060308.final draft Med Guide

MEDICATION GUIDE
PegIntron™/REBETOL® Combo Pack containing
PegIntron™ REDIPEN® Single-dose Delivery System (peginterferon alfa-2b) and
REBETOL® (ribavirin, USP) Capsules

Including appendix with instructions for using PegIntron™ REDIPEN® Single-dose Delivery System

Read this Medication Guide carefully before you start taking PegIntron™/REBETOL® Combo Pack containing **PegIntron™ (Peg In-tron)** and REBETOL® **(REB-eh-tole)**. Read the Medication Guide each time you refill your prescription because there may be new information. The information in this Medication Guide does not take the place of talking with your health care provider (doctor, nurse, nurse practitioner, or physician's assistant).

What is the most important information I should know about PegIntron™/REBETOL® Combo Pack therapy?

PegIntron™/REBETOL® Combo Pack is a treatment for some people who are infected with hepatitis C virus. However, PegIntron™/REBETOL® Combo Pack therapy can have serious side effects that may cause death in rare cases. Before you decide to start treatment, you should talk to your health care provider about the possible benefits and side effects of PegIntron™/REBETOL® Combo Pack therapy. If you begin treatment you will need to see your health care provider regularly for medical examinations and lab tests to make sure your treatment is working and to check for side effects.

REBETOL® capsules may cause birth defects and/or death of an unborn child. If you are pregnant, you or your male partner must not take PegIntron™/REBETOL® Combo Pack therapy. You must not become pregnant while either you or your partner are being treated with PegIntron™/REBETOL® Combo Pack therapy, or for 6 months after stopping therapy. During this time you must use two forms of birth control and you must have pregnancy test to show that you are not pregnant. Men and women should use birth control while taking the combination therapy and for 6 months afterwards. If you or your partner are being treated and you become pregnant, either during treatment or within 6 months of stopping treatment, call your health care provider right away. There is a Ribavirin Pregnancy Registry that collects information about pregnancy outcomes in female patients and female partners of male patients exposed to ribavirin. You or your health care provider are encouraged to contact the Registry at 1-800-593-2214.

Be assured that any information you tell the Registry will be kept confidential. (See **"What should I avoid while taking PegIntron™/REBETOL® Combo Pack therapy?"**)

If you are taking PegIntron™/REBETOL® Combo Pack therapy you should call your health care provider immediately if you develop any of these symptoms:

New or worsening mental health problems, such as thoughts about killing or hurting yourself or others, trouble breathing, chest pain, severe stomach or lower back pain, bloody diarrhea or bloody bowel movements, high fever, bruising, bleeding, or decreased vision.

The most serious possible side effects of PegIntron™/REBETOL® Combo Pack therapy include:

Problems with Pregnancy. PegIntron™/REBETOL® Combo Pack therapy can cause death, serious birth defects, or other harm to your unborn child. . If you are a woman of childbearing age, you must not become pregnant during treatment and for 6 months after you have stopped therapy. You must have a negative pregnancy test immediately before beginning treatment, during treatment, and for 6 months after you have stopped therapy. Both males and female patients must use effective forms of birth control during treatment and for the 6 months after treatment is completed. Male patients should use a condom. If you are a female, you must use birth control even if you believe that you are not fertile or that your fertility is low. You should talk to your health care provider about birth control for you and your partner.

Mental health problems and suicide. PegIntron™/REBETOL® Combo Pack therapy may cause patients to develop mood or behavioral problems. These can include irritability (getting easily upset) and depression (feeling low, feeling bad about yourself, or feeling hopeless). Some patients may have aggressive behavior. Former drug addicts may fall back into drug addiction or overdose. Some patients think about hurting or killing themselves or other people and some have killed (suicide) or hurt themselves or others. You must tell your health care provider if you are being treated for a mental illness or had treatment in the past for any mental illness, including depression and suicidal behavior. You should tell your health care provider if you have ever been addicted to drugs or alcohol.

Heart problems. Some patients taking PegIntron™/REBETOL® Combo Pack therapy may develop problems with their heart, including low blood pressure, fast heart rate, and very rarely, heart attacks. Tell your health care provider if you have had any heart problems in the past.

Blood problems. PegIntron™/REBETOL® Combo Pack therapy commonly lowers two types of blood cells (white blood cells and platelets). In some patients, these blood counts may fall to dangerously low levels. If your blood counts become very low, this could lead to infections or bleeding.

