

How to Use ENBREL[®] (etanercept)

INSTRUCTIONS FOR PREPARING AND GIVING AN INJECTION

Introduction

The following instructions are for preparing and giving a dose of ENBREL. ENBREL is given as an injection under the skin. ENBREL should be used under the guidance and supervision of a doctor. Your/your child's doctor or nurse will assist you in preparing and injecting your first dose (or first few doses) of ENBREL. Do not attempt to prepare or inject ENBREL on your own until you understand how to mix the powder and liquid and inject a dose. If you are having difficulty giving an injection, we encourage you to ask a family member or other caregiver to become involved with your treatment and learn how to give your injection.

FOR USE IN CHILDREN: The appropriate dose for your child will vary depending on your child's body weight. Your child's doctor will inform you of the correct amount of drug to use. If your child's doctor has instructed you to use one vial of ENBREL solution for more than one dose, YOU SHOULD NOT USE THE SAME NEEDLE AND SYRINGE. The supplied syringe and 25 gauge needle should be used only once. Contact your/your child's doctor or healthcare provider to obtain additional syringes (1 mL) and needles (25 or 27 gauge). For further instructions for use in children, please see Steps 2 and 3.

SINCE THE PRODUCT WAS FIRST INTRODUCED, SERIOUS INFECTIONS, SOME INVOLVING DEATH, HAVE BEEN REPORTED IN PATIENTS USING ENBREL. MANY OF THESE INFECTIONS OCCURRED IN PATIENTS WHO WERE PRONE TO INFECTIONS, SUCH AS THOSE PATIENTS WITH ADVANCED OR POORLY CONTROLLED DIABETES. ALSO, RARE CASES OF TUBERCULOSIS HAVE BEEN REPORTED. ENBREL SHOULD BE DISCONTINUED IN PATIENTS WITH SERIOUS INFECTIONS. DO NOT START ENBREL IF YOU/ YOUR CHILD HAVE AN INFECTION OR IF

YOU/YOUR CHILD HAVE AN ALLERGY TO ENBREL OR ITS COMPONENTS. ENBREL SHOULD BE USED WITH CAUTION IN PATIENTS PRONE TO INFECTION. CONTACT YOUR/YOUR CHILD'S DOCTOR IF YOU HAVE ANY QUESTIONS ABOUT ENBREL OR INFECTIONS.

There have been reports of serious nervous system disorders such as multiple sclerosis, seizures or inflammation of the nerves of the eyes. Tell your doctor if you/your child had any of these disorders or if you/your child develop these disorders after starting ENBREL. There also have been rare reports of serious blood disorders, some involving death. **Contact your/your child's doctor immediately if you/your child develop symptoms such as persistent bruising, bleeding, paleness, or fever.** It is unclear if ENBREL has caused these nervous system or blood disorders. If your/your child's doctor confirms serious blood problems, you/your child may need to stop using ENBREL.

Some patients have developed a condition that resembles lupus. Manifestations of this condition may include joint discomfort, rash on the cheeks or arms that is sensitive to the sun, and blood test changes. If you develop these problems, your doctor may decide to discontinue ENBREL therapy.

Some people have reported redness, itching, pain, swelling, bleeding, and/or bruising where the injection was given. If you/your child experience any of these symptoms, and they concern you, contact your/your child's doctor, nurse, or pharmacist.

NOTE: The needle cover is made from latex. If you or your child are allergic to latex, talk to your/your child's doctor before using.

ENBREL dose trays should be stored in the refrigerator at 36° to 46°F (2° to 8°C). **DO NOT FREEZE ENBREL.**

Any questions about therapy with ENBREL (for example, what to do if you miss a dose) should be directed to your/your child's doctor, nurse, or pharmacist. A toll-free information service is also available: 1-888-4ENBREL (1-888-436-2735).

Step 1: Setting up for an injection

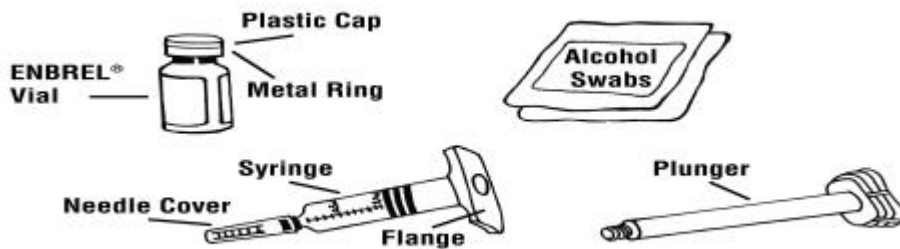
Select a clean, well-lit, flat working surface, such as a table.

