IMPORTANT INFORMATION
Please Read Before Use

TRUFILL® n-Butyl Cyanoacrylate (n-BCA) Liquid Embolic System

n-Butyl Cyanoacrylate

STERILE EO

Sterilized using dry heat, and Sterilized using ethylene oxide gas.

Tantalum Powder

STERILE R

Sterilized using Irradiation.

Ethiodized Oil

STERILE A

Sterile using aseptic processing techniques.

RX Only

Description
The TRUFILL® n-Butyl Cyanoacrylate (n-BCA) Liquid Embolic System is an artificial embolization device, comprised of TRUFILL n-Butyl Cyanoacrylate (n-BCA), TRUFILL Ethiodized Oil and TRUFILL Tantalum Powder. These components must be used as a system. They are not intended for use as individual components.

The TRUFILL System is used under fluoroscopic guidance to obstruct or reduce blood flow to cerebral arteriovenous malformations (AVMs) via superselective catheter delivery.
Upon contact with body fluids or tissue, the mixture polymerizes into a solid material. The n-BCA is a clear, free-flowing liquid that polymerizes via an anionic mechanism. Ethiodized oil is a straw-to-amber colored, oily fluid containing iodinated poppy seed oil and is used as a radiopaque polymerizing retardant. The amount of ethiodized oil used will vary the rate of polymerization. Tantalum powder is a finely ground, irregularly shaped, dark gray metal that can be used with ethiodized oil to make the n-BCA radiopaque.

The **TRUFILL** n-Butyl Cyanoacrylate (n-BCA) Liquid Embolic System is available in two kit configurations:

<table>
<thead>
<tr>
<th>Product Code</th>
<th>Description</th>
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<tbody>
<tr>
<td>631-400</td>
<td>Two 1 g tubes of n-BCA, one 10 mL vial of Ethiodized Oil and one 1 g vial of Tantalum Powder</td>
</tr>
<tr>
<td>631-500</td>
<td>One 1 g tube of n-BCA, one 10 mL vial of Ethiodized Oil and one 1 g vial of Tantalum Powder</td>
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**Indications**

The **TRUFILL** n-BCA Liquid Embolic System is indicated for the embolization of cerebral arteriovenous malformations (AVMs) when pre-surgical devascularization is desired.

**Contraindications**

Separate use of the individual components of the **TRUFILL** n-BCA Liquid Embolic System is contraindicated. The components must be used as a system. Ethiodized oil alone should not be injected:

- Intravascularly
- Intrathecally
- Intrabronchially
Use of the TRUFILL n-BCA Liquid Embolic System is contraindicated when any of the following conditions exist:

- Optimal catheter placement is not possible
- A previous history of reactions to cyanoacrylates exists
- A previous history of hypersensitivity to ethiodized oil exists
- A previous history of reactions to iodine exists
- Provocative testing indicates intolerance to the occlusion procedure
- Vasospasm stops blood flow
- High blood flow precludes safe infusion of an embolic agent

WARNINGS

- The safety and effectiveness of the TRUFILL n-BCA Liquid Embolic System as a long-term implant has not been established.
- Performing therapeutic embolizations to occlude blood vessels is a high risk procedure. Perform the procedure only under the direction of personnel with interventional training and thorough knowledge of angiographic techniques.
- Prior to injection it is essential to determine, via fluoroscopy, the radiopacity of the mixture by comparison with a similar syringe containing contrast. Inadequate visualization of the mixture could cause inappropriate embolization.
- The n-BCA is a fast-setting adhesive capable of adhering to most body tissues. It will polymerize in the presence of anionic media, such as body fluids or tissues. Proper handling is required to avoid premature polymerization and occlusion of the delivery system or adherence of the catheter tip to the vessel wall.
- TRUFILL Ethiodized Oil should never be used as a radiopaque contrast agent to assess hemodynamics and should be used only to prepare the TRUFILL n-BCA Liquid Embolic System.
• AVM embolization could influence blood flow patterns, thereby subjecting arteries supplying the AVM or the brain proximal to the AVM to increased pressures. Increased arterial pressures can result in hemorrhagic complications.
• Laboratory studies have determined that TRUFILL Ethiodized Oil can elute over time.
• Life threatening and fatal reactions can occur without warning. A fully equipped emergency cart and resuscitation equipment must be readily available at all times, along with personnel competent in recognizing and treating reactions of all severity.