REBETOL® can cause anemia, which is a decrease in the number of red blood cells. This can be dangerous, especially for patients who already have heart or circulatory (cardiovascular) or breathing problems. Talk with your health care provider before taking PegIntron™/REBETOL® Combo Pack therapy if you have, or have ever had any cardiovascular problems. Your health care provider should check your red blood cell count

before you start therapy and often during the first 4 weeks of therapy. Your red blood cell count may be checked more often if you have any heart or breathing problems.

- **Do not take REBETOL Capsules or Oral Solution alone to treat hepatitis C infection.** REBETOL Capsules should be used in combination with interferon alfa-2b (INTRON A) or in combination with peginterferon alfa-2b (PegIntron) for treating chronic hepatitis C infection in adults. In children, safety and effectiveness of REBETOL Capsules or Oral Solution has only been shown when used in combination with interferon alfa-2b (INTRON A). Your health care provider or pharmacist should give you a copy of the INTRON A or PegIntron Medication Guide. They have additional important information about combination therapy not covered in this guide. PegIntron™/REBETOL® Combo Pack is not approved for the treatment of chronic hepatitis C in children.

Body organ problems. Certain symptoms like severe stomach pain may mean that your internal organs are being damaged. Cases of weakness, loss of coordination, and numbness due to stroke have been reported in patients taking combination PegIntron/REBETOL, including patients with few or no reported risk factors for stroke.

For other possible side effects, see "What are the possible side effects of PegIntron™/REBETOL® Combo Pack therapy" in this Medication Guide.

What is PegIntron™/REBETOL® Combo Pack therapy?

PegIntron™/REBETOL® Combo Pack consists of two medications used to treat hepatitis C infection. Patients with hepatitis C have the virus in their blood and in their liver. PegIntron™ reduces the amount of virus in the body and helps the body's immune system fight the virus. REBETOL® (ribavirin) is a drug that helps to fight the viral infection, but does not work when used by itself to treat chronic hepatitis C.

It is not known if PegIntron™/REBETOL® Combo Pack therapy can cure hepatitis C (permanently eliminate the virus), or if it can prevent liver failure or liver cancer that is caused by hepatitis C infection.

It is also not known if PegIntron™/REBETOL® Combo Pack therapy will prevent one infected person from infecting another person with hepatitis C.

Who should not take PegIntron™/REBETOL® Combo Pack therapy?

Do not take PegIntron™/REBETOL® Combo Pack therapy if you:

- are pregnant, planning to get pregnant during treatment or during the 6 months after treatment, or breast-feeding

- are a male patient with a female sexual partner who is pregnant, or plans to become pregnant at any time while you are being treated with REBETOL®, or during the 6 months after your treatment has ended.

- have hepatitis caused by your immune system attacking your liver (autoimmune hepatitis) or unstable liver disease.

- had an allergic reaction to another alpha interferon or are allergic to any of the ingredients in PegIntron™ or REBETOL® Capsules. If you have any doubts, ask your health care provider.

- Do not take PegIntron™/REBETOL® Combo Pack therapy if you have abnormal red blood cells such as sickle-cell anemia or thalassemia major.

If you have any of the following conditions or serious medical problems, discuss them with your health care provider before taking PegIntron™/REBETOL® Combo Pack therapy:

- depression or anxiety
- sleep problems
- high blood pressure
- previous heart attack, or other heart problems
- liver problems (other than hepatitis C infection)
- any kind of autoimmune disease (where the body's immune system attacks the body's own cells), such as psoriasis, systemic lupus erythematosus, rheumatoid arthritis
- thyroid problems
- diabetes
- colitis (inflammation of the bowels)
- cancer
- hepatitis B infection
- HIV infection
- kidney problems
- bleeding problems
- alcoholism
- drug abuse or addiction
- body organ transplant and are taking medicine that keeps your body from rejecting your transplant (suppresses your immune system).

How should I take PegIntron™/REBETOL® Combo Pack therapy?