Take the ENBREL dose tray out of the refrigerator and place it on your flat working surface.

Wash your hands with soap and warm water.

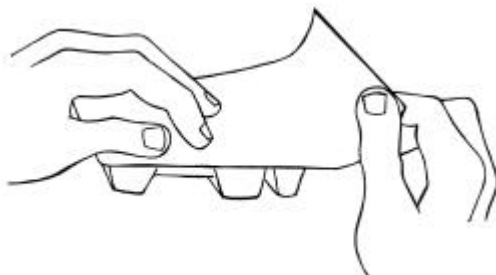
The dose tray should contain five items as pictured below:

- One prefilled diluent syringe containing 1 mL of diluent
- One plunger
- One ENBREL vial
- Two alcohol swabs



If these five items are not included in the dose tray, contact your pharmacist. Also, check the expiration date on the dose tray. If the expiration date has passed, do not use the dose tray. Contact your pharmacist.

Peel the paper seal off the dose tray.



Check the expiration (Exp.) date on the ENBREL vial label and prefilled diluent syringe label. The dates should be the current month and year or later. If the expiration date has passed, do not use the ENBREL vial or prefilled diluent syringe. Contact your pharmacist.

Inspect the volume of diluent in the syringe with the covered needle pointing down. Use the unit markings on the side of the syringe to make sure there is at least 1 mL of liquid in the syringe. If the level of liquid is below the 1 mL mark, do not use. Call 1-888-4ENBREL (1-888-436-2735) for assistance.

Step 2: Preparing the ENBREL solution

There are three methods for preparing the ENBREL solution:

- The Free-Hand method (see Step 2A)
- The Mixing Station method (see Step 2B)
- The Dose Preparation Guide method (see Step 2C)

For those patients who may not be able to use the free-hand method to prepare the dose due to their arthritis of the hands, the other methods are provided as alternatives. Contact your doctor or nurse if you have questions about which method to use.

For Use in Children:

For use in children, **you may be instructed by your child's healthcare provider to withdraw more than one dose from the same ENBREL vial.** The vial of ENBREL should be labeled with the date immediately after mixing the ENBREL powder and liquid. Write this date in the area marked "Mixing Date:" on the supplied sticker and

attach the sticker to the vial. Store the vial in the refrigerator at 36° to 46°F (2° to 8°C) as soon as possible, but always within 4 hours of mixing the solution. The ENBREL solution must be used within 14 days of the mixing date. You should discard the vial and any remaining solution if it is not used within 14 days. **THE STABILITY AND STERILITY OF THE MIXED ENBREL SOLUTION CANNOT BE GUARANTEED AFTER 14 DAYS. To prepare additional doses from the same vial of ENBREL solution, skip to Step 3.** Note that you will need one new needle (25 or 27 gauge) and one syringe (1 mL) for each additional dose. The supplied syringe and needle should never be reused. The Mixing Station and Dose Preparation Guide methods cannot be used to prepare additional doses because only the syringe supplied with the ENBREL dose tray is compatible with these devices. You may wish to contact your doctor or nurse on the use of the free-hand method if you have been trained in the use of the other methods and are unsure of how to prepare ENBREL using the free-hand method.

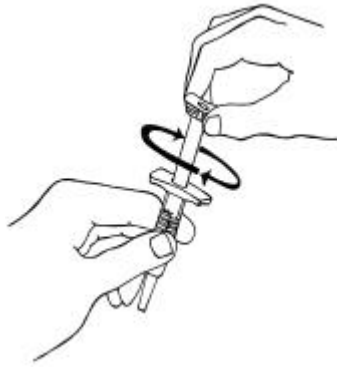
Step 2A: Free-Hand Method

To use the Free-Hand method, follow the steps below.

