

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

PATIENT MEDICATION INFORMATION

PrEnbrel®

etanercept injection

Single-use Prefilled Syringe

Read this carefully before you start taking **ENBREL** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **ENBREL**.

Serious Warnings and Precautions

- **Serious infections.** There have been cases where patients taking ENBREL or other TNF-blocking agents have developed serious infections, including tuberculosis (TB) and infections caused by bacteria, viruses or fungi that have spread throughout their body. Some patients have died from these infections. In very rare cases, hepatitis B recurred in patients with previous hepatitis. If you tend to get infections easily or if you develop an infection while taking ENBREL, you should tell your doctor right away.
- **Malignancies.** There have been cases, sometimes fatal, of unusual cancers in children and teenage patients who started using TNF-blocking agents, including ENBREL, at less than 18 years of age.

What is ENBREL used for?

ENBREL is a medicine for treating people with moderate to severe forms of rheumatoid arthritis (RA), juvenile idiopathic arthritis (JIA) and a type of disease called psoriatic (sore-ee-ah-tick) arthritis (PsA). ENBREL is also for treating adults with a type of arthritis called ankylosing spondylitis (ank-e-low-sing spond-e-lie-tis) (AS). ENBREL is also for adults with moderate to severe psoriasis (sore-l-ah-sis) (PsO) and children with severe psoriasis (PsO). RA, JIA, PsA and AS are inflammatory diseases that affect the joints in your body. PsO is an inflammatory disease that affects the skin and can cause raised, thick, red and scaly patches (“psoriatic skin lesions”) that can appear anywhere on the body. PsA is usually seen in patients with PsO and affects both the joints and the skin.

How does ENBREL work?

ENBREL is a type of protein called a tumour necrosis factor (TNF) blocker that blocks the action of a substance your body makes called TNF-alpha. TNF-alpha is made by your body’s immune system. People with immune diseases like RA, JIA, PsA and PsO, as well as patients with AS, have too much TNF-alpha in their bodies, which can cause inflammation and lead to painful, swollen joints and raised thick, red, scaly patches (“psoriatic skin lesions”) that can appear anywhere on the body. ENBREL can reduce the amount of TNF in the body to normal levels, helping to treat joint damage and skin lesions. In patients with inflammatory arthritis, ENBREL may be effective in reducing signs and symptoms of inflammatory arthritis (such as pain, morning stiffness and fatigue), may help improve your ability to do simple daily activities (such as dressing, walking and climbing stairs), and may help prevent damage to your bones and joints. In patients with psoriatic skin conditions, ENBREL may be effective in clearing skin and improving quality of life (such as personal relationships, work and daily activities, and treatment satisfaction).

When can I expect to see results from taking ENBREL?

Improvement may be seen as early as 1 week after starting ENBREL in adults, and within 2 weeks in children with JIA and 4 weeks with PsO. In clinical trials, full effect was usually seen by 3 months in both adults and children and was sustained with continued treatment.

In clinical trials with PsA, one quarter of patients saw improvement in their joint symptoms within 1 month, one half of patients saw improvement within 3 months, and three quarters of patients saw improvement within 9 months of treatment with ENBREL.

During the PsA clinical trials, approximately 2% of patients treated with ENBREL stopped taking ENBREL due to side effects and up to 5% of ENBREL-treated patients stopped taking ENBREL due to lack of improvement.

What are the ingredients in ENBREL?

Medicinal ingredients: etanercept

Non-medicinal ingredients: L-arginine hydrochloride, sodium chloride, sucrose, and Water for Injection, USP.

ENBREL comes in the following dosage forms:

Single-use prefilled syringes are available in 25 mg* (0.51 mL of a 50 mg/mL solution of etanercept, minimum deliverable volume of 0.47 mL) and 50 mg (0.98 mL of a 50 mg/mL solution of etanercept, minimum deliverable volume of 0.94 mL) dosage strengths.

Single-use prefilled SureClick® autoinjectors are available in a 50 mg (0.98 mL of a 50 mg/mL of etanercept, minimum deliverable volume of 0.94 mL) dosage strength.

Multiple-use vial: ENBREL is also available as a lyophilized powder in a multiple-use vial containing 25 mg etanercept per vial.

Do not use ENBREL if you:

- have ever had an allergic reaction to ENBREL or any of the ingredients in ENBREL.

The needle cover on the prefilled syringe is composed of dry natural rubber, which is made from latex. If you know you are allergic to latex, talk to your healthcare provider before using ENBREL in the prefilled syringe.

- have an infection that has spread through your body (sepsis).

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take ENBREL. Talk about any health conditions or problems you may have, including if you:

- have an infection. This could put you at risk for serious side effects from ENBREL.
- have symptoms of an infection such as fever, sweats or chills, cough or flu-like symptoms, shortness of breath, blood in your phlegm, weight loss, muscle aches, warm, red, or painful areas on your skin, sores on your body, diarrhea or stomach pain, burning when you urinate or urinate more often than normal, and feel very tired.
- have a history of infections that keep coming back or other conditions — like diabetes, HIV, or a weak immune system — that might increase your risk of infections.

* 25 mg single-use prefilled syringe is not available in Canada.

- have tuberculosis (TB), or have been in close contact with someone who has or has had TB. You will need to be evaluated for TB. Your doctor should test you for TB before starting ENBREL.
- were born in, lived in, or traveled to countries where there is a risk for getting TB. Ask your doctor if you are not sure.
- live in, have lived in or have traveled to, areas where there is a greater risk for certain kinds of fungal infections (histoplasmosis, coccidioidomycosis, blastomycosis). These infections may develop or become more severe if you take ENBREL. If you don't know if you have lived in an area where these infections are common, ask your doctor.
- have or have had hepatitis B.
- have or have had persistent numbness, tingling and muscle weakness or a disease such as multiple sclerosis, Guillain-Barré or a Guillain-Barré-like syndrome, which causes inflammation of the nervous system, either in the brain and spinal cord or nerves going to your hands and feet.
- have been newly diagnosed or are being treated for congestive heart failure.
- are scheduled to have major surgery.
- have recently received or are scheduled to receive a vaccine. All vaccines should be brought up-to-date before starting ENBREL. Patients taking ENBREL should not receive live vaccines.
- use the medication Kineret® (anakinra), Orencia® (abatacept) or cyclophosphamide (see The following may interact with ENBREL below).
- have been around someone with varicella zoster (chicken pox, shingles).

Know the medicines you take. Keep a list of them to show your doctor and pharmacist each time you get a new medicine.

Your doctor should monitor you closely for signs and symptoms of TB during treatment with ENBREL even if you have tested negative for TB. If you develop any of the symptoms of TB (a dry cough that doesn't go away, weight loss, fever, night sweats) call your doctor.

If you are not sure or have any questions about any of this information, ask your doctor.

Other warnings you should know about:

All medicines have side effects. Medicines, like ENBREL, that affect your immune system can cause serious side effects. The possible serious side effects include:

- **Nervous system diseases.** There have been rare cases of disorders that affect the nervous system of people taking ENBREL or other TNF-blockers, such as multiple sclerosis, seizures or inflammation of the nerves of the eyes. Signs that you could be experiencing a problem affecting your nervous system include: numbness or tingling throughout your body, problems with your vision, weakness in your arms and/or legs, and dizziness.
- **Blood problems.** In some patients the body may fail to produce enough of the blood cells that can help your body fight infections or help you to stop bleeding. This can lead to death. If you develop a fever that doesn't go away, bruise or bleed very easily or look very pale or feel faint, call your doctor right away. Your doctor may decide to stop treatment. Some people have also had symptoms that resemble lupus (rash on your face and arms that gets worse in the sun) that may go away when you stop taking ENBREL.

- **Heart problems.** You should also tell your doctor if you have ever been treated for heart failure. If you have, your doctor may choose not to start you on ENBREL, or may want to monitor you more closely. Symptoms include shortness of breath or swelling of your ankles and feet.
- **Allergic reactions.** Some patients have had allergic reactions to ENBREL. If you develop a severe rash, swollen face or difficulty breathing while taking ENBREL, call your doctor right away.
- **Malignancies.** Patients with inflammatory diseases including RA, AS or PsO, particularly those with highly active disease, may be at higher risk for lymphoma (a type of cancer). For children and adults taking TNF-blocker medicines including ENBREL, the chances of getting lymphoma or other cancers may increase. Whether treatment with ENBREL might influence the development and course of malignancies in adults is unknown.
- **Liver problems (autoimmune hepatitis).** Liver problems can happen in people who use TNF-blocker medicines, including ENBREL. These problems can lead to liver failure and death. Call your doctor right away if you have any of these symptoms: feel very tired, skin or eyes look yellow, poor appetite or vomiting, pain on the right side of your stomach (abdomen). These symptoms may occur several months after starting and even after ENBREL has been stopped.
- **Psoriasis.** Some people using ENBREL developed new psoriasis or worsening of psoriasis they already had. Tell your doctor if you develop red scaly patches or raised bumps which may be filled with pus. Your doctor may decide to stop your treatment with ENBREL.
- **Serious infections.** ENBREL can lower the ability of your immune system to fight infections. So, taking ENBREL can make you more prone to getting infections or make any infection that you may have worse. Some people have serious infections while taking ENBREL including infections that spread through the body such as tuberculosis (TB), legionellosis (usually a bacterial pneumonia), and listeriosis (usually from contaminated food). Other infections caused by viruses, fungi, bacteria or parasites may occur. Some people have died from these infections.

Can I take ENBREL if I am pregnant or breastfeeding?

The safe use of ENBREL has not been established in pregnant women.

You should tell your doctor if you are pregnant, become pregnant or are thinking about becoming pregnant. If you took ENBREL during pregnancy, talk to your doctor prior to administration of live vaccines to your infant.

ENBREL can pass into breast milk. ENBREL has not been studied in nursing mothers, and therefore its effects on nursing babies are not known. Talk to your healthcare provider about the best way to feed your baby while taking ENBREL.

If you are not sure or have any questions about any of this information, ask your doctor.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with ENBREL:

It is important that you tell your doctor about any other medicines (for example, high blood pressure medicine) you are taking for other conditions before you start taking ENBREL. You should also tell your doctor about any over-the-counter drugs, herbal medicines and vitamin and mineral supplements you are taking.

If you have diabetes and are taking medication to control your diabetes, your doctor may decide you need less anti-diabetic medicine while taking ENBREL.

General Information about ENBREL

Medicines are sometimes prescribed for purposes not mentioned in the Consumer Information leaflet. **Do NOT** use ENBREL for a condition for which it was not prescribed. **Do NOT** give ENBREL to other people, even if they have the same condition.

Can I take ENBREL if I am taking other medicines for my RA, JIA, PsA, AS or other conditions?

In adults, ENBREL can be used in combination with methotrexate. However, little is known of the interaction of ENBREL with methotrexate and other drugs in children with JIA.

Taking ENBREL with Kineret® (anakinra) is not recommended because this may increase your risk of getting a serious infection.

Taking ENBREL with Orencia® (abatacept) is not recommended because this may increase your risk for serious side effects.

Taking ENBREL with cyclophosphamide (used to treat cancer or immune diseases) is not recommended. You may have a higher chance for getting certain cancers when taking ENBREL with cyclophosphamide.

How to take ENBREL:

ENBREL is given as an injection under the skin.

You may continue to use other medicines that help treat your condition while taking ENBREL, such as non-steroidal anti-inflammatory drugs (NSAIDs) and prescription steroids, as recommended by your doctor.

Usual dose:

If you have RA, PsA or AS, the recommended dose of ENBREL for adults is 50 mg per week given as one injection using a 50 mg single-use prefilled syringe or two injections using the 25 mg* single-use prefilled syringe. Your doctor will tell you whether the two injections with the 25 mg* single-use prefilled syringe should be given on the same day once a week or on two different days (3 or 4 days apart) in the same week.