Your health care provider will determine the correct dose (based on your weight). PegIntron™/REBETOL® Combo Pack therapy is given for one year. Take your prescribed dose of PegIntron™ ONCE A WEEK, on the same day of each week and at approximately the same time. Take the medicine for the full year and do not take more than the prescribed dose. REBETOL® Capsules should be taken with food. It is important to follow your dosing schedule and your health care providers instructions on how to take your medicines. Under no circumstances should REBETOL Capsules be opened, crushed or broken. When you take REBETOL® with food, more of the medicine (70% more on average) is taken up by your body. You should take REBETOL® the same way every day (twice a day with food) to

keep the medicine in your body at a steady level. This will help your health care provider to decide how your treatment is working and how to change the number of REBETOL® capsules you take if you have side effects from REBETOL®. **Be sure to read the Medication Guide for PegIntron™/REBETOL® for complete instructions on how to take this medicine.**

You should be completely comfortable with how to prepare PegIntron™, how to set the dose you take, and how to inject yourself before you use PegIntron™ for the first time. PegIntron™ comes as a REDIPEN® single-use delivery system. See the attached appendix for detailed instructions for preparing and giving a dose of PegIntron™.

If you miss a dose of the PegIntron™ product, take the missed dose as soon as possible during the same day or the next day, then continue on your regular dosing schedule. If several days go by after you miss a dose, check with your health care provider about what to do. Do not double the next dose or take more than one dose a week without talking to your health care provider. Call your health care provider right away if you take more than your prescribed PegIntron™ dose. Your health care provider may wish to examine you more closely, and take blood for testing.

If you miss a dose of REBETOL® capsules, take the missed dose as soon as possible during the same day. If an entire day has gone by, check with your health care provider about what to do. Do not double the next dose.

You must get regular blood tests to help your health care provider check how the treatment is working and to check for side effects.

Tell your health care provider if you are taking or planning to take other prescription or non-prescription medicines, including vitamin and mineral supplements and herbal medicines.

What should I avoid while taking PegIntron™/REBETOL® Combo Pack therapy?

- If you are pregnant do not start taking PegIntron™/REBETOL® Combo Pack therapy.
- Avoid becoming pregnant while taking PegIntron™/REBETOL® Combo Pack therapy.

PegIntron™/REBETOL® Combo Pack therapy may harm your unborn child (death or serious birth defects) or cause you to lose your baby (miscarry). **If you or your partner becomes pregnant during treatment or during the 6 months after treatment with PegIntron™/REBETOL® Combo Pack therapy, immediately report the pregnancy to your health care provider. You or your health care provider should call 1-800-593-2214.** By calling this number, information about you and/or your partner will be added to a pregnancy registry that will be used to help you and your health care provider make decisions about your treatment for hepatitis in the future. You, your partner, and/or your health care provider will be asked to provide follow-up information on the outcome of the pregnancy. Be assured that any information you tell the Registry will be kept confidential.

- **Breastfeeding**. The medicine may pass through your milk and harm the baby.

- **Drinking alcohol**, including beer, wine, and liquor. This may make your liver disease worse.
- **Taking other medicines**. Take only medicines prescribed or approved by your health care provider. These include prescription and nonprescription medicines and herbal supplements.

What are the most common side effects of REBETOL Capsules and Oral Solution?
The most serious possible side effects of REBETOL Capsules and Oral Solution are:

- **Harm to unborn children.** REBETOL Capsules and Oral Solution may cause birth defects or death of an unborn child. (For more details, see "**What is the most important information I should know about REBETOL Capsules or Oral Solution?**")

- **Anemia.** Anemia is a reduction in the number of red blood cells you have which can be dangerous, especially if you have heart or breathing problems. Tell your health care provider right away if you feel tired, have chest pain or shortness of breath. These may be signs of low red blood cell counts.

- Do not breast-feed your baby while taking PegIntron™.

What are the possible side effects of PegIntron™/REBETOL® Combo Pack therapy?

Possible, serious side effects include:
Mental health problems including suicide, blood problems, heart problems, body organ problems. See "What is the most important information I should know about PegIntron™/REBETOL® Combo Pack therapy?"

Other body organ problems. A few patients have lung problems (such as pneumonia or inflammation of the lung tissue), inflammation of the kidney, and eye disorders.

New or worsening autoimmune disease. Some patients taking PegIntron™/REBETOL® Combo Pack therapy develop autoimmune diseases (a condition where the body's immune cells attack other cells or organs in the body), including rheumatoid arthritis, systemic lupus erythematosus, and psoriasis. In some patients who already have an autoimmune disease, the disease worsens on PegIntron™/REBETOL® Combo Pack therapy.