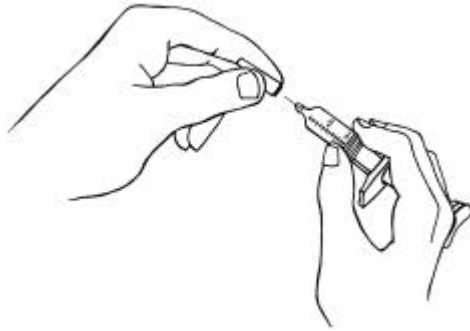
1. Remove the pink plastic cap from the ENBREL vial. Do not remove the gray stopper or silver metal ring around the top of the vial.



2. Use one alcohol swab to clean the gray stopper on the ENBREL vial. After cleaning, place the ENBREL vial upright on a flat surface. Do not touch the stopper with your hands.
3. Slide the plunger into the syringe, turning clockwise until a slight resistance is felt (that is, more force is required to turn the plunger).

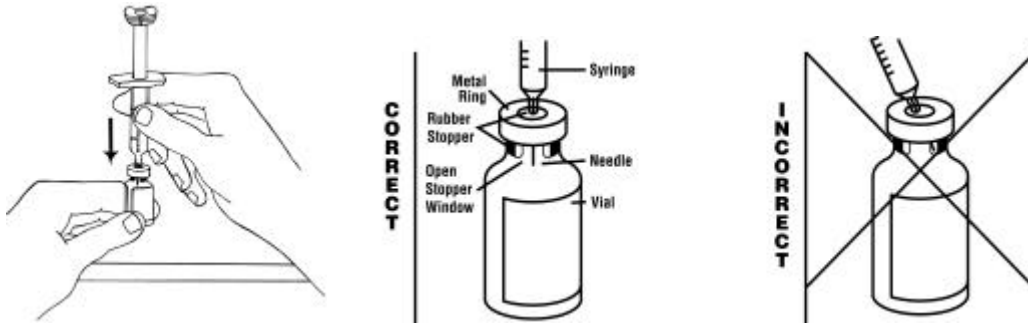


4. Pull the needle cover straight off the syringe. **DO NOT** touch the needle or allow it to touch any surface. **DO NOT** touch or bump the plunger; doing so could cause the solution to leak out.

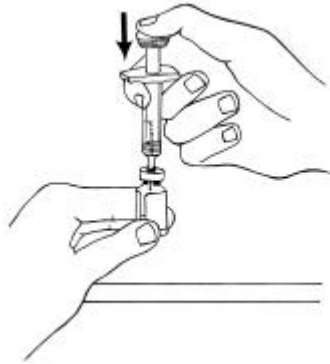


ADDING DILUENT

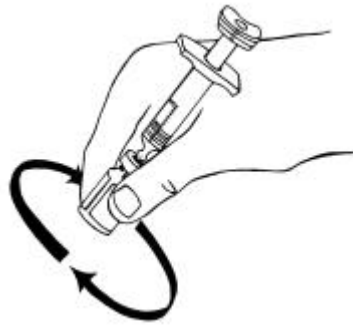
5. With the ENBREL vial upright on the flat working surface, insert the needle straight down through the center ring of the gray stopper (see illustrations). If the needle is correctly lined up, you should feel a slight resistance and then a “pop” as the needle goes through the center of the stopper. Look for the needle tip inside the stopper window. If the needle is not correctly lined up with the center of the stopper, you will feel constant resistance as it goes through the stopper and no “pop”. The needle may enter at an angle and bend, break or prevent proper addition of diluent into the vial.



6. Push the plunger down VERY SLOWLY until all liquid from the syringe is in the vial. Adding the liquid too fast will cause a lot of foaming (bubbles).



7. Leave the syringe in place. Gently swirl the vial between fingers in a circular motion to dissolve the powder (see illustration). **DO NOT SHAKE.** Wait until all the powder dissolves (usually less than 10 minutes). The solution should be clear and colorless. After the powder has completely dissolved, foam (bubbles) may still be present. This is normal. **Do not inject the solution if it contains lumps, flakes, or particles.** If all the powder in the vial is not dissolved or there are particles present after 10 minutes, call 1-888-4ENBREL (1-888-436-2735) for assistance.



WITHDRAWING THE ENBREL SOLUTION FROM THE VIAL

With the needle in the vial, turn the vial upside down. Holding the vial at eye level, slowly pull the plunger down to the unit markings on the side of the syringe that correspond with your/your child's dose. For adult patients, remove the entire volume (1 mL), unless otherwise instructed by your doctor. For pediatric patients, remove only the portion of the solution as instructed by your child's doctor. As the solution level drops in the vial, you may need to partially withdraw the needle to keep the tip of the needle in the solution. Some white foam may remain in the vial — this is normal.



