12-13-06-revsied MedGuide Powder-Final Draft

MEDICATION GUIDE

PegIntron™

Peginterferon alfa-2b

Including appendix with instructions for using PegIntron™ Powder for Injection

Read this Medication Guide carefully before you start taking PegIntron™ (**Peg In-tron**) or PegIntron™/REBETOL (**REB-eh-tole**) combination therapy. 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).

If you are taking PegIntron™/REBETOL combination therapy, also read the Medication Guide for REBETOL (ribavirin, USP) Capsules.

What is the most important information I should know about PegIntron™ and PegIntron™/REBETOL combination therapy?

PegIntron™ (peginterferon) is a treatment for some people who are infected with hepatitis C virus. However, PegIntron™ and PegIntron™/REBETOL combination 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™ or PegIntron™/REBETOL combination 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 combination therapy. You must not become pregnant while either you or your partner are being treated with the combination PegIntron™/REBETOL therapy, or for 6 months after stopping therapy. 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.

If you are taking PegIntron™ or PegIntron™/REBETOL 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™ and PegIntron™/REBETOL therapy include:

Problems with Pregnancy. **Combination PegIntron™/REBETOL 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™ and PegIntron™/REBETOL therapies 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™ or PegIntron™/REBETOL 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™ and PegIntron™/REBETOL therapies commonly lower 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 therapy causes a decrease in the number of red blood cells you have (anemia). This can be dangerous, especially for patients who already have heart or circulatory (cardiovascular) problems. Talk with your health care provider before taking combination PegIntron™/REBETOL therapy if you have, or have ever had any cardiovascular problems.

Body organ problems. Certain symptoms like severe stomach pain may mean that your internal organs are being damaged.

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

What is PegIntron™ and PegIntron™/REBETOL combination therapy?

The PegIntron™ product is a drug used to treat adults who have a lasting (chronic) infection with hepatitis C virus and who show signs that the virus is damaging the liver.

PegIntron™/REBETOL combination therapy consists of two medications also 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™ or PegIntron™/REBETOL therapies 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™ or PegIntron™/REBETOL combination therapy will prevent one infected person from infecting another person with hepatitis C.

Who should not take PegIntron™ or PegIntron™/REBETOL therapy?

Do not take PegIntron™ or PegIntron™/REBETOL 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 combination 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™ or PegIntron™/REBETOL 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™ or PegIntron™/REBETOL?

Your health care provider will decide whether you will take PegIntron™ therapy alone or the combination of PegIntron™/REBETOL, as well as the correct dose (based on your weight). PegIntron™ and PegIntron™/REBETOL are 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. 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 REBETOL (ribavirin, USP) for complete instructions on how to take the REBETOL capsules.**

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 in two different forms, a powder in a single-use vial and 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™ or PegIntron™/REBETOL therapies?

- If you are pregnant do not start taking PegIntron™/REBETOL combination therapy.
- Avoid becoming pregnant while taking PegIntron™ or PegIntron™/REBETOL.

PegIntron™ and PegIntron™/REBETOL 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 combination therapy, immediately report the pregnancy to your health care provider. You or your health care provider should call (800) 727-7064.** 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.

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

What are the possible side effects of PegIntron™ and PegIntron™/REBETOL combination 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™ and PegIntron™/REBETOL combination 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™ or PegIntron™/REBETOL 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™ and PegIntron™/REBETOL combination therapy.

Common but less serious side effects include:

Flu-like symptoms. Most patients who take PegIntron™ or PegIntron™/REBETOL 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™ or PegIntron™/REBETOL combination 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™ and PegIntron™/REBETOL treatment. Hair loss stops and hair growth returns after therapy is stopped.

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

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™, ask your health care provider. Your health care provider or pharmacist can give you information about PegIntron™ that was written for health care professionals. Do not use PegIntron™ for a condition for which it was not prescribed. Do not share this medication with other people.

If you are taking PegIntron™/REBETOL combination therapy, also read the Medication Guide for REBETOL (ribavirin, USP) Capsules.

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

Manufactured by: Schering Corporation, Kenilworth, NJ 07033 USA
DATE

<u>How do I prepare and inject the PegIntron™ Dose?</u>
Before you inject PegIntron™, the powder must be mixed with **0.7 mL** of the supplied DILUENT for PegIntron™, Sterile Water for Injection (diluent). You should carefully follow the directions given to you by your health care provider.

The vial of mixed PegIntron™ should be used immediately. DO NOT prepare more than one vial at a time. If you don't use the vial of the prepared solution right away, it must be stored in a refrigerator and used within 24 hours.

Storing PegIntron™

PegIntron™ Powder should be stored at room temperature (25 ^{o} C, 77^{o}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. The solution contains no preservatives. DO NOT FREEZE.