Common but less serious side effects include:

Flu-like symptoms. Most patients who take PegIntron™/REBETOL® Combo Pack therapy have "flu-like" symptoms (headache, muscle aches, tiredness, and fever). Some of these symptoms (fever, headache) usually lessen after the first few weeks of therapy. You can reduce some of these symptoms by injecting your PegIntron™ dose at bedtime. Over-the-counter pain and fever reducers, such as acetaminophen or ibuprofen, can be used to prevent or reduce the fever and headache.

Extreme fatigue (tiredness). Many patients become extremely tired while on PegIntron™/REBETOL® Combo Pack therapy.

Appetite problems. Nausea, loss of appetite, and weight loss, occur commonly.

Thyroid problems. Some patients develop changes in the function of their thyroid. Symptoms of thyroid changes include the inability to concentrate, feeling cold or hot all the time, a change in your weight, and changes to your skin.

Blood sugar problems. Some patients develop problems with the way their body controls their blood sugar, and may develop high blood sugar or diabetes.

Skin reactions. Redness, swelling, and itching are common at the site of injection. If after several days these symptoms do not disappear, contact your health care provider. You may get a rash during therapy. If this occurs, your health care provider may recommend medicine to treat the rash.

Hair thinning. Hair thinning is common during PegIntron™/REBETOL® Combo Pack treatment. Hair loss stops and hair growth returns after therapy is stopped.

These are not all of the side effects of PegIntron™/REBETOL® Combo Pack therapy. Your health care provider or pharmacist can give you a more complete list.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

General advice about prescription medicines:
Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. If you have any concerns about PegIntron™/REBETOL® Combo Pack therapy, ask your health care provider. Your health care provider or pharmacist can give you information about PegIntron™/REBETOL® Combo Pack therapy that was written for health care professionals. Do not use PegIntron™/REBETOL® Combo Pack therapy for a condition for which it was not prescribed. Do not share this medication with other people.

How do I store my PegIntron™/REBETOL® Combo Pack package?

The PegIntron™/REBETOL® Combo Pack package should be stored in the refrigerator at 2°-8°C (36°-46°F).

When separated, the individual bottle of REBETOL® Capsules should be stored at room temperature 25°C (77°F).

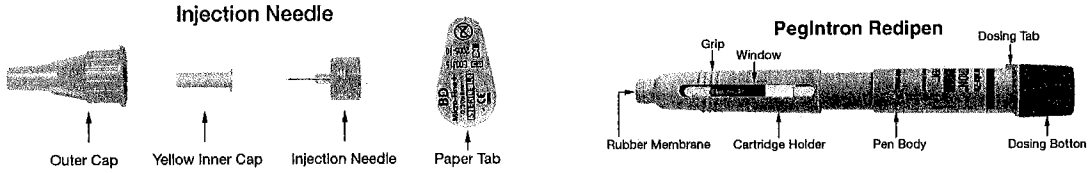
When separated, the PegIntron™ REDIPEN® should be stored in the refrigerator at 2°-8°C (36°-46°F); avoid exposure to heat. After mixing, the PegIntron™ solution should be used

immediately but may be stored in the refrigerator up to 24 hours at 2°-8°C (36°-46°F). The solution contains no preservatives. DO NOT FREEZE.

How do I prepare and inject the PegIntron™ REDIPEN® Dose?

The PegIntron™ REDIPEN® system is for a single use, by one person only, ONCE A WEEK. The REDIPEN® must not be shared. Use only the injection needle provided in the packaging for the PegIntron™ REDIPEN® system. If you have problems with the REDIPEN® system or the PegIntron™ solution, you should contact your health care provider, or pharmacist.

The following instructions explain how to prepare and inject yourself with the PegIntron™ REDIPEN® system. Please read the instructions carefully and follow them step by step. Your health care provider will instruct you on how to self-inject with the PegIntron™ REDIPEN®. Do not attempt to inject yourself unless you are sure you understand the procedure and requirements for self-injection.



How to use the PegIntron™ REDIPEN® Single-dose Delivery System.