If you have PsO, the recommended starting dose of ENBREL for adult patients is a 50 mg dose twice a week (3 or 4 days apart) for 3 months. After 3 months, your doctor will tell you to reduce your dose to 50 mg once per week, using one 50 mg single-use prefilled syringe or two 25 mg* single-use prefilled syringes.

* 25 mg single-use prefilled syringe is not available in Canada

The recommended dose of ENBREL for children with JIA or PsO is based on the child's body weight. Your child's doctor will tell you the correct amount of ENBREL your child should take. **The 50 mg single-use prefilled syringe is only recommended for children weighing 63 kg (138 pounds) or more.** ENBREL should be given by, or under the supervision of, a responsible adult.

Make sure you have been shown how to inject ENBREL before you do it yourself. You can call your doctor or the toll-free information line at 1-877-9ENBREL (1-877-936-2735) if you have any questions about ENBREL or about giving yourself or your child an injection. Someone you know can also help you with your injection. Remember to take this medicine just as your doctor has told you and do not miss any doses.

Overdose:

Call your doctor if you accidentally inject ENBREL more frequently than instructed.

If you think you have taken too much ENBREL, contact your healthcare professional, hospital emergency department or regional poison control centre immediately, even if there are no symptoms.

Missed Dose:

If you forget to use ENBREL, inject your dose as soon as you remember. Then, take your next dose at your regular(ly) scheduled time. In case you are not sure when to inject ENBREL, call your healthcare provider. A toll-free information service is also available: 1-877-9ENBREL (1-877-936-2735).

Instructions for preparing and giving an injection of ENBREL:

The following instructions are for preparing and giving a dose of ENBREL using a single-use prefilled syringe.

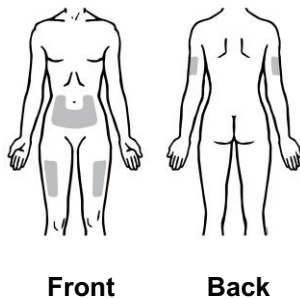
STEP 1: Setting up for an injection

1. Select a clean, well-lit, flat working surface, such as a table.
2. Take the ENBREL carton containing the prefilled syringes out of the refrigerator and place it on your flat working surface. Remove one prefilled syringe and place it on your working surface. **Do NOT** shake the prefilled syringe of ENBREL. Place the carton containing any remaining prefilled syringes back into the refrigerator (2°C to 8°C). **Do NOT** freeze. You may also store the carton of unused prefilled syringes at room temperature, up to 27°C for up to 60 days. If you have any questions about storage, contact your doctor, nurse, or pharmacist for further instructions.
3. Check the expiration date on the prefilled syringe. If the expiration date has passed, or if it has been stored at room temperature beyond 60 days (whichever comes first), **do NOT** use the prefilled syringe and contact your pharmacist or call 1-877-9ENBREL (1-877-936-2735) for assistance.
4. **Do NOT** use the prefilled syringe if the needle cover is missing or not securely attached. Call 1-877-9ENBREL (1-877-936-2735).
5. For a more comfortable injection, allow the ENBREL in the prefilled syringe to reach room temperature (approximately 15 to 30 minutes). **Do NOT** remove the needle cover while allowing it to reach room temperature. **Do NOT** warm ENBREL in any other way (for example, **do NOT** warm it in a microwave oven or in hot water).

6. Assemble the additional supplies you will need for your injection. These include an alcohol swab, a cotton ball or gauze, and a sharps disposal container (see **Step 4: Disposing of Supplies**).
7. Wash your hands thoroughly with soap and warm water.
8. Make sure the solution in the prefilled syringe is clear and colourless. You may notice small white particles in the solution. These particles are formed from ENBREL and this is acceptable. However, **do NOT inject the solution if it is cloudy or discoloured, or contains large or coloured particles** or if the prefilled syringe appears cracked or broken. Call 1-877-9ENBREL (1-877-936-2735) for assistance.

STEP 2: Choosing and Preparing an Injection Site

1. Three recommended injection sites for ENBREL using a prefilled syringe include the:
 - front of the middle thigh;
 - abdomen (stomach area), except for the **five-centimetre** (two-inch) area right around the navel (belly button); and
 - outer area of the upper arm.



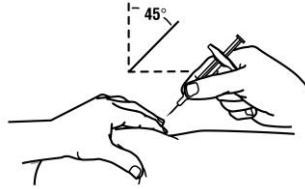
2. Rotate the site for each injection. Make sure that the new injection is given at least one inch from sites of recent injections. **Do NOT** inject into areas where the skin is tender, bruised, red, or hard. Avoid areas with scars or stretch marks.
3. If you have psoriasis, you should try not to inject directly into any raised, thick, red, or scaly skin patches (“psoriasis skin lesions”).
4. To prepare the area of skin where ENBREL is to be injected, wipe the injection site with an alcohol swab. **Do NOT** touch this area again before giving the injection.

STEP 3: Injecting ENBREL Using a Prefilled Syringe

Do NOT remove the needle cover from the prefilled syringe until you are ready to inject.

1. Pick up the prefilled syringe from your flat working surface. Hold the barrel of the prefilled syringe with one hand and pull the needle cover straight off. To avoid damaging the needle, **do NOT** twist or bend the needle cover while you are removing it, and **do NOT** try to put the needle cover back onto the prefilled syringe. When you remove the needle cover, there may be a drop of liquid at the end of the needle; this is normal. **Do NOT** touch the needle or allow it to touch any surface. **Do NOT** touch or bump the plunger. Doing so could cause the liquid to leak out.
2. Holding the syringe with the needle pointing up, check the syringe for air bubbles, gently tap the syringe with your finger until the air bubbles rise to the top of the syringe. Slowly push the plunger up to force the air bubbles out of the syringe.

3. Holding the syringe in one hand like a pencil, use the other hand to gently pinch a fold of skin at the cleaned injection site and hold it firmly.
4. Insert the needle at a slight angle (45 degrees) to the skin. With a quick, “dart like” motion insert the needle into the skin.



5. After the needle is inserted, let go of the skin. Slowly push the plunger all the way down to inject ENBREL.
6. When the syringe is empty, remove the needle from 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 the injection site with a bandage.

STEP 4: Disposing of Supplies

- The syringe should **NEVER** be reused. **NEVER** recap a needle.
- Immediately throw away the used syringe in a sharps disposal container. A container made specifically for disposing of used syringes and needles may be used. **Do NOT** recycle the container.
- 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 provincial or local laws regarding the proper disposal of needles and syringes.
- Used alcohol swabs should be placed in the trash.

All questions should be handled by a doctor, nurse, or pharmacist familiar with ENBREL. A toll-free information service is also available: 1-877-9ENBREL (1-877-936-2735).

What are possible side effects from using ENBREL?

Like all medicines, ENBREL can cause side effects. Most side effects are mild to moderate. However, some may be serious and require treatment.

What are the common side effects?

In studies comparing ENBREL to placebo (inactive injection), side effects that occurred more frequently in patients treated with ENBREL were:

- Reactions where the injection was given. These reactions are usually mild and include redness, swelling, itching, or bruising. These usually go away within 3 to 5 days. If you have pain, redness or swelling around the injection site that doesn’t go away or gets worse, call your doctor.
- Upper respiratory infections (sinus infections)
- Headaches

These are not all the possible side effects you may feel when taking ENBREL. If you experience any side effects not listed here, contact your healthcare professional.

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
VERY COMMON Injection site reactions		√	
COMMON Upper respiratory tract infections (sinus infections)		√	
Headaches	√		
UNCOMMON Serious infections		√	√
Tuberculosis		√	
Nerve disorders		√	

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, talk to your healthcare professional.

<p>Reporting Side Effects</p> <p>You can report any suspected side effects associated with the use of health products to Health Canada by:</p> <ul style="list-style-type: none"> • Visiting the Web page on Adverse Reaction Reporting (http://www.hc-sc.gc.ca/dhp-mpps/medeff/report-declaration/index-eng.php) for information on how to report online, by mail or by fax; or • Calling toll-free at 1-866-234-2345. <p><i>NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.</i></p>
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Storage:

Keep out of the reach and sight of children.

The ENBREL prefilled syringe should be refrigerated at 2°C to 8°C. **Do NOT freeze ENBREL.** Refrigerated ENBREL remains stable until the expiration date printed on the syringe.

ENBREL may be transferred to room temperature storage (up to 27°C). Upon removal from the refrigerator, it must be used within 60 days. Protect from direct sunlight, sources of heat, and humidity until ready to use.

If you want more information about ENBREL:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the [Health Canada website](#); the manufacturer's website www.amgen.ca, or by contacting the ENLIVEN[®] Services information support line, toll free at: 1-877-9ENBREL (1-877-936-2735). Additional information can be found at www.enbrel.ca.

This leaflet was prepared by AMGEN CANADA INC. for IMMUNEX CORPORATION

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PATIENT MEDICATION INFORMATION

PrEnbrel®

etanercept injection

Single-use Prefilled SureClick® Autoinjector

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- **Malignancies.** There have been cases, sometimes fatal, of unusual cancers in children and teenage patients who started using TNF-blocking agents, including ENBREL, at less than 18 years of age.

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How does ENBREL work?

ENBREL is a type of protein called a tumour necrosis factor (TNF) blocker that blocks the action of a substance your body makes called TNF-alpha. TNF-alpha is made by your body’s immune system. People with immune diseases like RA, JIA, PsA and PsO, as well as patients with AS, have too much TNF-alpha in their bodies, which can cause inflammation and lead to painful, swollen joints and raised thick, red, scaly patches (“psoriatic skin lesions”) that can appear anywhere on the body. ENBREL can reduce the amount of TNF in the body to normal levels, helping to treat joint damage and skin lesions. In patients with inflammatory arthritis, ENBREL may be effective in reducing signs and symptoms of inflammatory arthritis (such as pain, morning stiffness and fatigue), may help improve your ability to do simple daily activities (such as dressing, walking and climbing stairs), and may help prevent damage to your bones and joints. In patients with psoriatic skin conditions, ENBREL may be effective in clearing skin and improving quality of life (such as personal relationships, work and daily activities, and treatment satisfaction).

When can I expect to see results from taking ENBREL?

Improvement may be seen as early as 1 week after starting ENBREL in adults, and within 2 weeks in children with JIA and 4 weeks with PsO. In clinical trials, full effect was usually seen by 3 months in both adults and children and was sustained with continued treatment.

In clinical trials with PsA, one quarter of patients saw improvement in their joint symptoms within 1 month, one half of patients saw improvement within 3 months, and three quarters of patients saw improvement within 9 months of treatment with ENBREL.

During the PsA clinical trials, approximately 2% of patients treated with ENBREL stopped taking ENBREL due to side effects and up to 5% of ENBREL-treated patients stopped taking ENBREL due to lack of improvement.

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Medicinal ingredients: etanercept

Non-medicinal ingredients: L-arginine hydrochloride, sodium chloride, sucrose, and Water for Injection, USP.

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Single-use prefilled SureClick® autoinjectors are available in a 50 mg (0.98 mL of a 50 mg/mL of etanercept, minimum deliverable volume of 0.94 mL) dosage strength.

Multiple-use vial: ENBREL is also available as a lyophilized powder in a multiple-use vial containing 25 mg etanercept per vial.

Do not use ENBREL if you:

- have ever had an allergic reaction to ENBREL or any of the ingredients in ENBREL.

The needle cover on the prefilled syringe is composed of dry natural rubber, which is made from latex. If you know you are allergic to latex, talk to your healthcare provider before using ENBREL in the prefilled syringe.

- have an infection that has spread through your body (sepsis).