Precautions
• Store in a cool, dark, dry place.
• Inspect the sterile package carefully. Do not use if:
  • the package or seal appears damaged,
  • the contents appear damaged,
  • the expiry date has passed.
• Angiography is necessary for pre-embolization evaluation, operative control, and post-embolization follow-up.
• Verify that the n-BCA is a clear and free-flowing liquid prior to use. Discard material that is thickened or discolored. Use of a 21 or 23 gauge needle to aspirate the n-BCA into an appropriate injection syringe is recommended.
• The n-BCA will adhere to most surfaces. Avoid contact with non-disposable surfaces or surfaces that cannot be cleaned with acetone.
• Gloves and eye/face protection are recommended when handling n-BCA.
• Verify that the catheters and accessories used in direct contact with the system are clean and compatible with the material and do not trigger polymerization or degrade upon contact. Refer to “Accessories” under the “Recommended Procedure” section of these Instructions for Use.
• Do not use with any device containing polycarbonate. Cyanoacrylates cause polymers containing polycarbonate to deteriorate.

Training
Serious, including fatal, consequences can result with the use of the TRUFILL n-BCA Liquid Embolic System without adequate training. Contact your Codman Neurovascular sales representative for information on training courses.

Adverse Events
A total of 104 patients (52 TRUFILL n-BCA Liquid Embolic System, 52 poly-vinyl alcohol (PVA) (control)) were enrolled for safety evaluation in a clinical trial for the treatment of cerebral AVMs. Two patients who were randomized to PVA, but who received n-BCA after failed attempts to effectively embolize with PVA, have their complications listed (n-BCA or PVA) by when they occurred, i.e., during embolization or during surgical resection. Four of the five complications these patients experienced occurred during the PVA embolization stage and therefore are listed as PVA complications. One complication (other – considerable bleeding) occurred during resection after n-BCA embolization and, therefore, is listed as an n-BCA complication. Therefore, the number of patients used for calculation of the incidence of adverse events in the n-BCA group is 54. Fifty-two percent of the patients in the n-BCA group and 54% of the patients in the PVA group (n-BCA: 51.9%, N = 28, and PVA: 53.9%, N = 28) had at least one complication. There was one unanticipated adverse device event (UADE) reported for a patient in the n-BCA group during the study, described in Table 1. Two patients died during the treatment period; one due to cerebellar hemorrhage (n-BCA) and the other due to intracerebral hemorrhage (PVA),
and 2 patients (PVA) died post-resection. The treatment period was defined as from pre-surgical embolization up through surgical resection. All reported adverse events that occurred in the n-BCA System cohort in the pivotal clinical study are listed in Table 1. The adverse events are listed in descending order according to frequency as observed for the study treatment group.

Adverse events associated with embolization procedures (including those observed during the clinical study), can occur at any time during or after the procedure. These adverse events include (in alphabetical order): allergic reaction, AVM rupture, catheter glued inside vessel, death, early polymerization, headache, hemorrhage, infection/inflammation, late polymerization, neurological deficits, occluded catheter, passage of embolic material into normal vessels adjacent to the lesion, pulmonary embolism, seizure, stroke or cerebral infarction, thromboembolism, vasospasm, vessel dissection, and vessel perforation.

**Clinical Study**

**Study Design**

A prospective, multi-center, single-blind, randomized study was conducted to determine whether the TRUFILL n-BCA Liquid Embolic System was as safe and effective as PVA for use in the obliteration of cerebral AVMs when pre-surgical devascularization is desired. The primary effectiveness endpoint was the degree of vascular occlusion (percent nidus/lesion reduction and number of vessels occluded) as determined by the angiographic core laboratory. Secondary effectiveness endpoints were the length of time to resect the AVM and the number of transfusions required/total blood loss during the surgery. Primary safety outcomes for comparison to control treatment were the incidences of
device-related complications, procedural complications, intracranial events, and unanticipated adverse device effects. Other safety measures, clinical neurological examinations, Glasgow Outcome Scores, and NIH Stroke Scale scores, were summarized at each of the follow-up time periods: post procedure, pre surgery, and post surgery. Patients enrolled in the study were those who had an AVM that required preoperative devascularization as determined angiographically. Patients with Spetzler-Martingrade III, IV and V AVMs were treated. Patients with grade I and II lesions were treated if the anticipated benefit of the embolization was greater than the risk of the embolization procedure, and if the AVM feeding pedicle was located in an area that was difficult to surgically access. Conjunctive therapy using coils was permitted prior to embolization to slow the flow rate (if needed) or if a portion of the AVM contained blood vessels that were larger than the largest size of PVA available. Patients who had been previously embolized with PVA or cyanoacrylate and patients with a known sensitivity to iodine containing contrast reagents were excluded from the study.