Preparation

1. Find a clean, well-lit, non-slip flat working surface and assemble all of the supplies you will need for an injection. All of the supplies you will need are in the PegIntron™ REDIPEN® package. The package contains:
   - a PegIntron™ REDIPEN® Single-dose Delivery System
   - one disposable needle
   - two alcohol swabs, and
   - dosing tray (The dosing tray is the bottom half of the REDIPEN® package.)
2. Take the PegIntron™ REDIPEN® out of the refrigerator and allow the medicine to come to room temperature. Before removing the REDIPEN® from the carton, check the expiration date printed on the PegIntron™ REDIPEN® carton to make sure that the expiration date has not passed. Do not use if the expiration date has passed.
3. After taking the PegIntron™ REDIPEN® out of the carton, look in the window of the REDIPEN® and make sure the PegIntron™ in the cartridge holder window is a white, to off- white tablet that is whole, in pieces, or powdered.
4. Wash your hands thoroughly with soap and water, rinse, and towel dry. It is important to keep your work area, your hands, and the injection site clean to minimize the risk of infection.

1. Mix the Drug

Key points:

Before you mix the PegIntron™, make sure it is at room temperature. It is important that you keep the PegIntron™ REDIPEN® UPRIGHT (Dosing Button down) as shown in Figure 1.

a. Hold the PegIntron™ REDIPEN® **UPRIGHT (Figure 1a)** in the dosing tray on a hard, flat, non-slip surface with the dosing button **down.** You may want to hold the REDIPEN® using the grip.

b. To mix the powder and the liquid, keep the REDIPEN® upright in the dosing tray and press the top half of the REDIPEN® downward toward the hard, flat, non-slip surface **until you hear the click (Figure 1b).**Once you've heard the click, you will notice in the window that both dark stoppers are now touching. The dosing button should be flush with the pen body.

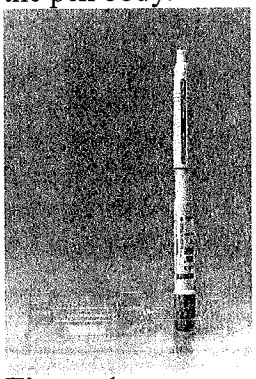


Figure 1a

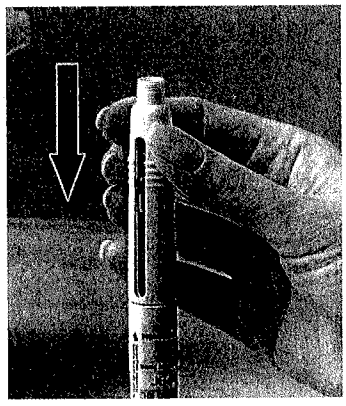


Figure 1b

c. Wait several seconds for the powder to completely dissolve.

d. **Gently turn the PegIntron™ REDIPEN® upside down twice (Figure 2). To avoid excessive foaming, DO NOT SHAKE.**

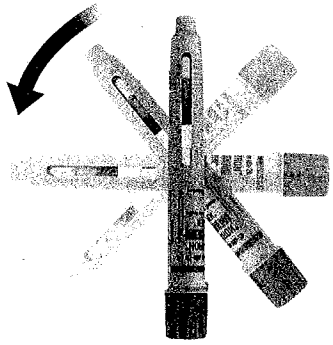


Figure 2

e. Keep the PegIntron™ REDIPEN® **UPRIGHT**, with the dosing button down. Then, look through the REDIPEN® window to see that the mixed PegIntron™ solution is completely dissolved. The solution should be clear and colorless **before use**. Before attaching the needle, it is normal to see some small bubbles in the REDIPEN® window, near the top of the solution. Do not use the solution if it is discolored, or not clear, or if particulates are present.

f. **Place the PegIntron™ REDIPEN® back into the dosing tray provided in the packaging (Figure 3). The dosing button will be on the bottom.**

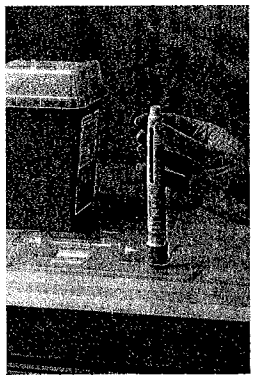


Figure 3

2. Attach the Needle

a. Wipe the rubber membrane of the PegIntron™ REDIPEN® with one alcohol swab.

b. Remove the protective paper tab from the injection needle, but do NOT remove either the outer cap or the yellow inner cap from the injection needle. Keeping the PegIntron™ REDIPEN® UPRIGHT in the dosing tray, FIRMLY push the injection needle straight into the REDIPEN® rubber membrane, and screw it firmly in place, in a clockwise direction (**Figure 4**). Remember to leave the needle caps in place when you attach the needle to the REDIPEN®. Pushing the needle through the rubber membrane, "primes" the needle and allows the extra liquid and air in the pen to be removed.