With the needle still inserted in the vial, check for air bubbles in the syringe. Gently tap the syringe to make any air bubbles rise to the top of the syringe (see illustration). Slowly push the plunger up to remove the air bubbles. If you push solution back into the vial, slowly pull back on the plunger to draw the correct amount of solution back into the syringe.



SKIP TO STEP 4 FOR INSTRUCTIONS ON HOW TO SELECT AND PREPARE THE INJECTION SITE

Step 2B: Mixing Station Method

The mixing station is a device that is made to hold the vial and supplied syringe in place to guide the needle into the vial correctly. The mixing station is provided in the *Dosing System* starter kit that contains items designed to help you prepare and inject a dose of ENBREL. The *Dosing System*, which is not a part of this package, is available at no charge upon request through your/your child's doctor by calling 1-888-4ENBREL. A videotape and "Step-by-Step Visual Guide" are also provided in the *Dosing System*. If you choose to use the mixing station method, follow the instructions on the videotape and "Step-by-Step Visual Guide" provided in the *Dosing System*.

Step 2C: Dose Preparation Guide Method

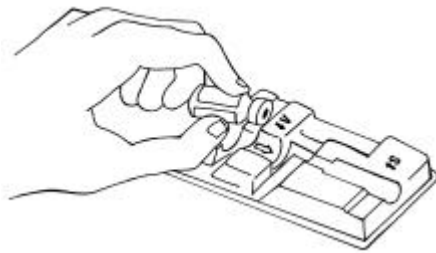
The Dose Preparation Guide method involves using the preparation guide on the underside of the dose tray. The tray underside is specially made to hold the vial and supplied syringe in place while the ENBREL solution is prepared. To use this method follow the steps below.

1. Remove the contents of the tray and turn the tray over.

2. Remove the pink plastic cap from the ENBREL vial. Do not remove the gray stopper or silver metal ring around the top of the vial.



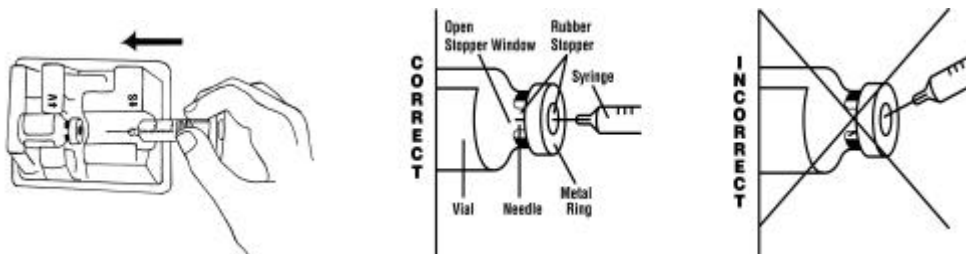
3. Use one alcohol swab to clean the gray stopper on the ENBREL vial. After cleaning, do not touch the stopper with your hands.
4. Press the ENBREL vial into the space next to the ↓V mark in the Dose Preparation Guide; the gray stopper must face the center of the tray. Turn the vial so the open stopper window (see illustration) is facing up.



5. Pull the needle cover straight off the syringe. **DO NOT** touch the needle or allow it to touch any surface.



6. With the needle pointing at the gray stopper in the top of the vial, line up the “0.5 mL” mark on the syringe with the edge of the Dose Preparation Guide (see illustrations). Keep the syringe and needle level so the needle does not touch the tray. Slide the syringe into the Dose Preparation Guide until the needle touches the center ring of the vial’s gray stopper. It may be necessary to rotate the vial slightly to get the needle correctly lined up with the center of the stopper. If the needle is correctly lined up, you should feel a slight resistance and then a “pop” as you push the needle through the center of the stopper. If necessary, turn the vial again so the stopper window is up and visible. Look for the needle tip inside the stopper window. If the needle is not correctly lined up with the center of the stopper, you will feel constant resistance as it goes through the stopper and no “pop”. The needle may enter at an angle and bend, break, or prevent addition of diluent into the vial.