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take ENBREL. Talk about any health conditions or problems you may have, including if you:

- have an infection. This could put you at risk for serious side effects from ENBREL.
- have symptoms of an infection such as fever, sweats or chills, cough or flu-like symptoms, shortness of breath, blood in your phlegm, weight loss, muscle aches, warm, red, or painful areas on your skin, sores on your body, diarrhea or stomach pain, burning when you urinate or urinate more often than normal, and feel very tired.
- have a history of infections that keep coming back or other conditions — like diabetes, HIV, or a weak immune system — that might increase your risk of infections.

* 25 mg single-use prefilled syringe is not available in Canada.

- have tuberculosis (TB), or have been in close contact with someone who has or has had TB. You will need to be evaluated for TB. Your doctor should test you for TB before starting ENBREL.
- were born in, lived in, or traveled to countries where there is a risk for getting TB. Ask your doctor if you are not sure.
- live in, have lived in or have traveled to, areas where there is a greater risk for certain kinds of fungal infections (histoplasmosis, coccidioidomycosis, blastomycosis). These infections may develop or become more severe if you take ENBREL. If you don't know if you have lived in an area where these infections are common, ask your doctor.
- have or have had hepatitis B.
- have or have had persistent numbness, tingling and muscle weakness or a disease such as multiple sclerosis, Guillain-Barré or a Guillain-Barré-like syndrome, which causes inflammation of the nervous system, either in the brain and spinal cord or nerves going to your hands and feet.
- have been newly diagnosed or are being treated for congestive heart failure.
- are scheduled to have major surgery.
- have recently received or are scheduled to receive a vaccine. All vaccines should be brought up-to-date before starting ENBREL. Patients taking ENBREL should not receive live vaccines.
- use the medication Kineret® (anakinra), Orencia® (abatacept) or cyclophosphamide (see the following may interact with ENBREL below).
- have been around someone with varicella zoster (chicken pox, shingles).

Know the medicines you take. Keep a list of them to show your doctor and pharmacist each time you get a new medicine.

Your doctor should monitor you closely for signs and symptoms of TB during treatment with ENBREL even if you have tested negative for TB. If you develop any of the symptoms of TB (a dry cough that doesn't go away, weight loss, fever, night sweats) call your doctor.

If you are not sure or have any questions about any of this information, ask your doctor.

Other warnings you should know about:

All medicines have side effects. Medicines, like ENBREL, that affect your immune system can cause serious side effects. The possible serious side effects include:

- **Nervous system diseases.** There have been rare cases of disorders that affect the nervous system of people taking ENBREL or other TNF-blockers, such as multiple sclerosis, seizures or inflammation of the nerves of the eyes. Signs that you could be experiencing a problem affecting your nervous system include: numbness or tingling throughout your body, problems with your vision, weakness in your arms and/or legs, and dizziness.
- **Blood problems.** In some patients the body may fail to produce enough of the blood cells that can help your body fight infections or help you to stop bleeding. This can lead to death. If you develop a fever that doesn't go away, bruise or bleed very easily or look very pale or feel faint, call your doctor right away. Your doctor may decide to stop treatment. Some people have also had symptoms that resemble lupus (rash on your face and arms that gets worse in the sun) that may go away when you stop taking ENBREL.

- **Heart problems.** You should also tell your doctor if you have ever been treated for heart failure. If you have, your doctor may choose not to start you on ENBREL, or may want to monitor you more closely. Symptoms include shortness of breath or swelling of your ankles and feet.
- **Allergic reactions.** Some patients have had allergic reactions to ENBREL. If you develop a severe rash, swollen face or difficulty breathing while taking ENBREL, call your doctor right away.
- **Malignancies.** Patients with inflammatory diseases including RA, AS or PsO, particularly those with highly active disease, may be at higher risk for lymphoma (a type of cancer). For children and adults taking TNF-blocker medicines including ENBREL, the chances of getting lymphoma or other cancers may increase. Whether treatment with ENBREL might influence the development and course of malignancies in adults is unknown.
- **Liver problems (autoimmune hepatitis).** Liver problems can happen in people who use TNF-blocker medicines, including ENBREL. These problems can lead to liver failure and death. Call your doctor right away if you have any of these symptoms: feel very tired, skin or eyes look yellow, poor appetite or vomiting, pain on the right side of your stomach (abdomen). These symptoms may occur several months after starting and even after ENBREL has been stopped.
- **Psoriasis.** Some people using ENBREL developed new psoriasis or worsening of psoriasis they already had. Tell your doctor if you develop red scaly patches or raised bumps which may be filled with pus. Your doctor may decide to stop your treatment with ENBREL.
- **Serious infections.** ENBREL can lower the ability of your immune system to fight infections. So, taking ENBREL can make you more prone to getting infections or make any infection that you may have worse. Some people have serious infections while taking ENBREL including infections that spread through the body such as tuberculosis (TB), legionellosis (usually a bacterial pneumonia), and listeriosis (usually from contaminated food). Other infections caused by viruses, fungi, bacteria or parasites may occur. Some people have died from these infections.

Can I take ENBREL if I am pregnant or breastfeeding?

The safe use of ENBREL has not been established in pregnant women.

You should tell your doctor if you are pregnant, become pregnant or are thinking about becoming pregnant. If you took ENBREL during pregnancy, talk to your doctor prior to administration of live vaccines to your infant.

ENBREL can pass into breast milk. ENBREL has not been studied in nursing mothers, and therefore its effects on nursing babies are not known. Talk to your healthcare provider about the best way to feed your baby while taking ENBREL.

If you are not sure or have any questions about any of this information, ask your doctor.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with ENBREL:

It is important that you tell your doctor about any other medicines (for example, high blood pressure medicine) you are taking for other conditions before you start taking ENBREL. You

should also tell your doctor about any over-the-counter drugs, herbal medicines and vitamin and mineral supplements you are taking.

If you have diabetes and are taking medication to control your diabetes, your doctor may decide you need less anti-diabetic medicine while taking ENBREL.

General Information about ENBREL

Medicines are sometimes prescribed for purposes not mentioned in the Consumer Information leaflet. **Do NOT** use ENBREL for a condition for which it was not prescribed. **Do NOT** give ENBREL to other people, even if they have the same condition.

Can I take ENBREL if I am taking other medicines for my RA, JIA, PsA, AS or other conditions?

In adults, ENBREL can be used in combination with methotrexate. However, little is known of the interaction of ENBREL with methotrexate and other drugs in children with JIA.

Taking ENBREL with Kineret[®] (anakinra) is not recommended because this may increase your risk of getting a serious infection.

Taking ENBREL with Orencia[®] (abatacept) is not recommended because this may increase your risk for serious side effects.

Taking ENBREL with cyclophosphamide (used to treat cancer or immune diseases) is not recommended. You may have a higher chance for getting certain cancers when taking ENBREL with cyclophosphamide.

How to take ENBREL:

ENBREL is given as an injection under the skin.

You may continue to use other medicines that help treat your condition while taking ENBREL, such as non-steroidal anti-inflammatory drugs (NSAIDs) and prescription steroids, as recommended by your doctor.

Usual dose:

If you have RA, PsA or AS, the recommended dose of ENBREL for adults is 50 mg per week given as one injection using a 50 mg single-use prefilled SureClick[®] autoinjector.

If you have PsO, the recommended starting dose of ENBREL for adult patients is a 50 mg dose twice a week (3 or 4 days apart) for 3 months. After 3 months, your doctor will tell you to reduce your dose to 50 mg once per week using one 50 mg single-use prefilled SureClick[®] autoinjector.

The recommended dose of ENBREL for children with JIA or PsO is based on the child's body weight. Your child's doctor will tell you the correct amount of ENBREL your child should take.

The 50 mg single-use prefilled SureClick[®] autoinjector is only recommended for children weighing 63 kg (138 pounds) or more. ENBREL should be given by, or under the supervision of, a responsible adult.

Make sure you have been shown how to inject ENBREL before you do it yourself. You can call your doctor or the toll-free information line at 1-877-9ENBREL (1-877-936-2735) if you have any questions about ENBREL or about giving yourself or your child an injection. Someone you know can also help you with your injection. Remember to take this medicine just as your doctor has told you and do not miss any doses.

Overdose:

Call your doctor if you accidentally inject ENBREL more frequently than instructed.

If you think you have taken too much ENBREL, contact your healthcare professional, hospital emergency department or regional poison control centre immediately, even if there are no symptoms.

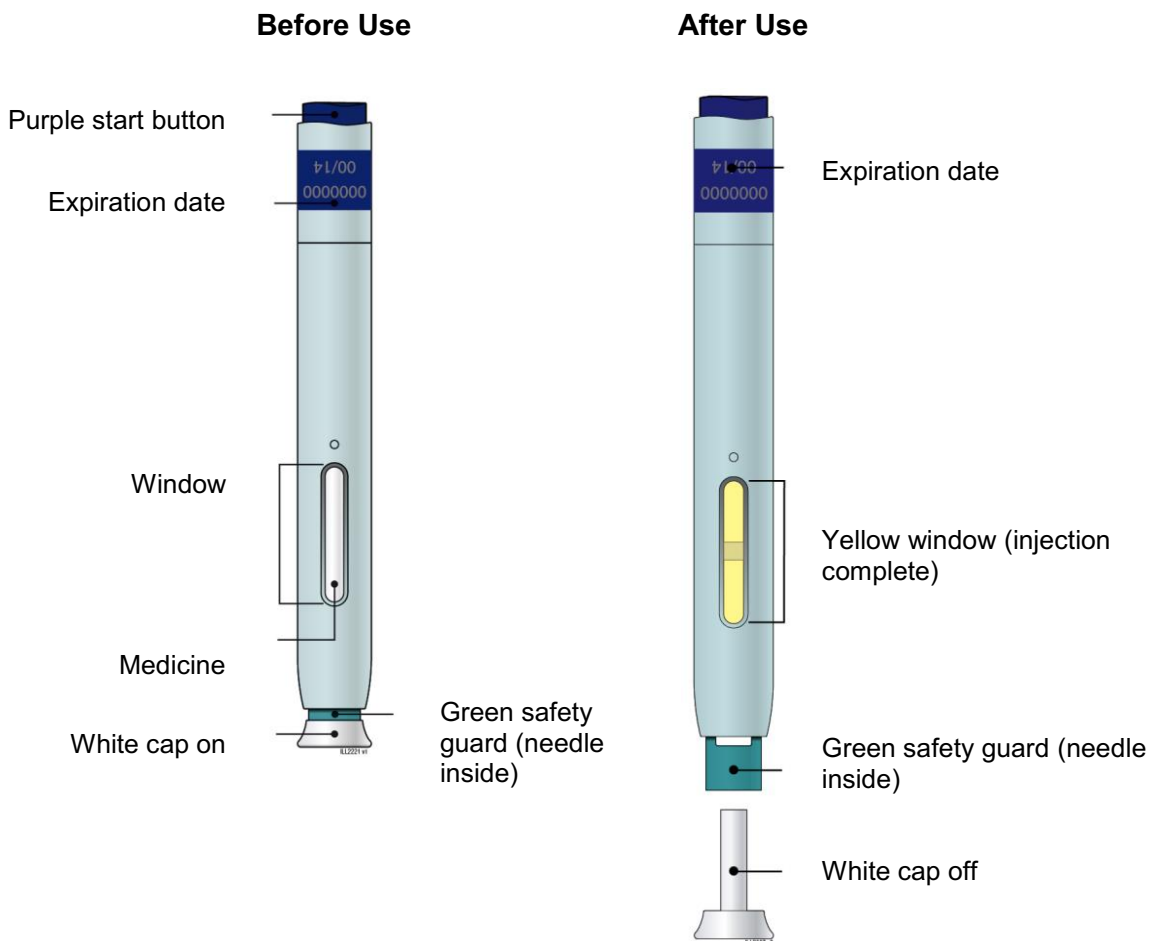
Missed Dose:

If you forget to use ENBREL, inject your dose as soon as you remember. Then, take your next dose at your regular(ly) scheduled time. In case you are not sure when to inject ENBREL, call your healthcare provider. A toll-free information service is also available: 1-877-9ENBREL (1-877-936-2735).