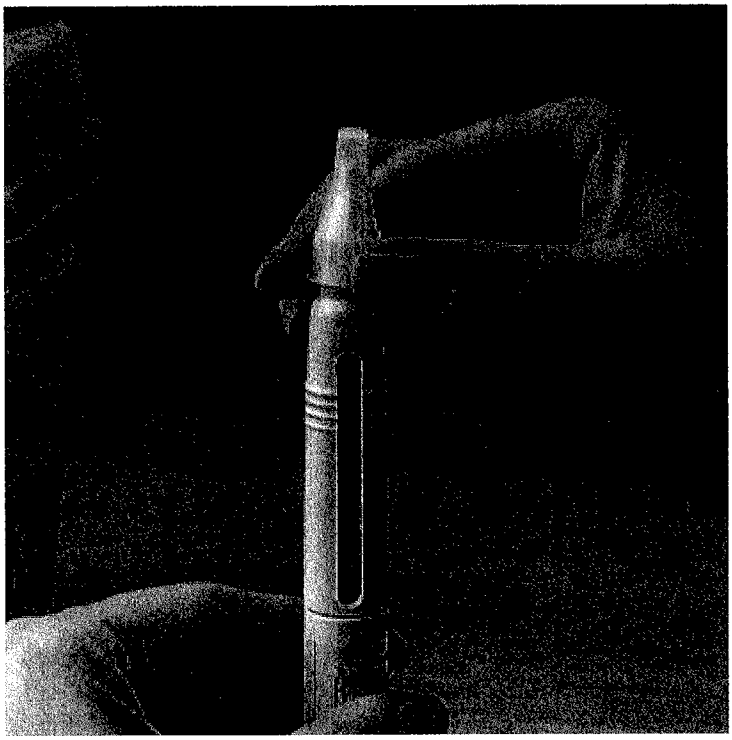


Figure 4

NOTE: Some fluid will trickle out. This is **normal.** The dark stoppers move up and you will no longer see the fluid in the window once the needle is successfully primed.

3. Dialing the Dose

a. **Remove the PegIntron™ REDIPEN® from the dosing tray (Figure 5a).**
Holding the PegIntron™ REDIPEN® firmly, pull the dosing button out as far as it will go. -You will see a dark band.

Do not push the dosing button in until you are ready to self-inject the PegIntron™ dose.

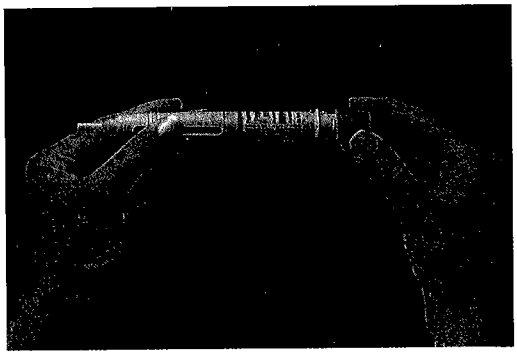


Figure 5a

b. Turn the dosing button until your prescribed dose is lined up with the dosing tab (**Figure 5b**). The dosing button will turn freely. If you have trouble dialing your dose, check to make sure the dosing button has been pulled out **as far** as it will go (**Figure 5c**).

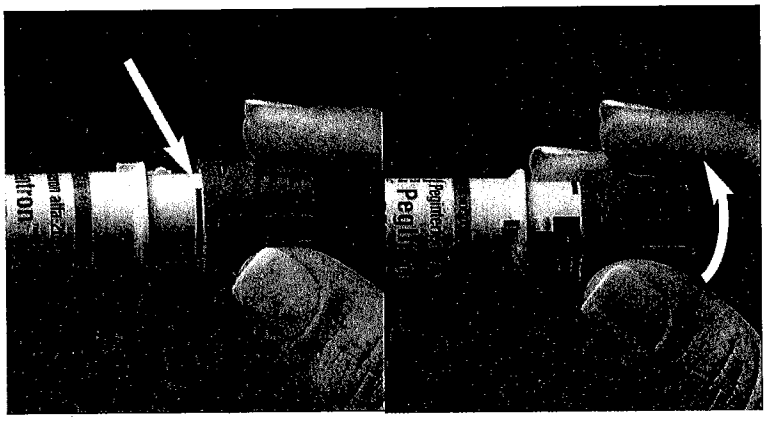


Figure 5b **Figure 5c**

c. Carefully lay the PegIntron™ REDIPEN® down on a hard, flat, non-slip surface. Do NOT remove either of the needle caps and do NOT push the dosing button in until you are ready to self-inject the PegIntron™ dose.

