<td>167</td>
<td>168</td>
</tr>
<tr>
<td>N. patients treated</td>
<td>239</td>
<td>242</td>
<td>167</td>
<td>166</td>
</tr>
<tr>
<td>Patients completed</td>
<td>228 (95%)</td>
<td>215 (88%)</td>
<td>164 (98%)</td>
<td>162 (96%)</td>
</tr>
<tr>
<td>N. control sutures/strips/staples/missing</td>
<td>194/46/1</td>
<td>116/45/5/0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wound Closure Assessment</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Immediate: Additional Devices</td>
<td>18 (7.5%)</td>
<td>13 (5.4%)</td>
<td>2 (1.2%)</td>
<td>11 (6.6%)</td>
</tr>
<tr>
<td>@ 5-10 days: 100% epidermal apposition</td>
<td>169 (75.1%)</td>
<td>199 (88.8%)</td>
<td>140 (84.3%)</td>
<td>160 (96.4%)</td>
</tr>
<tr>
<td>&gt;50% epidermal apposition</td>
<td>205 (91.1%)</td>
<td>214 (95.5%)</td>
<td>163 (98.2%)</td>
<td>165 (99.4%)</td>
</tr>
<tr>
<td>@ 3 months: Cosmesis Score *= 0 (optimal)</td>
<td>188 (82.5%)</td>
<td>180 (83.7%)</td>
<td>128 (78.0%)</td>
<td>128 (78.9%)</td>
</tr>
<tr>
<td>Median Time for Treatment (Minutes)</td>
<td>1.5</td>
<td>6.0</td>
<td>1.3</td>
<td>2.9</td>
</tr>
</tbody>
</table>

* Cosmesis: Modified Hollander Cosmesis Scale

The study population included patients at least one year of age, in good general health, who signed informed consent and agreed to follow-up visits. Patients were excluded if presenting with: significant multiple trauma, peripheral vascular disease, insulin dependent diabetes mellitus, blood clotting disorder, keloid formation or hypertrophy history (patient or family), cyanocrylate or formaldehyde allergy, burst or stellate lacerations due to crush or hard blow, animal or human bite, and decubitus ulcer.

Follow-up was at 5-10 days and at 3 months. All wounds were assessed by visual inspection at 5-10 days after wound closure. The total kinds of wounds treated in the study were 46.1% lacerations and 53.9% incisions.

The incisions were comprised of 47.8% excisions of skin lesions, 27.4% minimally invasive surgery punctures, and 24.8% general surgery incisions.

For wounds closed without subcuticular stitches, mean wound length was 1.5 cm, mean wound width was 2.5 mm, and mean wound depth was 0.8 mm. For wounds closed with subcuticular stitches, mean wound length was 3.2 cm, mean wound width was 5.5 mm, and mean wound depth was 3.8 mm.

6. Do not apply liquid or ointment medications onto wounds closed with high viscosity DERMABOND adhesive because these substances can weaken the polymerized film, leading to wound dehiscence.

7. Protective dry dressings such as gauze, may be applied only after high viscosity DERMABOND adhesive is applied. Do not apply liquid or ointment medications onto wounds closed with high viscosity DERMABOND adhesive.

8. Patients should be instructed to not pick at the polymerized film of high viscosity DERMABOND adhesive. Picking at the film can disrupt its adhesion to the skin and cause dehiscence of the wound. Picking at the film can be discouraged by an overlying dressing.

9. Apply a dry protective dressing for children or other patients who may not be able to follow instructions for proper wound care.

10. Patients treated with high viscosity DERMABOND adhesive should be provided the printed instruction sheet entitled: How to Care for Your Wound After It’s Treated With High Viscosity DERMABOND Topical Skin Adhesive. This instruction sheet should be reviewed with each patient or guardian to assure understanding of the proper care for the treatment site.

11. Patients should be instructed that until the polymerized film of high viscosity DERMABOND adhesive has sloughed naturally (usually in 5-15 days), there should be only transient wetting of the treatment site. Patients may shower and bathe the site gently. The site should not be scrubbed, soaked, or exposed to prolonged wetness until after the film has sloughed naturally and the wound has healed closed. Patients should be instructed not to go swimming during this period.