Instructions for preparing and giving an injection of ENBREL:

The following instructions are for preparing and giving a dose of ENBREL using a single-use prefilled SureClick[®] autoinjector. Your doctor, nurse, or pharmacist will tell you how much ENBREL you need and how often it should be injected. **Each ENBREL SureClick[®] autoinjector can be used one time.**

Guide to Parts



Important: Needle is inside the green safety guard.

Important

Before you use an ENBREL SureClick® autoinjector, read this important information:

Storing your ENBREL SureClick® autoinjectors

- Store the ENBREL SureClick® autoinjector in original carton to protect from light or damage.
- Store the ENBREL SureClick® autoinjector in the refrigerator at 2°C to 8°C.
- You may store the unused autoinjectors at room temperature, up to 27°C, for up to 60 days.
 - Once ENBREL has reached room temperature, do not put it back in the refrigerator.
- Do not store the ENBREL SureClick® autoinjector in extreme heat or cold.
- **Do not** freeze.
- **Do not** shake.
- **Keep ENBREL SureClick® autoinjector out of the reach of children.**

If you have any questions about storage, contact your healthcare professional or call 1-877-9ENBREL (1-877-936-2735).

Using your ENBREL SureClick® autoinjectors

- It is important that you do not try to give the injection unless you or your caregiver has received training from your healthcare professional.
- **Do not** use an ENBREL SureClick® autoinjector after the expiration date on the label or if it has been stored at room temperature beyond 60 days (whichever comes first).
- **Do not** shake the ENBREL SureClick® autoinjector.
- **Do not** remove the white cap from ENBREL SureClick® autoinjector until you are ready to inject.
- **Do not** use an ENBREL SureClick® autoinjector if it has been dropped on a hard surface. Part of the ENBREL SureClick® autoinjector may be broken even if you cannot see the break. Use a new ENBREL SureClick® autoinjector, and call 1-877-9ENBREL (1-877-936-2735).
- The white cap on ENBREL SureClick® autoinjector contains dry natural rubber, which is made from latex. Tell your healthcare professional if you are allergic to latex.
- **Children must weigh at least 63 kg (138 pounds)** to use ENBREL SureClick® autoinjector. Children who weigh less than 63 kg (138 pounds) should use a different form of ENBREL.

A healthcare professional familiar with ENBREL should be able to answer all of your questions. For more information, call 1-877-9ENBREL (1-877-936-2735).

STEP 1: Prepare

A. Remove one ENBREL SureClick® autoinjector from the package.

Carefully lift autoinjector straight up out of the box.

Put the original package with any unused autoinjectors back in the refrigerator.

You may also store the unused autoinjectors at room temperature, up to 27°C for up to 60 days.

For a more comfortable injection, leave the autoinjector at room temperature for at least **30** minutes before injecting.

Do not put the autoinjector back in the refrigerator once it has reached room temperature.

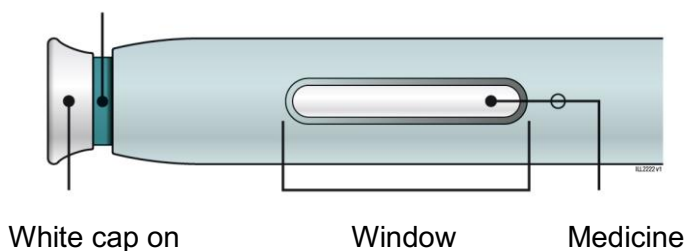
Do not try to warm the autoinjector by using a heat source such as hot water or microwave.

Do not shake the autoinjector.

Do not remove the white cap from the autoinjector yet.

B. Inspect the ENBREL SureClick® autoinjector.

Green safety guard (needle inside)



Make sure the medicine in the window is clear and colourless.

It is okay if you see small white particles in the medicine.

Do not use the autoinjector if:

- The medicine is cloudy or discoloured or contains large lumps, flakes, or coloured particles
- Any part appears cracked or broken
- The white cap is missing or not securely attached
- The expiration date printed on the label has passed or if it has been stored at room temperature beyond 60 days (whichever comes first)

In all cases, use a new autoinjector, and call 1-877-9ENBREL (1-877-936-2735).

C. Gather all materials needed for your injection.

Wash your hands thoroughly with soap and water.

On a clean, well-lit work surface, place the:

- New autoinjector
- Alcohol wipes
- Cotton ball or gauze pad
- Adhesive bandage
- Sharps disposal container. See **“Step 4: Finish”**



D. Prepare and clean your injection site.

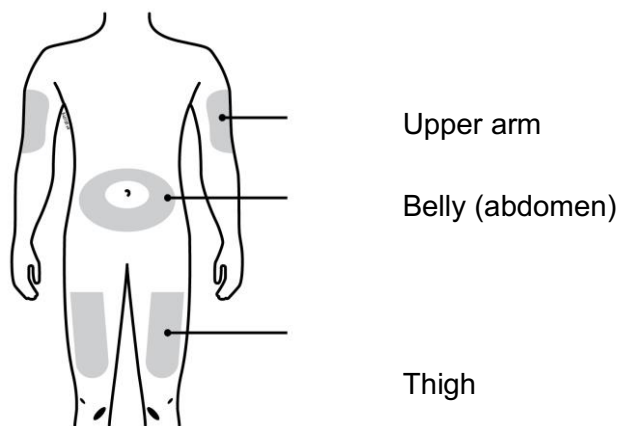
Only use these injection sites:

- Your thigh

- Stomach area (abdomen), except for a **five-centimetre** (two inches) area right around your navel (belly button)
- Outer area of upper arm (only if someone else is giving you the injection)

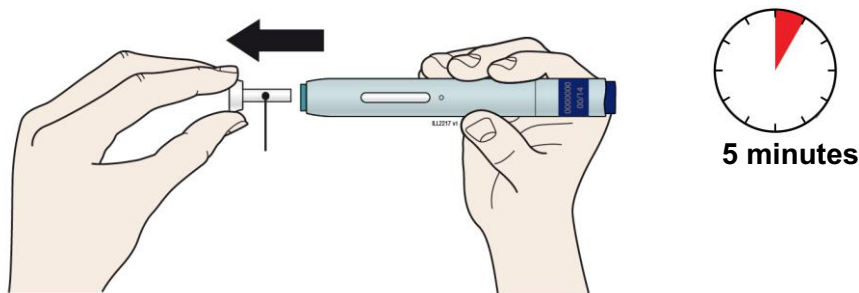
Clean injection site with an alcohol wipe. Let your skin dry.

- **Do not** touch this area again before injecting.
- Choose a different site each time you give yourself an injection. If you need to use the same injection site, just make sure it is not the same spot on that site you used for the last time.
 - **Do not** inject into areas where the skin is tender, bruised, red, or hard. Avoid injecting into areas with scars or stretch marks.
- If you have psoriasis, you should avoid injecting directly into raised, thick, red, or scaly skin patch or lesion.



Step 2: Get ready

- E. Pull white cap straight off, only when you're ready to inject. **Do not** leave the white cap off for more than **five minutes**. This can dry out the medicine.



White Cap

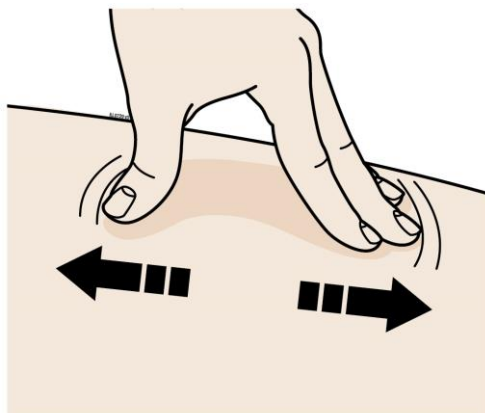
It is normal to see a drop of liquid at the end of the needle or green safety guard.

- **Do not** twist or bend the white cap.
- **Do not** put the white cap back onto the autoinjector.
- **Do not** put fingers into the green safety guard.

- **Do not** remove the white cap from the autoinjector until you are ready to inject.

F. Create a firm surface at the selected injection site (thigh, stomach, or outer areas of the upper arm), by using the Stretch method or the Pinch method.

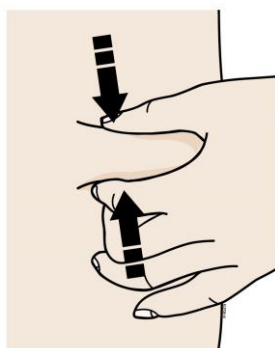
Stretch method



Stretch skin firmly by moving your thumb and fingers in opposite directions, creating an area about **5 centimetres (2 inches)** wide.

OR

Pinch method

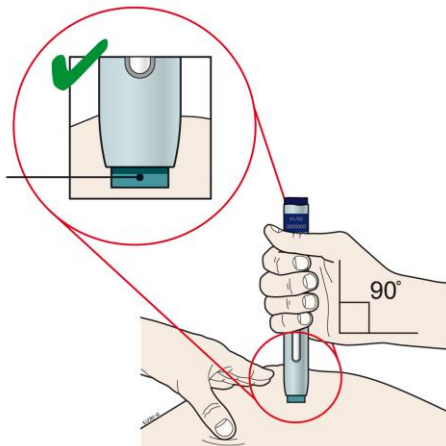


Pinch skin firmly between your thumb and fingers, creating an area about **5 centimetres (2 inches)** wide.

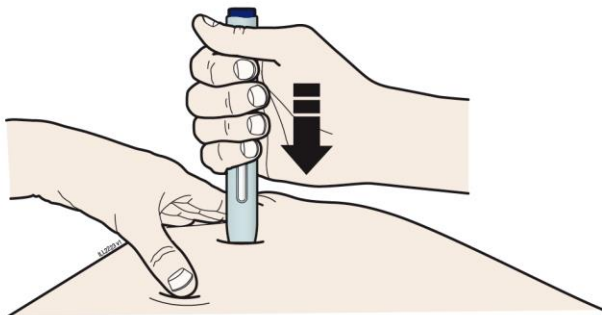
Important: Keep the skin stretched or pinched while injecting.

STEP 3: Inject

G. Keep holding the stretched or pinched skin. With the white cap off, **put** the green safety guard on your skin at 90 degrees. The **needle is inside** the green safety guard. Do not push the purple start button yet.



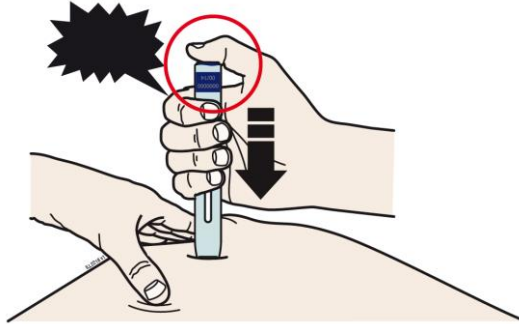
H. Firmly **push** the autoinjector down onto skin until it stops moving.



Important: You must push all the way down but do not touch the purple start button until you're ready to inject.

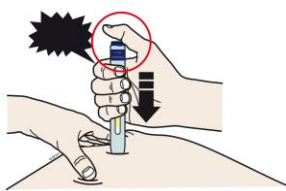
I. When you're ready to inject, **press** the purple start button.