Preparing the PegIntron™ solution

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 for an injection are in the PegIntron™ Powder for Injection package. The package contains:
   - a vial of PegIntron™ powder
   - a 1.25 mL vial of DILUENT
   - 2 disposable syringes, and
   - alcohol swabs
2. Check the date printed on the PegIntron™ carton to make sure that the expiration date has not passed. Remove one vial and look at the contents. The PegIntron™ in the vial should appear as a white to off-white tablet-like solid, that is whole/in pieces or as a loose powder.

   If you have already mixed the PegIntron™ solution and it has been stored properly in the refrigerator, take it out of the refrigerator and allow the solution to come to room temperature.
3. Wash your hands thoroughly with soap and water, rinse and towel dry. It is important to keep your work area, your hands, and injection site clean to minimize the risk of infection.

   The disposable syringes have needles that are already attached and cannot be removed. Each syringe has a clear plastic safety sleeve that is pulled over the needle for disposal after use. The safety sleeve should remain tight against the flange while using the syringe and moved over the needle only when ready for disposal (**Figure A).**
   The syringes and needles are for single use only.

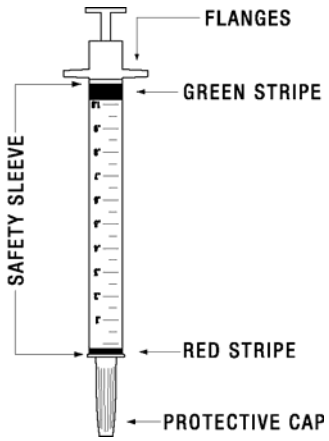

Figure A

4. Remove the protective wrapper from ONE of the syringes provided and use for the following steps 5-7. Make sure that the syringe safety sleeve is sitting against the flange (**Figure A**).

5. Remove the protective plastic cap from the tops of both the supplied DILUENT and the PegIntron™ vials. Clean the rubber stopper on the top of both vials with an alcohol swab.

6. Carefully remove the protective cap straight off of the needle to avoid damaging the needle point. Fill the syringe with air by pulling the plunger to 0.7 mL (**Figure B**). Hold the DILUENT vial upright. Do not touch the cleaned top of the vial with your hands (**Figure C**). Insert the needle through the center of the rubber stopper of the DILUENT vial, and inject the air from the syringe into the vial (**Figure D**). Turn the vial upside down and make sure the tip of the needle is in the liquid. **Withdraw only 0.7 mL of DILUENT** by pulling the plunger back to 0.7 mL mark on the side of the syringe (**Figure E**). Remove the needle from the vial (**Figure F**). **Discard the remaining DILUENT.**

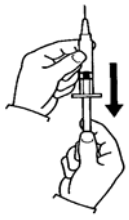

Figure B

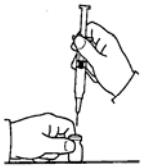

Figure C

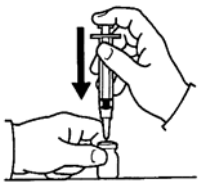

Figure D

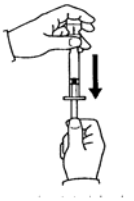

Figure E

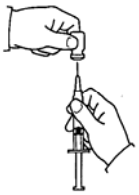

Figure F

7. Insert the needle through the center of the rubber stopper of the PegIntron™ vial, and place the needle tip against the glass wall of the vial (**Figure G**). SLOWLY inject the 0.7 mL DILUENT so that the stream of DILUENT runs down the side of the vial. To prevent bubbles from forming, DO NOT AIM THE STREAM of diluent directly on the tablet-like SOLID or POWDER in the bottom of the vial. Remove the needle from the vial.
Firmly grasp the safety sleeve and pull it over the exposed needle until you hear a click. The green stripe on the safety sleeve will completely cover the red stripe on the needle. (See **Figure O** in the section: "Injecting the PegIntron™ dose.") Discard the syringe and needle in the puncture proof container.

8. GENTLY swirl the vial in a gentle circular motion (**Figure H**), until the PegIntron™ is completely dissolved. **DO NOT SHAKE** the vial. If any powder remains undissolved in the vial, gently turn the vial upside down until all of the powder is dissolved. It is not unusual for the solution to appear cloudy or bubbly for a few minutes. If air bubbles do form, wait until the solution has settled and all bubbles have risen to the top before withdrawing your dose from the vial.

Figure G

Figure H

9. After the solution has settled and is completely dissolved it should be clear, colorless, and without particles, but there may be a ring of foam or bubbles on the surface, this is normal. Do not use it if you see particles or the color is not correct**.**
10. After the PegIntron™ powder is dissolved but before you withdraw your dose, clean the rubber stopper again with an alcohol swab.