**Patient Accounting**

A total of 104 patients were enrolled into the study, 52 patients were randomized into each treatment group. Three patients of the PVA group were determined not able to be evaluated for the effectiveness analysis. Two crossover patients were randomized to PVA, but were treated with n-BCA and one PVA patient was not used for effectiveness analyses due to inadequate source documentation. Four n-BCA patients were not embolized and therefore not included in the effectiveness analyses. Two patients were not embolized due to an inability to subselect the feeder vessel. One patient was not embolized because the physician deemed the location and type of AVM too dangerous to embolize. Finally, one patient was embolized
with coils at Stage 1 and was to receive n-BCA during Stage 2 but withdrew consent. Therefore the total number of patients who were included in the primary effectiveness endpoint analysis was 9; 48 patients in the n-BCA group and 49 patients in the PVA group. The safety data set included 54 n-BCA and 52 PVA patients. Two patients who were randomized to PVA, but who received n-BCA after failed attempts to effectively embolize with PVA, have their complications listed (n-BCA or PVA) by when they occurred, i.e., during embolization or during surgical resection. Four of the five complications these patients experienced occurred during the PVA embolization stage and therefore are listed as PVA complications. One complication (other – considerable bleeding) occurred during resection after n-BCA embolization and, therefore, is listed as an n-BCA complication.

**Methods**

Preembolization and postembolization angiograms were obtained to determine the extent of occlusion achieved. The angiograms were sent to the angiographic core laboratory where anterior/posterior (AP) and lateral views of the nidus and selective arteriograms of the selected feeding pedicles were evaluated.

**Primary Effectiveness Results**

The primary effectiveness endpoint was the degree of vascular occlusion (percent nidus/lesion reduction and number of vessels occluded). Staged embolizations (more than one embolization procedure per patient) were allowed. The mean percent reduction in lesion volume and the mean number of feeding vessels occluded per patient and per stage are listed in Table 2.
**Secondary Effectiveness/Safety Results**

Additional parameters assessed included the time of resection and the blood volume replacement needed (units of blood, fluid/colloid, or amount from autologous blood recovery device.) Results for the time of resection and blood volume replacement are reported in Table 3.

**How Supplied**

This product is for SINGLE USE ONLY; DO NOT RESTERILIZE. Codman & Shurtleff will not be responsible for product that is resterilized, nor accept for credit or exchange product that has been opened but not used.

As long as the inner unit is not opened or damaged, the product is sterile and nonpyrogenic.

**Storage and Handling**

Remove the components from the carton just prior to use. Protect the ethiodized oil from light.

**Directions for Use**

**Recommended Accessories**

**Caution:** Do not use with syringes containing polycarbonate. Verify syringe material before use.

- The **TRUFILL** n-BCA Liquid Embolic System is designed to be delivered under fluoroscopy to targeted lesions through the **PROWLER** and **TRANSIT** families of microcatheters.
- The n-BCA, Ethiodized Oil, and Tantalum Powder (if used) mixture should be prepared using a 1mL to 10 mL syringe (made of polyethylene or polypropylene).
- To inject the mixture through the infusion catheter, a 1 mL to 3 mL syringe with Luer lock made of polyethylene or polypropylene is recommended.
• A 21 or 23 gauge needle is recommended to aspirate and/or transfer the n-BCA, the ethiodized oil and the mixture.
• A sterile 25 mL to 50 mL glass beaker or equivalent is recommended for preparation of the mixture.

**Pre-Embolization**
Serious, including fatal, consequences can result with the use of the TRUFILL n-BCA Liquid Embolic System without adequate training. Contact your Codman Neurovascular sales representative for information on training courses.

1. Prior to use, perform baseline angiography to determine the vascular supply to the lesion. The angiogram should demonstrate the route of the catheter entry as well as identify relevant collateral circulation.
2. Introduce the infusion catheter according to standard technique. Position the infusion catheter as close as possible to the treatment site to avoid inadvertent occlusion of normal vessels.
3. Perform contrast injections to assess hemodynamics prior to embolization.

**Caution:** The ethiodized oil must not be used as a radiopaque contrast agent to assess hemodynamics and must be used only to prepare the n-BCA mixture. Ethiodized oil is contraindicated for intravascular, intrathecal or intrabronchial use.

**Recommended Mixtures**
1. Radiopacity of the n-BCA mixture is accomplished by adding ethiodized oil and tantalum powder to the n-BCA. These additives will also extend the polymerization time of the n-BCA.
2. Recommended ratios of n-BCA to ethiodized oil and tantalum powder vary depending on the location of injection (feeding pedicle or intranidal), the diameters of the pedicle
and nidal component supplied, tortuosity/linearity of the pedicle, presence of AV fistulae, and flow rates. Therapeutic embolization should not be performed when high blood flow precludes the safe infusion of embolic agent. Higher concentrations of ethiodized oil increase the polymerization time, which allows the physician to penetrate the nidus more distally. Higher concentrations of n-BCA result in a faster polymerization rate, which will allow the physician to embolize the nidus more proximally. Ratios used in the prospective, randomized clinical study of the TRUFILL System varied from 10% to 70% n-BCA and 30% to 80% ethiodized oil by volume. Ratios outside these parameters have not been tested clinically and are not recommended. Guidelines are recommended in Table 4.