“click”

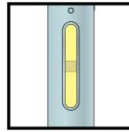


J. Keep **pushing** down on your skin. Then lift your thumb while still holding the autoinjector on your skin. Your injection could take about **15 seconds**.

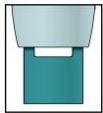
“click”



15 seconds



Window turns from clear to yellow when the injection is done. You may hear a second click.



Note: After you remove autoinjector from your skin, the needle will be automatically covered.

Important: When you remove the autoinjector, if the window has not turned yellow, or if it looks like the medicine is still injecting, this means you have not received a full dose. Call your healthcare professional immediately.

Step 4: Finish

K. Discard the used autoinjector and the white cap.



Put the used SureClick® autoinjector in a sharps disposal container right away after use. **Do not** throw away (dispose of) the SureClick® autoinjector in your household trash.

If you do not have a sharps disposal container, you may use a household container that is:

- Made of a heavy-duty plastic,
- Can be closed with a tight-fitting, puncture-resistant lid without sharps being able to come out,
- Upright and stable during use,
- Leak-resistant, and
- Properly labeled to warn of hazardous waste inside the container.
- When your sharps disposal container is almost full, you will need to follow your community guidelines for the right way to dispose of your sharps disposal container. There may be provincial or local laws about how you should throw away used needles and syringes. Talk with your doctor about proper disposal. **Do not** reuse the autoinjector.
- **Do not** recycle the autoinjector or sharps disposal container or throw them into household trash.

Important: Always keep the sharps disposal container out of the reach of children.

L. Examine the injection site.

If there is blood, press a cotton ball or gauze pad on your injection site. **Do not** rub injection site. Apply an adhesive bandage if needed.

Commonly asked questions

What will happen if I press the purple start button before I am ready to do the injection on my skin?

Even when you press the purple start button, the injection will only happen when the green safety guard is also pushed into the autoinjector.

Can I move the autoinjector around on my skin while I am choosing an injection site?

It is okay to move the autoinjector around on the injection site as long as you **do not** press the purple start button. However, if you press the purple start button and the green safety guard is pushed into the autoinjector, the injection will begin.

Can I release the purple start button after I start my injection?

You can release the purple start button, but continue to hold the autoinjector firmly against your skin during the injection.

Will the purple start button pop up after I release my thumb?

The purple start button may not pop up after you release your thumb if you held your thumb down during the injection. This is okay.

What do I do if I didn't hear a second click?

If you didn't hear a second click, you can confirm a complete injection by checking that the window has turned yellow.

Whom do I contact if I need help with the autoinjector or my injection?

If you have any questions about the autoinjector or about your injection, ask your doctor, nurse, or pharmacist, or call 1-877-9ENBREL (1-877-936-2735) for help.

What are possible side effects from using ENBREL?

Like all medicines, ENBREL can cause side effects. Most side effects are mild to moderate. However, some may be serious and require treatment.

What are the common side effects?

In studies comparing ENBREL to placebo (inactive injection), side effects that occurred more frequently in patients treated with ENBREL were:

- Reactions where the injection was given. These reactions are usually mild and include redness, swelling, itching, or bruising. These usually go away within 3 to 5 days. If you have pain, redness or swelling around the injection site that doesn't go away or gets worse, call your doctor.
- Upper respiratory infections (sinus infections)
- Headaches

These are not all the possible side effects you may feel when taking ENBREL. If you experience any side effects not listed here, contact your healthcare professional.

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
VERY COMMON Injection site reactions		√	
COMMON Upper respiratory tract infections (sinus infections)		√	
Headaches	√		
UNCOMMON Serious infections		√	√
Tuberculosis		√	
Nerve disorders		√	

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, talk to your healthcare professional.

<p>Reporting Side Effects</p> <p>You can report any suspected side effects associated with the use of health products to Health Canada by:</p> <ul style="list-style-type: none"> • Visiting the Web page on Adverse Reaction Reporting (http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/index-eng.php) for information on how to report online, by mail or by fax; or • Calling toll-free at 1-866-234-2345. <p><i>NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.</i></p>
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Storage:

The ENBREL single-use prefilled SureClick® autoinjector should be refrigerated at 2°C to 8°C. **Do not freeze. Do not shake.** Refrigerated ENBREL remains stable until the expiration date printed on the syringe.

ENBREL may be transferred to room temperature storage (up to 27°C). Upon removal from the refrigerator, it must be used within 60 days. Protect from direct sunlight, sources of heat, and humidity until ready to use.

Keep out of the reach of children.

If you want more information about ENBREL:

- Talk to your healthcare professional

- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the [Health Canada website](#); the manufacturer's website www.amgen.ca, or by contacting the ENLIVEN[®] Services information support line, toll free at: 1-877-9ENBREL (1-877-936-2735). Additional information can be found at www.enbrel.ca.

This leaflet was prepared by AMGEN CANADA INC. for IMMUNEX CORPORATION

Last revised: March 19, 2021

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READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

PATIENT MEDICATION INFORMATION

PrEnbrel®

etanercept for injection

Multiple-use Vial

Read this carefully before you start taking **ENBREL** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **ENBREL**.

Serious Warnings and Precautions

- **Serious infections.** There have been cases where patients taking ENBREL or other TNF-blocking agents have developed serious infections, including tuberculosis (TB) and infections caused by bacteria, viruses or fungi that have spread throughout their body. Some patients have died from these infections. In very rare cases, hepatitis B recurred in patients with previous hepatitis. If you tend to get infections easily or if you develop an infection while taking ENBREL, you should tell your doctor right away.
- **Malignancies.** There have been cases, sometimes fatal, of unusual cancers in children and teenage patients who started using TNF-blocking agents, including ENBREL, at less than 18 years of age.

What is ENBREL used for?

ENBREL is a medicine for treating people with moderate to severe forms of rheumatoid arthritis (RA), juvenile idiopathic arthritis (JIA) and a type of disease called psoriatic (sore-ee-ah-tick) arthritis (PsA). ENBREL is also for treating adults with a type of arthritis called ankylosing spondylitis (ank-e-low-sing spond-e-lie-tis) (AS). ENBREL is also for adults with moderate to severe psoriasis (sore-l-ah-sis) (PsO) and children with severe psoriasis (PsO). RA, JIA, PsA and AS are inflammatory diseases that affect the joints in your body. PsO is an inflammatory disease that affects the skin and can cause raised, thick, red and scaly patches (“psoriatic skin lesions”) that can appear anywhere on the body. PsA is usually seen in patients with PsO and affects both the joints and the skin.

How does ENBREL work?

ENBREL is a type of protein called a tumour necrosis factor (TNF) blocker that blocks the action of a substance your body makes called TNF-alpha. TNF-alpha is made by your body’s immune system. People with immune diseases like RA, JIA, PsA and PsO, as well as patients with AS, have too much TNF-alpha in their bodies, which can cause inflammation and lead to painful, swollen joints and raised thick, red, scaly patches (“psoriatic skin lesions”) that can appear anywhere on the body. ENBREL can reduce the amount of TNF in the body to normal levels, helping to treat joint damage and skin lesions. In patients with inflammatory arthritis, ENBREL may be effective in reducing signs and symptoms of inflammatory arthritis (such as pain, morning stiffness and fatigue), may help improve your ability to do simple daily activities (such as dressing, walking and climbing stairs), and may help prevent damage to your bones and joints. In patients with psoriatic skin conditions, ENBREL may be effective in clearing skin and improving quality of life (such as personal relationships, work and daily activities, and treatment satisfaction).

When can I expect to see results from taking ENBREL?

Improvement may be seen as early as 1 week after starting ENBREL in adults, and within 2 weeks in children with JIA and 4 weeks with PsO. In clinical trials, full effect was usually seen by 3 months in both adults and children and was sustained with continued treatment.

In clinical trials with PsA, one quarter of patients saw improvement in their joint symptoms within 1 month, one half of patients saw improvement within 3 months, and three quarters of patients saw improvement within 9 months of treatment with ENBREL.

During the PsA clinical trials, approximately 2% of patients treated with ENBREL stopped taking ENBREL due to side effects and up to 5% of ENBREL-treated patients stopped taking ENBREL due to lack of improvement.

What are the ingredients in ENBREL?

Medicinal ingredients: etanercept

Non-medicinal ingredients: mannitol, sucrose, tromethamine

ENBREL comes in the following dosage forms:

ENBREL is available as a lyophilized powder in a **multiple-use vial** containing 25 mg etanercept per vial.

ENBREL is also available as a **single-use prefilled syringe** in 25 mg* (0.51 mL of a 50 mg/mL solution of etanercept, minimum deliverable volume of 0.47 mL) and 50 mg (0.98 mL of a 50 mg/mL solution of etanercept, minimum deliverable volume of 0.94 mL) dosage strengths.

ENBREL **single-use prefilled SureClick® autoinjectors** are available in a 50 mg (0.98 mL of a 50 mg/mL solution of etanercept, minimum deliverable volume of 0.94 mL) dosage strength.

Do not use ENBREL if you:

- have ever had an allergic reaction to ENBREL or any of the ingredients in ENBREL.
The needle cover on the prefilled syringe is composed of dry natural rubber, which is made from latex. If you know you are allergic to latex, talk to your healthcare provider before using ENBREL in the prefilled syringe.
- have an infection that has spread through your body (sepsis).

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take ENBREL. Talk about any health conditions or problems you may have, including if you:

- have an infection. This could put you at risk for serious side effects from ENBREL.
- have symptoms of an infection such as fever, sweats or chills, cough or flu-like symptoms, shortness of breath, blood in your phlegm, weight loss, muscle aches, warm, red, or painful areas on your skin, sores on your body, diarrhea or stomach pain, burning when you urinate or urinate more often than normal, and feel very tired.
- have a history of infections that keep coming back or other conditions - like diabetes, HIV, or a weak immune system — that might increase your risk of infections.

* 25 mg single-use prefilled syringe is not available in Canada.

- have tuberculosis (TB), or have been in close contact with someone who has or has had TB. You will need to be evaluated for TB. Your doctor should test you for TB before starting ENBREL.
- were born in, lived in, or traveled to countries where there is a risk for getting TB. Ask your doctor if you are not sure.
- live in, have lived in or have traveled to, areas where there is a greater risk for certain kinds of fungal infections (histoplasmosis, coccidioidomycosis, blastomycosis). These infections may develop or become more severe if you take ENBREL. If you don't know if you have lived in an area where these infections are common, ask your doctor.
- have or have had hepatitis B.
- have or have had persistent numbness, tingling and muscle weakness or a disease such as multiple sclerosis, Guillain-Barré or a Guillain-Barré-like syndrome, which causes inflammation of the nervous system, either in the brain and spinal cord or nerves going to your hands and feet.
- have been newly diagnosed or are being treated for congestive heart failure.
- are scheduled to have major surgery.
- have recently received or are scheduled to receive a vaccine. All vaccines should be brought up-to-date before starting ENBREL. Patients taking ENBREL should not receive live vaccines.
- use the medication Kineret[®] (anakinra), Orencia[®] (abatacept) or cyclophosphamide (see The following may interact with ENBREL below).
- have been around someone with varicella zoster (chicken pox, shingles).

Know the medicines you take. Keep a list of them to show your doctor and pharmacist each time you get a new medicine.

Your doctor should monitor you closely for signs and symptoms of TB during treatment with ENBREL even if you have tested negative for TB. If you develop any of the symptoms of TB (a dry cough that doesn't go away, weight loss, fever, night sweats) call your doctor.

If you are not sure or have any questions about any of this information, ask your doctor.