4. Injecting the PegIntron™ Dose

Choosing an Injection Site

The best sites for giving yourself an injection are those areas with a layer of fat between the skin and muscle, like your thigh, the outer surface of your upper arm, and abdomen. Do not inject yourself in the area near your navel or waistline. If you are very thin, you should only use the thigh or outer surface of the arm for injection.

You should use a different site each time you inject PegIntron™ to avoid soreness at any one site. Do not inject PegIntron™ into an area where the skin is irritated, red, bruised, infected, or has scars, stretch marks, or lumps.

a. Clean the skin where the injection is to be given with the second alcohol swab provided, and wait for the area to dry.

b. Remove the **outer** cap from the needle (**Figure 6a**). There may be some liquid around the yellow inner needle cap (**Figure 6b**). This is normal.

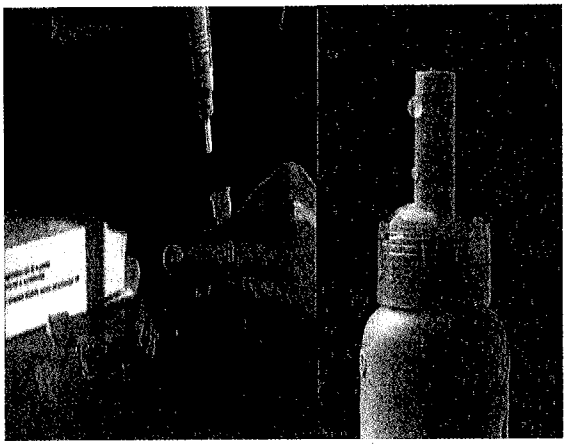


Figure 6a **Figure 6b**

c. Once the injection site is dry, remove the **yellow** inner needle cap (**Figure 6c**). You are now ready to inject.

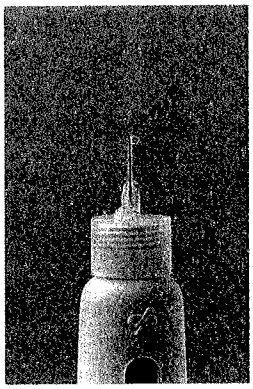


Figure 6c

d. **Hold the PegIntron™ REDIPEN ® with your fingers wrapped around the pen body barrel and your thumb on the dosing button (Figure 7).**

- With your other hand, pinch the skin in the area you have cleaned for injection.

- Insert the needle into the pinched skin at an angle of 45° to 90°.
- Press the dosing button down slowly and firmly until you can't push it any further.
- Keep your thumb pressed down on the dosing button for an additional 5 seconds to ensure that you get the complete dose.
- Remove the needle from your skin.

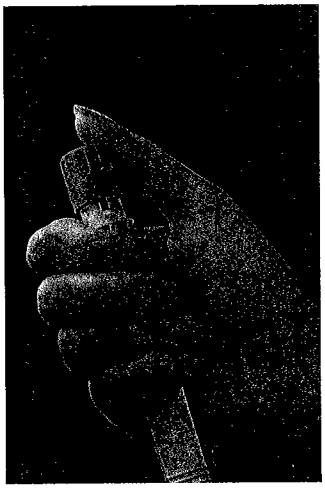


Figure 7

e. **Gently press the injection site with a small bandage or sterile gauze if necessary for a few seconds but** do not massage the injection site. If there is bleeding, cover with an adhesive bandage. **DO NOT RECAP THE NEEDLE and DO NOT REUSE the REDIPEN®.**

How do I Dispose of the REDIPEN®?

Discard the REDIPEN® and needle and any solution remaining in the REDIPEN® in a sharps container or other puncture-resistant container like a metal coffee can. DO NOT use glass or clear plastic containers. Ask your health care provider how to dispose of a full container. Always keep the container out of reach of children.

After 2 hours, check the injection site for redness, swelling, or tenderness. If you have a skin reaction and it doesn't clear up in a few days, contact your health care provider.

This Medication Guide has been approved by the U.S. Food and Drug Administration.

Manufactured by: Schering Corporation, Kenilworth, NJ 07033 USA

DATE 06/08