**Note:** If feeding pedicle injections suggest an AV fistula where venous opacification occurs upon contrast injection within 1/3 second, placement of a coil(s) to reduce flow should be considered prior to n-BCA injection. Coil placement was used in 15 of 77 (19%) treatment stages during the TRUFILL n-BCA System Clinical Study.

**Preparation of Mixture**

1. Snap the top off the neck of the ethiodized oil vial using a sterile alcohol wipe.
2. Put the desired amount of ethiodized oil and, if using, tantalum powder into a clean, sterile glass beaker. Mixing can be achieved by aspirating in and out of a syringe until the mixture appears homogenous.

**Caution:** Thoroughly mix the radiopacity agents prior to adding the n-BCA. Do not use tantalum powder alone with n-BCA.
3. To remove the TRUFILL n-BCA from the tube, attach the self-piercing cap to a Luer lock syringe and then attach the other end of the cap (with the syringe connected to it) to the n-BCA tube. While screwing the cap onto the tube you will first feel resistance which will ease when the seal of the tube is punctured. Continue twisting the cap onto the tube until resistance builds again, signaling a proper seal between the syringe, cap, and tube. Avoid spilling the n-BCA, by keeping the tube crimped side down and the cap with syringe up until a proper seal is achieved. To withdraw the n-BCA, turn the syringe-cap-tube assembly to the tube crimped side up and extract the desired amount of n-BCA into the syringe.

4. Inspect the n-BCA to verify that it is clear and free flowing. Discard any material that is thickened, discolored, or contains particulate matter prior to use.

5. Add the desired amount of n-BCA to the sterile glass beaker. Mix thoroughly as described above until the mixture appears homogenous.

**Warning:** Polymerization time, viscosity, and injection technique are interrelated and affect the progress of embolization. The appropriate formulation of any additives is dependent upon the expert evaluation of the relationship of anatomy, hemodynamics, and the catheter system. Figure 1 illustrates the polymerization rates obtained during in vitro testing in static bovine plasma.

**Warning:** A 0:1 ethiodized oil to n-BCA ratio should never be used. Refer to the “Recommended Mixtures” section for recommended ratios.
6. To determine whether your mixture is sufficiently radiopaque for visualization, compare it under fluoroscopy to a similar syringe full of contrast media.

![Approximate Polymerization Time](image)

**Figure 1**

**Injection of Mixture**

1. Prepare the infusion catheter by thoroughly rinsing the outside of the catheter hub and flushing the catheter with a 5% dextrose solution in water.

   **Note:** Do not rinse the glass beaker and/or the syringes with 5% dextrose prior to use. Prolonged contact of n-BCA with 5% dextrose could initiate the polymerization process.

2. Aspirate the mixture into an appropriate injection syringe through a 21 or 23 gauge needle to verify that no material is agglomerated. Verify that the mixture is well suspended and free of air bubbles.
3. Positioning the syringe tip slightly upwards (this will minimize the potential for agglomerated tantalum to obstruct the catheter lumen), inject the mixture through the infusion catheter, using hand control and high resolution fluoroscopic monitoring.

**Warning:** If resistance is met during injection, do not attempt to clear or overcome the resistance by applying increased pressure. If this occurs, determine the cause of resistance and remove the catheter, if necessary. Applying increased pressure could result in rupture of the catheter and deposition of the mixture in an undesired area.

4. After injection is completed, immediately aspirate with the injection syringe and rapidly withdraw the catheter to prevent adherence of the catheter tip and to ensure that no unpolymerized mixture will leak during catheter withdrawal.

**Note:** If the microcatheter tip becomes glued to the intracranial site, cut the microcatheter at the hub and remove the guiding catheter. Affix the microcatheter to the groin site. The microcatheter can then be removed during surgical resection of the AVM. If the microcatheter fractures during removal, distal migration or coiling of the microcatheter fragment could occur. Same-day surgical AVM resection must be considered to avoid the risk of thrombosis.

5. Following each injection, discard the infusion catheter.

6. Discard any opened and unused n-BCA, ethiodized oil, and tantalum powder.
Warranty
Codman & Shurtleff, Inc. warrants that this medical device is free from defects in both materials and workmanship. Any other express or implied warranties, including warranties of merchantability or fitness, are hereby disclaimed. Suitability for use of this medical device for any particular surgical procedure should be determined by the user in conformance with the manufacturer’s instructions for use. There are no warranties that extend beyond the description on the face hereof.
Do not reстерilize

Do not use if package is damaged

Prescription device only (USA)

Nonpyrogenic

Manufacturer

Made in

Quantity

Do not autoclave

Radiopaque