Other warnings you should know about:

All medicines have side effects. Medicines, like ENBREL, that affect your immune system can cause serious side effects. The possible serious side effects include:

- **Nervous system diseases.** There have been rare cases of disorders that affect the nervous system of people taking ENBREL or other TNF-blockers, such as multiple sclerosis, seizures or inflammation of the nerves of the eyes. Signs that you could be experiencing a problem affecting your nervous system include: numbness or tingling throughout your body, problems with your vision, weakness in your arms and/or legs, and dizziness.
- **Blood problems.** In some patients the body may fail to produce enough of the blood cells that can help your body fight infections or help you to stop bleeding. This can lead to death. If you develop a fever that doesn't go away, bruise or bleed very easily or look very pale or feel faint, call your doctor right away. Your doctor may decide to stop treatment. Some people have also had symptoms that resemble lupus (rash on your face and arms that gets worse in the sun) that may go away when you stop taking ENBREL.

- **Heart problems.** You should also tell your doctor if you have ever been treated for heart failure. If you have, your doctor may choose not to start you on ENBREL, or may want to monitor you more closely. Symptoms include shortness of breath or swelling of your ankles and feet.
- **Allergic reactions.** Some patients have had allergic reactions to ENBREL. If you develop a severe rash, swollen face or difficulty breathing while taking ENBREL, call your doctor right away.
- **Malignancies.** Patients with inflammatory diseases including RA, AS or PsO, particularly those with highly active disease, may be at higher risk for lymphoma (a type of cancer). For children and adults taking TNF-blocker medicines including ENBREL, the chances of getting lymphoma or other cancers may increase. Whether treatment with ENBREL might influence the development and course of malignancies in adults is unknown.
- **Liver problems (autoimmune hepatitis).** Liver problems can happen in people who use TNF-blocker medicines, including ENBREL. These problems can lead to liver failure and death. Call your doctor right away if you have any of these symptoms: feel very tired, skin or eyes look yellow, poor appetite or vomiting, pain on the right side of your stomach (abdomen). These symptoms may occur several months after starting and even after ENBREL has been stopped.
- **Psoriasis.** Some people using ENBREL developed new psoriasis or worsening of psoriasis they already had. Tell your doctor if you develop red scaly patches or raised bumps which may be filled with pus. Your doctor may decide to stop your treatment with ENBREL.
- **Serious infections.** ENBREL can lower the ability of your immune system to fight infections. So, taking ENBREL can make you more prone to getting infections or make any infection that you may have worse. Some people have serious infections while taking ENBREL including infections that spread through the body such as tuberculosis (TB), legionellosis (usually a bacterial pneumonia), and listeriosis (usually from contaminated food). Other infections caused by viruses, fungi, bacteria or parasites may occur. Some people have died from these infections.

Can I take ENBREL if I am pregnant or breastfeeding?

The safe use of ENBREL has not been established in pregnant women.

You should tell your doctor if you are pregnant, become pregnant or are thinking about becoming pregnant. If you took ENBREL during pregnancy, talk to your doctor prior to administration of live vaccines to your infant.

ENBREL can pass into breast milk. ENBREL has not been studied in nursing mothers, and therefore its effects on nursing babies are not known. Talk to your healthcare provider about the best way to feed your baby while taking ENBREL.

If you are not sure or have any questions about any of this information, ask your doctor.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with ENBREL:

It is important that you tell your doctor about any other medicines (for example, high blood pressure medicine) you are taking for other conditions before you start taking ENBREL. You should also tell your doctor about any over-the-counter drugs, herbal medicines and vitamin and mineral supplements you are taking.

If you have diabetes and are taking medication to control your diabetes, your doctor may decide you need less anti-diabetic medicine while taking ENBREL.

General Information about ENBREL

Medicines are sometimes prescribed for purposes not mentioned in the Consumer Information leaflet. **Do NOT** use ENBREL for a condition for which it was not prescribed. **Do NOT** give ENBREL to other people, even if they have the same condition.

Can I take ENBREL if I am taking other medicines for my RA, JIA, PsA, AS or other conditions?

In adults, ENBREL can be used in combination with methotrexate. However, little is known of the interaction of ENBREL with methotrexate and other drugs in children with JIA.

Taking ENBREL with Kineret[®] (anakinra) is not recommended because this may increase your risk of getting a serious infection.

Taking ENBREL with Orencia[®] (abatacept) is not recommended because this may increase your risk for serious side effects.

Taking ENBREL with cyclophosphamide (used to treat cancer or immune diseases) is not recommended. You may have a higher chance for getting certain cancers when taking ENBREL with cyclophosphamide.

How to take ENBREL:

ENBREL is given as an injection under the skin.

You may continue to use other medicines that help treat your condition while taking ENBREL, such as non-steroidal anti-inflammatory drugs (NSAIDs) and prescription steroids, as recommended by your doctor.

Usual dose:

If you have RA, PsA or AS, the recommended dose of ENBREL for adults is 50 mg per week (two 25 mg injections). Your doctor will tell you whether the two injections should be given on the same day once a week or on two different days (3 or 4 days apart) in the same week.

If you have PsO, the recommended dose of ENBREL is a 50 mg dose given twice a week (3 or 4 days apart) given for 3 months. After 3 months, your doctor will tell you to reduce your dose to 50 mg once per week.

The recommended dose of ENBREL for children with JIA or PsO is based on the child's body weight. Your child's doctor will tell you the correct amount of ENBREL your child should take and whether the dose should be given as one or two injections. Your child's doctor will also tell you whether the injection or injections should be given on the same day once a week or on two different days (3 or 4 days apart) in the same week. ENBREL should be given by, or under the supervision of, a responsible adult.

Make sure you have been shown how to inject ENBREL before you do it yourself. You can call your doctor or the toll-free information line at 1-877-9ENBREL (1-877-936-2735) if you have any

questions about ENBREL or about giving yourself or your child an injection. Someone you know can also help you with your injection. Remember to take this medicine just as your doctor has told you and do not miss any doses.

Overdose:

Call your doctor if you accidentally inject ENBREL more frequently than instructed.

If you think you have taken too much ENBREL, contact your healthcare professional, hospital emergency department or regional poison control centre immediately, even if there are no symptoms.

Missed Dose:

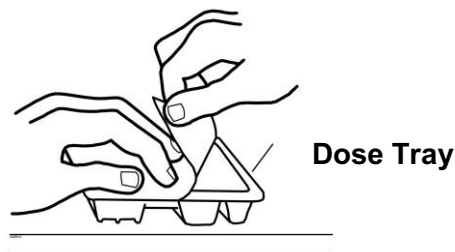
If you forget to use ENBREL, inject your dose as soon as you remember. Then, take your next dose at your regular(ly) scheduled time. In case you are not sure when to inject ENBREL, call your healthcare provider. A toll-free information service is also available: 1-877-9ENBREL (1-877-936-2735).

Instructions for preparing and giving an injection of ENBREL:

The following instructions are for preparing and giving a dose of ENBREL.

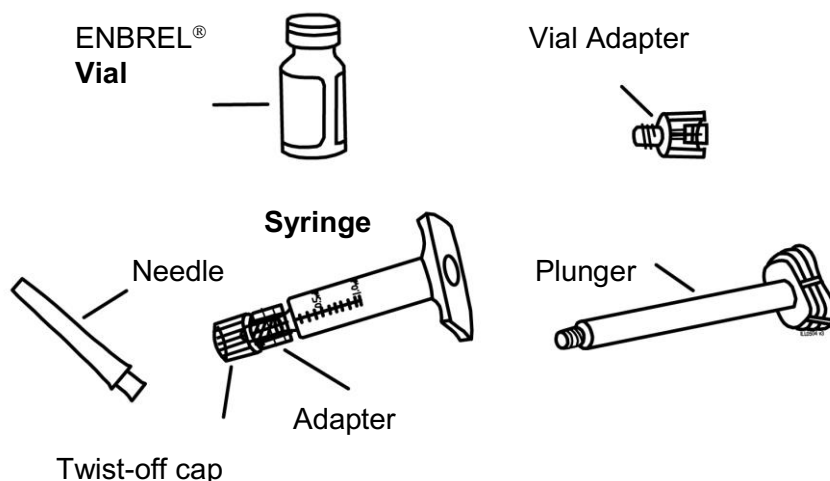
STEP 1: Setting Up for an Injection

1. Select a clean, well-lit, flat working surface, such as a table.
2. Take the ENBREL dose tray out of the refrigerator (2° to 8°C) and place it on your flat working surface.
You may also store the unopened dose tray at room temperature, up to 27°C for up to 60 days. **Do NOT** freeze. If you have any questions about storage, contact your doctor, nurse or pharmacist for further instructions.
3. Wash your hands thoroughly with soap and warm water.
4. Peel the paper seal off the dose tray and remove the contents.



5. The dose tray should contain the items shown in the diagram below. If any of the items are missing or if any item looks damaged, **do NOT** use the dose tray and consult your pharmacist, or call 1-877-9ENBREL (1-877-936-2735). Use only these items. The prefilled diluent syringe is specially designed for the preparation and administration of ENBREL. **Do NOT** use any other syringe.

- One prefilled diluent syringe containing 1 mL of liquid diluent, with attached adapter twist-off cap
- One plunger
- One ENBREL vial
- One 27-gauge needle in hard plastic cover
- One vial adapter



Alcohol swabs will also be required for injections and will need to be obtained or purchased separately.

6. Inspect the expiration (Exp.) dates on both 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, or if the unopened dose tray has been stored at room temperature beyond 60 days (whichever comes first), **do NOT** use the ENBREL vial or prefilled diluent syringe. Contact your pharmacist or call 1-877-9ENBREL (1-877-936-2735) for assistance.
7. Inspect the volume of diluent in the syringe with the twist-off cap 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. **Do NOT** use the diluent syringe **if the level of liquid is below the 1 mL mark or appears to be cracked or broken.** Call 1-877-9ENBREL (1-877-936-2735) for assistance.
8. **Do NOT** use the syringe if the twist-off cap is missing or not securely attached. Call 1-877-9ENBREL (1-877-936-2735).

STEP 2: Preparing the ENBREL Solution

There are two methods for preparing the ENBREL solution: one for single-use administration (Vial Adapter Method) and one for multiple-use administration in children (Free-hand Method). For some children, one vial of ENBREL solution can be used for more than one dose. The free-hand method should be used for children on ENBREL who are using one vial of ENBREL solution for more than one dose. **You should not use the vial adapter method if you will be using the vial more than once.** Ask your healthcare provider if you have questions about which method to use.

- **Vial Adapter Method:** Adult patients and children who use an entire vial of ENBREL should use the vial adapter device to assist with mixing the powder with the liquid and withdrawing ENBREL. A 27-gauge needle should be attached to the syringe to inject the dose. **This method should not be used for children withdrawing multiple doses from the same vial of ENBREL.** Instructions on using the vial adapter method are outlined in STEP 2A.
- **Free-hand Method:** For some children, one vial of ENBREL solution can be used for more than one dose. The free-hand method should be used for multiple-use administration in children on ENBREL, using a 25-gauge needle to assist with mixing the powder with the liquid and switching to a 27-gauge needle to inject the dose.

The instructions on preparing additional doses from the same vial are in STEP 2B. For each additional dose, you will need two new needles (one 25-gauge needle to withdraw the solution and one 27-gauge needle for the injection) and one new empty syringe (1 mL). **NEVER REUSE A SYRINGE OR NEEDLE.**

If you are using the vial of ENBREL for more than one dose, you should write the date you mixed the powder and liquid in the area marked "Mixing Date:" on the supplied sticker and attach the sticker to the ENBREL vial. After you have withdrawn the dose of ENBREL that you need, you must store the vial (in the dose tray) in the refrigerator at 2° to 8°C as soon as possible, but always within 4 hours of mixing the solution.

The reconstituted ENBREL solution must be used within 14 days after the mixing date if stored in the original vial at 2° to 8°C, with overall room temperature exposure of less than 12 hours during storage and handling. 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.