12. If removal of high viscosity DERMABOND adhesive is necessary for any reason, carefully apply petroleum jelly or acetone to the high viscosity DERMABOND film to help loosen the bond. Peel off the film, do not pull the skin apart.

HOW SUPPLIED
High viscosity DERMABOND adhesive is supplied sterile, in a pre-filled, single-use applicator. The applicator is comprised of a crushable glass ampule contained within a plastic vial with attached applicator tip. The product is also available with a pen applicator. The applicator contains the liquid adhesive. The applicator is packaged in a blister pouch to maintain the device sterile until opened or damaged.

STORAGE
Recommended storage conditions: below 30°C, 80°F, away from moisture, direct heat, and direct light. Do not use after expiry date.

STERILITY
High viscosity DERMABOND adhesive is originally sterilized by dry heat and ethylene oxide gas. Do not resterilize. Do not use if package is opened or damaged. Discard any unused material following completion of medical procedure.

If the primary method of closure was insufficient for closure, an additional securing device was placed. The time to perform treatment included the time required later to remove the closure device when applicable.

The Modified Hollander Cosmesis Scale (MHCS), a validated scale, was used to evaluate cosmesis at three months: step-off borders, edge inversion, contour irregularities, excess inflammation, wound margin separation, and overall appearance.

DIRECTIONS FOR USE
1. The application of high viscosity DERMABOND adhesive requires thorough wound cleansing. Follow standard surgical practice for wound preparation before application of high viscosity DERMABOND adhesive (i.e., anesthetize, irrigate, debride, obtain hemostasis and close deep layers).

2. Pat the wound dry with dry, sterile gauze to assure direct tissue contact for adherence of the high viscosity DERMABOND adhesive to the skin. Moisture accelerates high viscosity DERMABOND adhesive’s polymerization and may affect wound closure results.

3. To prevent inadvertent flow of liquid high viscosity DERMABOND adhesive to unintended areas of the body, the wound should be held in a horizontal position and the high viscosity DERMABOND adhesive should be applied from above the wound.

4. High viscosity DERMABOND adhesive should be used immediately after crushing the glass ampule, since the liquid high viscosity DERMABOND adhesive will flow freely from the tip for only a few minutes. Remove the applicator from the blister pouch. If using the pen applicator, refer to the instructions on the pouch for crushing the glass ampule and expressing the liquid adhesive. If using the plastic vial, hold the applicator with the thumb and a finger and away from the patient to prevent any unintentional placement of the liquid high viscosity DERMABOND adhesive into the wound or on the patient. While holding the applicator, and with applicator tip pointed upward, apply pressure at the midpoint of the ampule to crush the inner glass ampule. Invert and gently squeeze the applicator just sufficiently to express the liquid high viscosity DERMABOND adhesive to moisten the applicator tip.

5. Approximate wound edges with gloved fingers or sterile forceps. Slowly apply the liquid high viscosity DERMABOND adhesive in multiple (at least two) thin layers to the surface of the approximated wound edges using a gentle brushing motion. Wait approximately 30 seconds between applications or layers. Maintain manual approximation of the wound edges for approximately 60 seconds after the final layer.

NOTE: High viscosity DERMABOND adhesive polymerizes through an exothermic reaction. If the liquid high viscosity DERMABOND adhesive is applied so that large droplets are allowed to remain without being evenly spread, the patient may experience a sensation of heat or discomfort. The sensation may be higher on sensitive tissues. This can be minimized by applying high viscosity DERMABOND adhesive in multiple thin layers (at least two).

NOTE: Excessive pressure of the applicator tip against the wound edges or surrounding skin can result in forcing the wound edges apart and allowing high viscosity DERMABOND adhesive into the wound. High viscosity DERMABOND adhesive within the wound could delay wound healing and/or result in adverse cosmetic outcome.

NOTE: Full apposition strength is expected to be achieved about 2.5 minutes after the final layer is applied, although the top adhesive layer may remain tacky for up to approximately 5 minutes. Full polymerization is expected when the top high viscosity DERMABOND adhesive layer is no longer sticky.