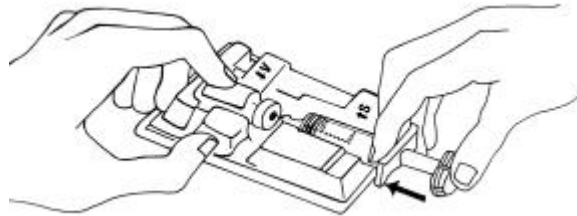


7. Slide the plunger into the syringe, turning clockwise until a slight resistance is felt (that is, until more force is required to turn the plunger).

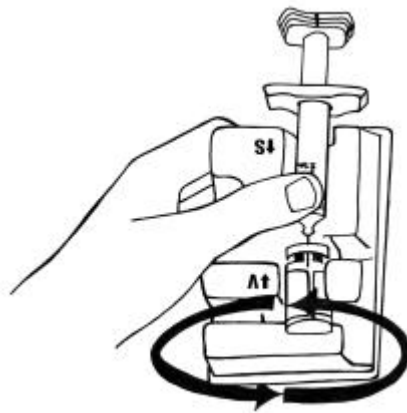


ADDING DILUENT

8. Push the plunger down VERY SLOWLY until all the liquid from the syringe is in the vial. Adding the liquid too fast will cause a lot of foaming (bubbles).

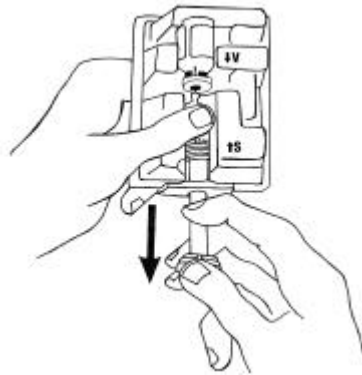


9. While holding the syringe in place, lift the Dose Preparation Guide so the vial is in an upright position. Gently move the Dose Preparation Guide in a circular motion to dissolve the powder (see illustration). **DO NOT SHAKE.** Wait until all the powder dissolves (usually less than 10 minutes). The solution should be clear and colorless. After the powder has completely dissolved, foam (bubbles) may still be present. This is normal. **Do not inject the solution if it contains lumps, flakes, or particles.** If all the powder in the vial is not dissolved or there are particles present after 10 minutes, call 1-888-4ENBREL (1-888-436-2735) for assistance.

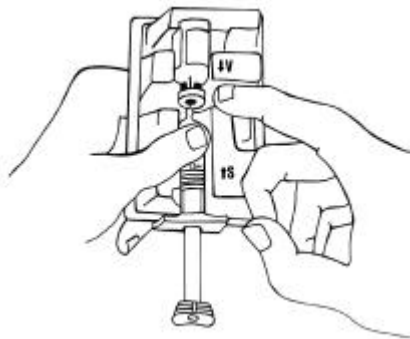


WITHDRAWING THE ENBREL SOLUTION FROM THE VIAL

10. With the needle in the vial, hold the Dose Preparation Guide with the vial upside down at eye level. Holding the Dose Preparation Guide at eye level, slowly pull the plunger down to the unit markings on the side of the syringe that correspond with your/your child's dose (see illustration). For adult patients, remove the entire volume (1 mL) unless otherwise instructed by your doctor. For children, remove only the portion of solution as instructed by your child's doctor. Some white foam may remain in the vial—this is normal.



11. With the needle still inserted in the vial, check the syringe for air bubbles. Gently tap the syringe to make any air bubbles rise to the top of the syringe. Slowly push the plunger up to remove the air bubbles. If you push solution back into the vial, slowly pull back the plunger to draw the solution back into the syringe.



SKIP TO STEP 4 FOR INSTRUCTIONS ON HOW TO SELECT AND PREPARE THE INJECTION SITE

Step 3: For Use In Children - Preparing additional doses from multiple-use ENBREL vials

For some children, one vial of ENBREL solution can be used for more than one dose. Your child's doctor will tell you if this is the case for your child. Contents of one vial of ENBREL solution should not be mixed with, or transferred into, the contents of another vial of ENBREL.