STEP 2A: Vial Adapter Method – For Single Use Only

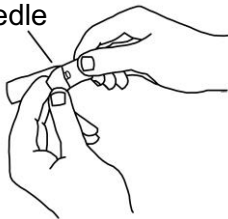
To use the Vial Adapter Method, follow the steps below:

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 ENBREL vial.

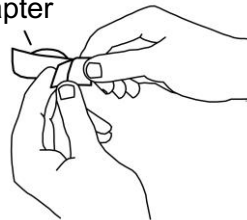


2. Place your ENBREL vial on a flat working surface or turn your dose tray upside down and place your ENBREL vial in the round space marked "V". Use one alcohol swab to clean the gray stopper on the ENBREL vial. **Do NOT** touch the stopper with your hands.
3. Partially open (only open part of) the package that contains the 27-gauge needle by peeling apart the tabs, and set aside. Open the package with the vial adapter by peeling apart the tabs. **Do NOT** touch the vial adapter's twist - on end or the spike inside.

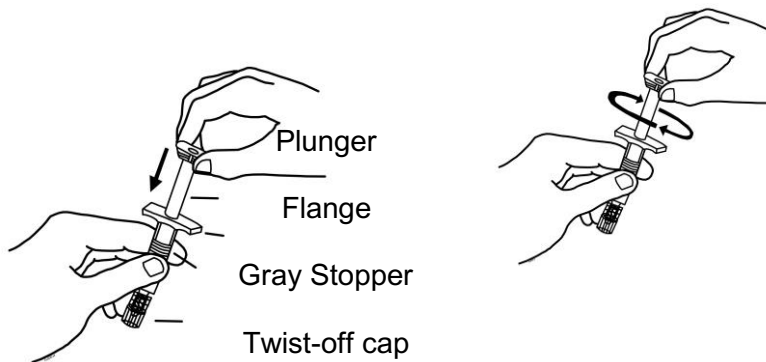
27 Gauge Needle



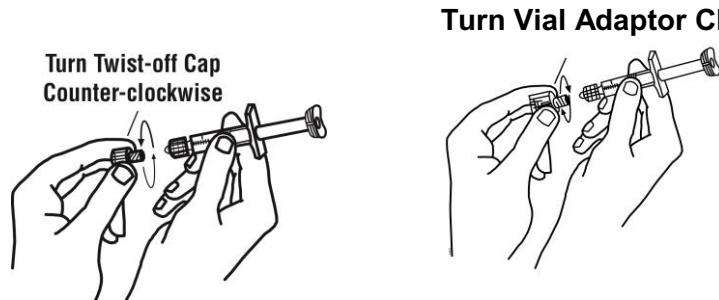
Vial Adapter



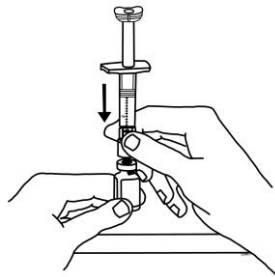
4. Slide the plunger into the syringe. Attach the plunger to the gray rubber stopper in the syringe by turning the plunger clockwise three times or until a slight resistance is felt.



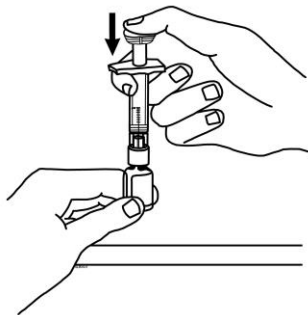
- Remove the twist-off cap from the prefilled diluent syringe by turning counter-clockwise. **Do NOT** bump or touch the plunger; doing so could cause the liquid to leak out. You may see a drop of liquid when removing the twist cap—this is normal. Once the twist cap is removed, holding the syringe and the vial adapter, twist the vial adapter onto the syringe, turning clockwise, until a slight resistance is felt. **Do NOT over-tighten.**



- Hold your ENBREL vial on a flat surface, grasp the sides of the vial adapter and place it over the top of the ENBREL vial. **Do NOT** bump or touch the plunger; doing so could cause the liquid to leak out. Press down until the vial adapter attaches to the ENBREL vial. The plastic spike inside the vial adapter should puncture the gray stopper. The vial adapter should fit snugly.

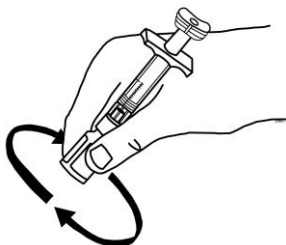


- Hold the ENBREL vial upright on your flat work surface and press the plunger down until all the liquid from the syringe is in the ENBREL vial. You may see foaming (bubbles) in the vial—this is normal.

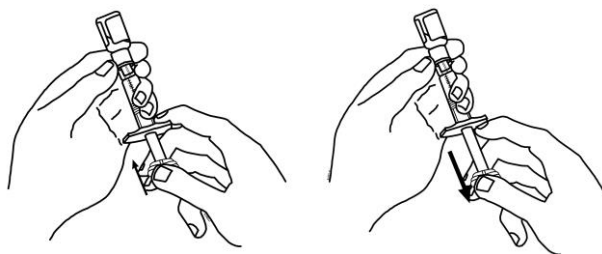


- Gently swirl the ENBREL vial between fingers in a circular motion to dissolve the powder (see illustration). If you used the dose tray to hold your ENBREL vial, take the vial (with the vial adapter and syringe still attached) out of the dose tray, and gently swirl in a circular motion to dissolve the powder. **DO NOT SHAKE.** Wait until all the powder dissolves (usually less than 10 minutes). The solution should be clear and colourless. After the

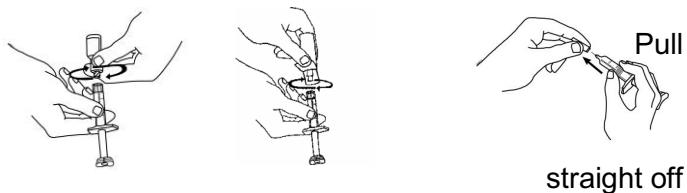
powder has completely dissolved, foam (bubbles) may still be present. This is normal. **Do NOT inject the solution if it is cloudy or discoloured, or if it contains large or coloured particles.** If all the powder in the ENBREL vial is not dissolved or there are particles present after 10 minutes, call 1-877-9ENBREL (1-877-936-2735) for assistance. **DO NOT WITHDRAW THE ENBREL SOLUTION INTO THE SYRINGE UNTIL YOU ARE READY TO INJECT.**



9. Turn the ENBREL vial upside down. Push the plunger all the way in to remove air from the syringe. Holding the syringe at eye level, slowly pull the plunger down to remove the entire volume (1 mL), unless otherwise instructed by your doctor. Be careful not to pull the plunger completely out of the syringe. Some white foam may remain in the ENBREL vial—this is normal.



10. 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.
11. To remove the syringe from the vial adapter, grasp the vial adapter and untwist the syringe. **Do NOT** touch or bump the plunger; doing so could cause the solution to leak out. Place the ENBREL vial with the vial adapter on your flat work surface. With the needle cover still on, in the partially opened paper packaging, twist the new 27-gauge needle onto the syringe until it fits snugly. Remove the paper packaging from the needle cover. Pull the hard plastic needle cover straight off the syringe. **Do NOT** touch the needle or allow it to touch any surface. You are now ready to inject ENBREL.



GO TO STEP 4 CHOOSING AND PREPARING AN INJECTION SITE.

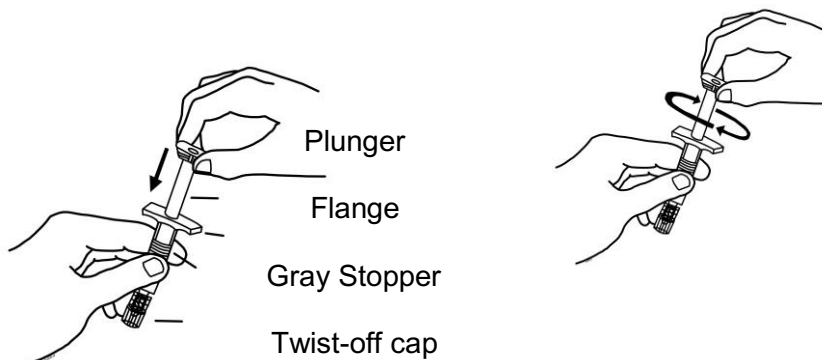
STEP 2B: Free-hand Method – For Use in Children

If you are preparing a dose from an ENBREL vial that was previously used, go to STEP 3: Preparing Additional Doses from Multiple-use ENBREL Vials.

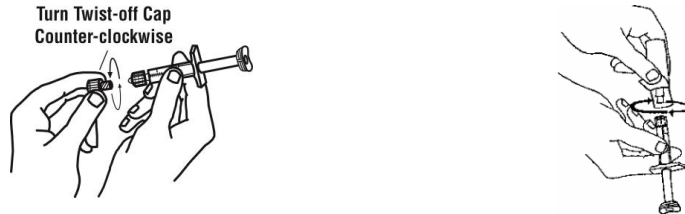
1. Remove the pink plastic cap from the ENBREL vial. **Do NOT** remove the gray stopper or silver metal ring around the top of the vial. Write the mixing date on the supplied “Mixing Date:” sticker and attach it to the ENBREL vial.



2. Use a new alcohol swab to clean the gray stopper on the ENBREL vial. After cleaning, place the ENBREL vial upright on a flat working surface. **Do NOT** touch the stopper with your hands.
3. Partially open (only open part of) the package that contains the 25-gauge needle by peeling apart the tabs, and set aside. The 25-gauge needle will be used to mix the liquid with the powder and for withdrawing ENBREL from the vial.
4. Slide the plunger into the flange end of the syringe, turning clockwise three times or until the plunger is attached to the gray stopper in the syringe.

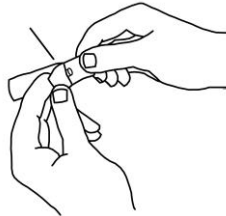


5. Remove the twist-off cap from the prefilled diluent syringe by turning counter-clockwise. Do NOT touch or bump the plunger; doing so could cause the solution to leak out. You may see a drop of liquid when removing the twist-off cap—this is normal. With the needle cover still on, in the partially opened paper packaging, twist the 25-gauge needle onto the syringe, until it fits snugly. Place the syringe on your flat work surface.

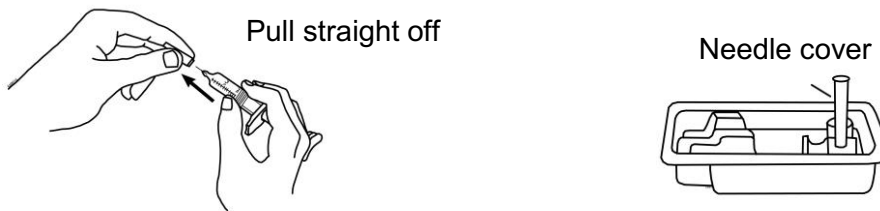


6. Prepare the 27-gauge needle by partially opening (only open part of) the package by peeling back the tabs; and set aside for later use. The 27-gauge needle will be used to inject ENBREL once the powder is mixed with the liquid.