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11. Unwrap the second syringe provided. You will use it to give yourself the injection. Carefully remove the protective cap from the needle and fill the syringe with air by pulling the plunger to the number on the side of the syringe (mL) that corresponds to your prescribed dose (**Figure J**). Hold the PegIntron™ vial upright. DO NOT touch the cleaned top of the vial with your hands (**Figure K**). Insert the needle into the vial containing the PegIntron™ solution and inject the air into the center of the vial (**Figure L**).

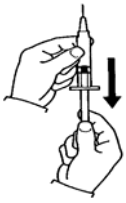

Figure J

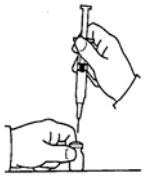

Figure K

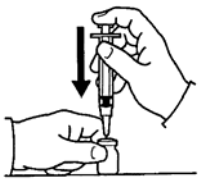

Figure L

12. Turn the PegIntron™ vial upside down. Be sure the tip of needle is in the PegIntron™ solution. While holding the vial and syringe with one hand slowly pull the plunger back to withdraw the exact amount of PegIntron™ into the syringe your health care provider told you to use (**Figure M**).

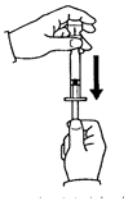

Figure M

13. Remove the needle from the vial (**Figure N**) and check for air bubbles in the syringe. If you see any bubbles, hold the syringe with the needle pointing up and gently tap the syringe gently until the bubbles rise. Then push the plunger in slowly until the bubbles disappear.

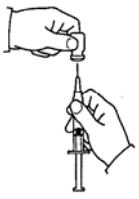

Figure N

Injecting the PegIntron™ Dose

Selecting the Site for Injection.

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™ solution into an area where the skin is irritated, red, bruised, infected or has scars, stretch marks, or lumps.

14. Clean the skin where the injection is to be given with an alcohol swab, and wait for the area to dry. Remove the protective cap from the needle. Make sure the safety sleeve of the syringe is pushed firmly against the syringe flange so that the needle is fully exposed (**Figure A**).

15. With one hand, pinch a 2-inch fold of loose skin. With your other hand, pick up the syringe and hold it like a pencil. Position the bevel of the needle facing up and insert the needle approximately ¼ inch into the pinched skin at approximately a 45- to 90-degree angle with a quick dart-like thrust. After the needle is in, remove the hand that you used to pinch your skin and use it to hold the syringe barrel. Pull the plunger of the syringe back very slightly. If blood comes into the syringe, the needle has entered a blood vessel. **Do not inject.** Withdraw the needle and discard the syringe as outlined in step 17. Repeat the above steps with a new vial to prepare a new syringe and inject the medicine at a new site. If no blood is present in the syringe, inject the medicine by gently pressing the plunger all the way down the syringe barrel.

16. Hold an alcohol swab near the needle and pull the needle straight out of the skin. Press the alcohol swab over the injection site for several seconds. Do not massage the injection site. If there is bleeding, cover it with a bandage.

17. After injecting your dose, firmly grasp the safety sleeve and pull it over the exposed needle until you hear a click, and the green stripe on the safety sleeve covers the red stripe on the needle (**Figure O**). Discard the syringe and needle in the Sharp's container supplied to you.

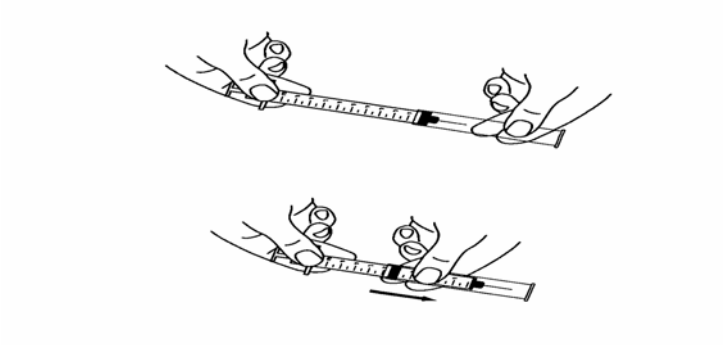

Figure O

18. 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 or nurse.

How do I dispose of the used syringes and needles?

Discard used safety lock syringes and needles in a Sharp's container or other puncture-proof container like a coffee can. DO NOT USE glass or clear plastic containers. Your health care provider or nurse will tell you how to dispose of a full container. Always keep the container out of reach of children.

Manufactured by: Schering Corporation, Kenilworth, NJ 07033 USA

DATE 12/06