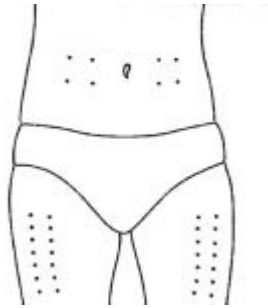
If you are preparing a dose from a vial that was previously used, follow the instructions below:

1. Select a clean, well-lit, flat working surface, such as a table.
2. Your doctor will tell you what type of syringe and needle (25 or 27 gauge only) to use. Alcohol swabs are available at a drug store. Place the new empty sterile syringe with a needle and two alcohol swabs on your flat working surface.
3. Take the vial of ENBREL solution out of the refrigerator and place it on your flat working surface.
4. Check the mixing date you wrote on the sticker on the vial and confirm that the mixed solution is less than 14 days old. **Discard the vial if more than 14 days have passed since the ENBREL solution was mixed.**
5. Wash your hands with soap and water.

6. Use one alcohol swab to clean the gray stopper on the ENBREL vial. Do not touch the stopper with your hands.
7. If the syringe and the needle are not pre-assembled, assemble them as instructed by your doctor.
8. Pull the needle cover straight off the syringe. DO NOT touch the needle or allow it to touch any surface.
9. With the ENBREL vial upright on your flat working surface, insert the needle straight down through the center ring of the gray stopper. Look for the needle tip inside the stopper window. If the needle is not correctly lined up with the center of the stopper, you will not feel a “pop” and you will feel constant resistance as you try to push the needle through the stopper. If you do not line the needle up correctly, it may enter at an angle and bend, break, or prevent proper withdrawal of ENBREL solution from the vial.
10. With the needle still in the vial, turn the vial upside down. Holding the vial at eye level, slowly pull the plunger down to the unit markings on the syringe that correspond to your child’s dose. As the solution level drops in the vial, you may need to partially withdraw the needle to keep the tip of the needle in the solution.
11. With the needle still inserted in the vial, check for air bubbles in the syringe. Gently tap the syringe to make any air bubbles rise to the top of the syringe. Slowly push the plunger up to remove the air bubbles. If you push solution back into the vial, slowly pull back on the plunger to draw the correct amount of solution back into the syringe.

Step 4: Choosing and preparing an injection site

1. Choose an injection site. Three recommended injection sites for ENBREL include: (1) the front of your middle thighs; (2) the abdomen, except for the two-inch area right around your navel; and, (3) the outer area of your upper arms.



2. Rotate the site for each injection. Make sure that the new injection is given at least one inch from sites of recent injections. Do not inject into areas where the skin is tender, bruised, red, or hard. Avoid areas with scars or stretch marks.
3. To prepare the area of skin where ENBREL is to be injected, wipe the injection site with a new alcohol swab. **DO NOT** touch this area again before giving the injection.

Step 5: Injecting the ENBREL Solution

1. Remove the syringe and needle from the vial. Do not touch the needle, or allow it to touch the surface.
2. With one hand, gently pinch the cleaned area of skin and hold it firmly. With the other hand, hold the syringe (like a pencil) at a 45° angle to the skin.
3. With a quick, "dart-like" motion, push the needle into the skin.



4. Let go of the skin with the other hand.
5. With your free hand, slowly push the plunger down to inject ENBREL.



6. When the syringe is empty, pull the needle out of the skin, being careful to keep it at the same angle it was when it was inserted.
7. Slight bleeding may occur. If needed, press a cotton ball or gauze over the injection site for 10 seconds. Do not rub the injection site. If needed, you may cover injection site with a bandage.
8. For Use In Children – If enough solution remains in the vial for another dose, refrigerate the vial after use. Otherwise, discard the vial and any remaining solution.

Step 6: Disposing of Supplies

1. The syringe and needle should **NEVER** be reused. **NEVER** recap a needle.

2. Dispose of both the used needle and syringe in a puncture-resistant container. A "SHARPS" container made specifically for disposing of used syringes and needles may be used. **DO NOT** recycle the container.
3. Keep the container out of the reach of children. When the container is about two-thirds full, dispose of it as instructed by your/your child's doctor, nurse, or pharmacist. Follow any special state or local laws regarding the proper disposal of needles and syringes.
4. The ENBREL vials and used swabs should be placed in the trash, unless otherwise instructed by your/your child's doctor, nurse, or pharmacist. The dose tray and cover may be recycled.

All questions should be answered by a doctor, nurse, or pharmacist familiar with ENBREL. A toll-free information service is also available: 1-888-4ENBREL (1-888-436-2735).

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