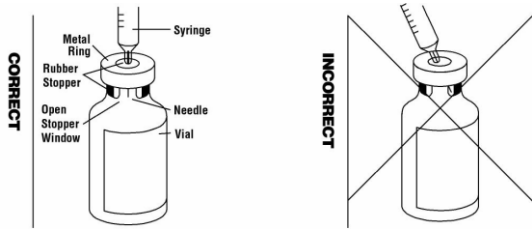
27 Gauge Needle



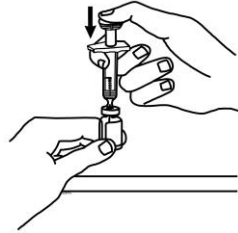
7. Hold the barrel of the syringe with one hand and remove the paper packaging off the 25-gauge needle. Pull the hard plastic needle cover straight off. To avoid damaging the needle, **do NOT** twist or bend the needle cover while you are removing it. **Do NOT** touch the needle or allow it to touch any surface. **Do NOT** touch or bump the plunger; doing so could cause the solution to leak out. Place the hard plastic needle cover (open side up) in the round space marked “N” in the ENBREL dose tray.



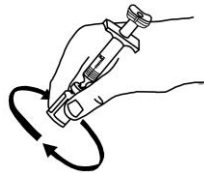
8. Place the ENBREL vial upright on the flat working surface. Hold the syringe with the needle facing up, and gently pull back on the plunger to pull a small amount of air into the syringe. Insert the needle straight down through the centre ring of the gray stopper (see illustrations). If the needle is correctly lined up, you should feel a slight resistance and then a “pop” as the needle goes through the centre of the stopper. Look for the needle tip inside the stopper window. If the needle is not correctly lined up with the centre of the stopper, you will feel a 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 the diluent into the ENBREL vial.



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

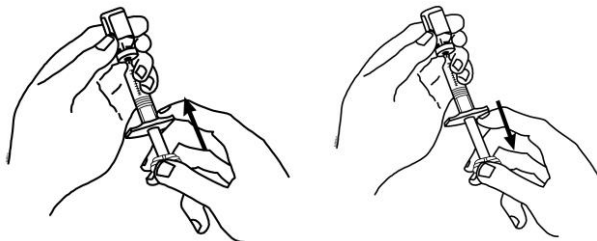


10. Leave the syringe in place. Gently swirl the ENBREX vial between fingers in a circular motion to dissolve the powder (see illustration below). **DO NOT SHAKE.** Wait until all the powder dissolves (usually less than 10 minutes). The solution should be clear and colourless. After the powder has completely dissolved, foam (bubbles) may still be present. This is normal. **Do NOT inject the solution if it is cloudy or discoloured or if it contains large coloured particles.**



If all the powder in the ENBREX vial is not dissolved or there are particles present after 10 minutes, call 1-877-9ENBREX (1-877-936-2735) for assistance.

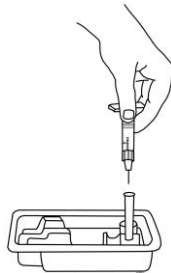
11. With the needle still in the vial, turn the vial upside down. Push the plunger all the way in to remove air from the syringe. Holding the syringe at eye level, slowly pull the plunger back to the mark on the side of the syringe that corresponds with the correct dose. Remove only the portion of the solution as instructed by your/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. Be careful not to pull the plunger completely out of the syringe. Some white foam may remain in the vial—this is normal.



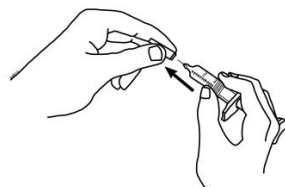
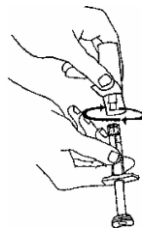
12. With the needle still inserted in the vial, check for air bubbles in the syringe. Gently tap the syringe to make any bubbles rise to the top of the syringe (see illustration below). Slowly push the plunger up to remove the air bubbles. If you push solution back into the vial, slowly pull back on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



13. Remove the syringe and needle from the ENBREL vial. Again, **Do NOT** touch the needle or allow it to touch any surface. Place the 25-gauge needle back into the hard plastic needle cover in the ENBREL dose tray, and push the syringe down until the needle is attached. Once the needle is secure in the needle cover, untwist the 25-gauge needle from the syringe and dispose of the needle in your sharps disposal container.



14. With the needle cover still on, in the partially opened paper packaging, twist the new 27-gauge needle onto the syringe until it fits snugly. Remove the paper packaging from the needle cover. **Do NOT** remove the needle cover from the syringe until you are ready to inject. Pull the hard plastic needle cover straight off the syringe. To avoid damaging the needle, **do NOT** twist or bend the needle cover while you are removing it, and **do NOT** try to put the needle cover back onto the syringe. When you remove the needle cover, there may be a drop of liquid at the end of the needle; this is normal. **Do NOT** touch the needle or allow it to touch any surface. You are now ready to inject ENBREL.



Pull straight off

GO TO STEP 4: CHOOSING AND PREPARING AN 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.

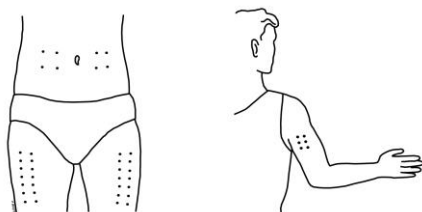
Do NOT re-use needles or syringes supplied with your ENBREL.

1. Select a clean, well-lit, flat working surface, such as a table.
2. Your doctor will tell you what type of syringe and needles (1 mL Luer-lok® syringe, and 25- and 27-gauge needles) to use. Alcohol swabs are available at a drugstore. Place the new empty sterile syringe with a 25-gauge needle (for withdrawing ENBREL), a 27-gauge needle (for injecting ENBREL) and two alcohol swabs on your flat working surface.
3. Take the vial of ENBREL solution that is stored in the dose tray out of the refrigerator and place it on your flat working surface. For a more comfortable injection, allow ENBREL to reach room temperature (approximately 15 to 30 minutes).
4. Check the mixing date you wrote on the sticker on the ENBREL vial and confirm that the mixed solution is less than 14 days old. **Do NOT** inject the solution if it is cloudy or discoloured, or if it contains large or coloured particles. **Discard the vial if more than 14 days have passed since the ENBREL solution was mixed.**
5. Wash your hands with soap and warm 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 25-gauge needle are not pre-assembled, assemble them as instructed by your doctor.
8. Prepare the 27-gauge needle by partially opening (only open part of) the package by peeling back the tabs. Set the 27-gauge needle aside. The 27-gauge needle will be used to inject the dose of ENBREL.
9. Hold the syringe and pull the hard plastic needle cover straight off. To avoid damaging the needle, **do NOT** twist or bend the needle cover while you are removing it. **Do NOT** touch the needle or allow it to touch any surface. Place the hard plastic needle cover (open side up) in the round space of the ENBREL dose tray marked "N".
10. Place the ENBREL vial upright on your flat working surface. Hold the syringe with the needle facing up, and gently pull back the plunger to pull a small amount of air into the syringe. Insert the 25-gauge needle straight down through the centre ring of the gray stopper. You should feel a slight resistance and then a "pop" as the needle goes through the centre of the stopper. Look for the needle tip inside the stopper window. If the needle is not correctly lined up with the centre of the stopper, you will not feel a "pop" and will feel constant resistance as you 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.

11. With the needle still in the vial, turn the vial upside down. Holding the syringe at eye level, slowly pull the plunger down to the mark on the syringe that corresponds 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.
12. 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 the solution back into the vial, slowly pull back on the plunger to draw the correct amount of solution back into the syringe.
13. Remove the syringe and needle from the ENBREL vial. **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. Place the 25-gauge needle back into the hard plastic needle cover in the ENBREL dose tray, and push the syringe down until the needle is attached. Once the needle is secure in the needle cover, untwist the 25-gauge needle from the syringe and dispose of it in your sharps disposal container.
14. With the needle cover still on, in the partially opened paper packaging, twist the new 27-gauge needle onto the syringe until it fits snugly. Remove the paper packaging from the needle cover. **Do NOT** remove the needle cover from the syringe until you are ready to inject. Pull the hard plastic needle cover straight off the syringe. To avoid damaging the needle, **do NOT** twist or bend the needle cover while you are removing it, and **do NOT** try to put the needle cover back onto the syringe. When you remove the needle cover, there may be a drop of liquid at the end of the needle; this is normal. **Do NOT** touch the needle or allow it to touch any surface. You are now ready to inject ENBREL.

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 **five** centimeters (two inches) around your navel (belly button); 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. With one hand, gently pinch the cleaned area of skin and hold it firmly. With the other hand, hold the syringe at about a 45° angle to the skin.



2. With a quick, “dart-like” short motion, push the needle into the skin.
3. Let go of the skin with the other hand.
4. With your free hand, slowly push the plunger down to inject ENBREL.



5. When the syringe is empty, remove the needle from the skin, being careful to keep it at the same angle it was when it was inserted.
6. 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 the injection site with a bandage.
7. If there is enough solution left in the ENBREL vial for another dose, write the date you mixed the powder and liquid in the area marked “Mixing Date:” on the sticker supplied with these instructions and attach the sticker to the ENBREL vial. Refrigerate the reconstituted (mixed) ENBREL vial (in the dose tray) after use. Prepare additional doses from the ENBREL vial as described in STEP 3. Otherwise, discard the ENBREL vial and any remaining solution.

STEP 6: Disposing of Supplies

1. The syringe, needle, and vial adapter should **NEVER** be reused. **NEVER** recap a needle. Instructions have been provided for children’s caregivers to help them safely switch from the 25-gauge needle used for mixing and withdrawing ENBREL to the 27-gauge needle used for injecting ENBREL.
2. Immediately throw away the used needle and syringe in a sharps disposal container. **Do NOT** remove the plunger from the syringe prior to disposal. A 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 provincial or local laws regarding the proper disposal of needles and syringes.

- The ENBREL vials, vial adapters, 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 handled by a doctor, nurse, or pharmacist familiar with ENBREL. A toll-free information service is also available: 1-877-9ENBREL (1-877-936-2735).

What are possible side effects from using ENBREL?

Like all medicines, ENBREL can cause side effects. Most side effects are mild to moderate. However, some may be serious and require treatment.

What are the common side effects?

In studies comparing ENBREL to placebo (inactive injection), side effects that occurred more frequently in patients treated with ENBREL were:

- Reactions where the injection was given. These reactions are usually mild and include redness, swelling, itching, or bruising. These usually go away within 3 to 5 days. If you have pain, redness or swelling around the injection site that doesn't go away or gets worse, call your doctor.
- Upper respiratory infections (sinus infections)
- Headaches

These are not all the possible side effects you may feel when taking ENBREL. If you experience any side effects not listed here, contact your healthcare professional.

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
VERY COMMON Injection site reactions		√	
COMMON Upper respiratory tract infections (sinus infections)		√	
Headaches	√		
UNCOMMON Serious infections		√	√
Tuberculosis		√	
Nerve disorders		√	

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, talk to your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on [Adverse Reaction Reporting](http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/index-eng.php) (<http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/index-eng.php>) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

The ENBREL dose tray containing sterile powder should be refrigerated at 2°C to 8°C. **Do NOT freeze ENBREL.** Unopened refrigerated ENBREL sterile powder remains stable until the expiration date printed on the vial.

Unopened ENBREL sterile powder may be transferred to room temperature storage (up to 27°C). Upon removal from the refrigerator, it must be used within 60 days. Protect from direct sunlight, sources of heat, and humidity until ready to use.

Reconstituted solutions of ENBREL prepared with the supplied Sterile Bacteriostatic Water for Injection, USP (0.9% benzyl alcohol) must be stored in the original vial for no more than 14 days at 2°C to 8°C, with overall room temperature exposure of less than 12 hours during storage and handling. Product stability and sterility of reconstituted solutions cannot be assured after 14 days. Discard reconstituted solution after 14 days.

Keep out of the reach of children.

If you want more information about ENBREL:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the [Health Canada website](#); the manufacturer's website www.amgen.ca, or by contacting the ENLIVEN[®] Services information support line, toll free at: 1-877-9ENBREL (1-877-936-2735). Additional information can be found at www.enbrel.ca.

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