MEDICATION GUIDE
REBETRON

Combination Therapy

containing

REBETOL (ribavirin, USP) Capsules

INTRON A (interferon alfa-2b, recombinant) Injection

REBETRON (REB-eh-tron) is the name for the combination of REBETOL (REB-eh-tole) and INTRON A (IN-tron aye). Read this medication guide carefully before you begin taking REBETRON Combination Therapy, and each time you refill your prescription in case there is new information. This summary does not tell you everything about REBETRON Combination Therapy. Your health care provider is the best source of information about these medicines. After reading this medication guide, talk with your health care provider if you have any questions about this treatment.

What is the most important information I should know about REBETRON Combination Therapy?

- **REBETRON Combination Therapy may cause birth defects and/or death of an unborn child. Therefore, if you are pregnant, you must not take REBETRON Combination Therapy.** If you could become pregnant, you must not become pregnant during therapy and for six months after you have stopped therapy. During this time you must use two forms of birth control, and you must have pregnancy tests that show that you are not pregnant.

  Female sexual partners of male patients being treated with REBETOL must not become pregnant during treatment and for six months after treatment has stopped. Therefore, two forms of birth control must be used during this time.

  If pregnancy occurs, report the pregnancy to your healthcare provider right away.

- **Treatment with REBETOL and INTRON A products can cause a dangerous drop in your blood cell counts**.
  REBETRON Combination Therapy can cause anemia, which is a decrease in the number of red blood cells. This can be dangerous, especially if you have heart or breathing problems. Tell your health care provider before taking REBETRON Combination Therapy if you have ever had any of these problems. Your health care provider should check your red blood cell count before starting therapy and often during the first 4 weeks of therapy. Your red blood cell count may be checked more often if you have heart or breathing problems.

- **REBETRON Combination Therapy** can cause a dangerous drop in the number of cells that help fight infections and stop bleeding, which might cause you to have an infection or abnormal bleeding.

- **Serious mental problems: REBETRON Combination Therapy may cause or worsen mood or behavioral problems.** These can include irritability (getting easily upset) and depression (feeling low, feeling bad about yourself). **Some patients, including some children, think about hurting or killing themselves or other people, and some have**

killed themselves (suicide) or hurt themselves or others. If you experience any of these thoughts or symptoms you should tell your health care provider right away. **See "What are the possible side effects of REBETRON Combination Therapy?" for important information on signs of mental problems.**

- **You should not take REBETOL Capsules alone to treat your hepatitis C virus infection**. REBETOL Capsules should be used only in combination with interferon alfa-2b (INTRON A) for the treatment of chronic hepatitis C infection; the combination is called REBETRON Combination Therapy.

What is REBETRON Combination Therapy?

REBETRON Combination Therapy is a treatment for some people who have chronic hepatitis C infection. It consists of two separate medicines, REBETOL Capsules (ribavirin) and INTRON A Injection (interferon), used in combination. INTRON A helps the body's immune system fight infections. "REBETOL" is the name given to the antiviral drug ribavirin made by Schering. It is not known how REBETOL and INTRON A work together to fight hepatitis C infection. REBETOL should not be used alone to treat chronic hepatitis C infection.

It is not known if treatment with REBETRON Combination Therapy will cure hepatitis C virus infections or prevent cirrhosis, liver failure, or liver cancer that can be caused by hepatitis C virus infections. It is not known if treatment with REBETRON Combination Therapy will prevent you from infecting another person with the hepatitis C virus.

You should use REBETRON Combination Therapy only if you have never been treated or your hepatitis C has returned after interferon therapy.

Who should not take REBETRON Combination Therapy?

Do not use these medicines if:

- You are a female and you are pregnant or plan to become pregnant at any time during your treatment with REBETRON Combination Therapy or during the 6 months after your treatment has ended.
- You 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 during treatment with REBETRON Combination Therapy or during the 6 months after your treatment has ended. **Please see "What is the most important information I should know about REBETRON Combination Therapy?" at the beginning of this Medication Guide.**
- You are breastfeeding. REBETOL and INTRON A products may pass through your milk and harm your baby. Talk with your health care provider about whether you should stop breast-feeding.
- You have autoimmune hepatitis (hepatitis caused by cells in your body attacking each other) because treatment with REBETOL and INTRON A can make this kind of liver problem worse.
- You are allergic to any of the ingredients in REBETOL Capsules or INTRON A Injection, or to any alpha interferon. (See ingredients listed at the end of this Medication Guide).

Tell your health care provider before starting REBETRON Combination Therapy if you have any of the following medical conditions or other serious medical problems:

- **mental health problems, such as depression or anxiety**. REBETRON Combination Therapy may make them worse. Tell your health care provider if you are being treated for a mental illness or had treatment in the past for any mental problems, including depression, suicidal behavior, or psychosis. Psychosis is loss of contact with reality, such as hearing voices or seeing things that are not there.
- **high blood pressure, other heart problems, or have had a heart attack**. The medicines in REBETRON Combination Therapy may worsen heart problems. Patients who have had certain heart problems should not take REBETRON Combination Therapy.
- **blood disorders**, including anemia (low red blood cell count), thalassemia (Mediterranean anemia), and sickle-cell anemia. REBETRON Combination Therapy can reduce the number of red blood cells you have. This may make you feel dizzy or weak and could worsen any heart problems you might have.
- **kidney problems**. If your kidneys do not work well, you may get worse side effects from REBETRON Combination Therapy and need a dose adjustment.
- **liver problems** (other than hepatitis C infection)
- **organ transplant**, and are taking medicine that keeps your body from rejecting your transplant (suppresses your immune system)
- **thyroid disease**. REBETRON Combination Therapy may make your thyroid disease worse or harder to treat. REBETRON Combination Therapy may be stopped if you develop thyroid abnormalities that cannot be controlled by medication.
- **lung problems.** REBETRON Combination Therapy can cause breathing problems or worsen breathing problems you already have.
- **alcoholism or drug abuse or addiction**
- **cancer**
- **infection with hepatitis B virus or human immunodeficiency virus (HIV),** the virus that causes AIDS.
- **diabetes.** REBETRON Combination Therapy may make your diabetes worse or harder to treat.
- **past interferon treatment for hepatitis C virus infection that did not work for you.**

How should I take REBETRON Combination Therapy?

- Your health care provider has determined the correct doses of REBETOL and INTRON A. Your doses of REBETOL and INTRON A may be lowered if you have side effects.
- **Under no circumstances should REBETOL capsules be opened, crushed or broken.**

The recommended dose of INTRON A Injection and REBETOL Capsules are shown in the table below.

If your weight is:	**Take this many REBETOL Capsules each day:**	**Inject this amount of INTRON A under your skin (subcutaneously)**
165 pounds or less	2 capsules in the AM 3 capsules in the PM	3 million international units 3times a week
More than 165 pounds	3 capsules in the AM 3 capsules in the PM	3 million international units 3times a week

Ask your health care provider about the right amount of INTRON A Injection and REBETOL Capsules needed to treat a child with hepatitis C. This amount will depend on a child's weight.

- You can take your REBETOL Capsules with or without food, but you should take it the same way every day.
- It is important to follow your dosing schedule and your health care provider's instructions on how to take your medicines.
- Take the medicines for as long as they are prescribed, and do not take more than the recommended doses.
- 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.
- If you miss a dose of INTRON A, take the missed dose as soon as possible during the same day or on the next day, and continue your regular dosing schedule. If several days go by without taking INTRON A, check with your health care provider about what to do. Do not double the next dose.
- 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.

Instructions on how to inject INTRON A are at the end of this Medication Guide.

What should I avoid while taking REBETRON Combination Therapy?

- **Pregnancy:** If you or your sexual partner becomes pregnant, tell your health care provider right away. (See "**What is the most important information I should know about therapy with Rebetron Combination Therapy**?" at the beginning of this Medication Guide.)

Talk with your health care provider about how to avoid pregnancy. If you or your sexual partner becomes pregnant while being treated with REBETRON Combination Therapy or during the 6 months after treatment ends, you must report the pregnancy to your health care provider right away. Your *health care provider* should call toll-free 1-800-727-7064. Your health care provider will be asked to give follow-up information about the pregnancy. Any information about your pregnancy that is reported about you will be confidential.

- Breastfeeding. The medicine may pass through your milk and harm the baby.
- Drinking alcohol, including beer, wine and liquor because this may make your liver disease worse.
- Do not inject yourself with Intron A if it is discolored or contains particles.
- Taking any medicines other than those prescribed or approved by your health care provider
- Ask your health care provider if there are other things you should avoid, in addition to alcohol (beer, wine, liquor), prescription and nonprescription drugs, and alternative medications (herbal medicine).

What are the possible side effects of REBETRON Combination Therapy?

Harm to unborn children. REBETRON Combination Therapy can harm your unborn child. It can cause birth defects and may kill your unborn child. (For more details, see

"**What is the most important information I should know about REBETRON Combination Therapy?**" at the beginning of this Medication Guide.)

- **Anemia**. REBETRON Combination Therapy causes anemia (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 counts.
- **Infections.** INTRON A therapy may lower your white blood cell count, making it easier for you to get serious infections. You must have your blood tested regularly during treatment to check for this problem.
- **Mental Problems**. Tell your health care provider if you have ever had any mental illness, including depression, suicidal behavior, or psychosis (loss of contact with reality such as hearing voices or seeing things that are not there). Also, tell your health care provider if you are taking any medications for these problems. **Tell your health care provider right away if you have the following:**

  - Start to feel unusually sad or have crying spells
  - **Lose interest in your usual activities**
  - **Have changes in your normal sleep patterns**
  - **Become more irritable than usual**
  - **Lose your appetite**
  - **Become unusually tired**
  - **Have trouble concentrating**
  - **Withdraw from family and friends**
  - **Have thoughts about hurting yourself or others.**

Tell your health care provider right away if you have any of the following symptoms. They may be signs of a serious side effect:

- trouble breathing, hives or swelling
- chest pain
- severe stomach or lower back pain
- bloody diarrhea or bloody stools (bowel movements). These may appear to be black and tarry.
- high fever
- bruising
- bleeding
- decreased vision

What are the most common side effects of REBETRON Combination Therapy?

- **"Flu-like" symptoms.** These include headache, feeling very tired (fatigue), muscle aches, and fever. These get better as treatment continues. You can reduce some of these flu-like symptoms by injecting your INTRON A about 2 hours before bedtime. Some health care providers suggest taking non-prescription pain and fever reducers, such as acetaminophen or ibuprofen before taking INTRON A. This may be helpful to prevent or relieve the fever and headache.
- **Feeling tired**
- **Hair thinning**
- **Rash and itching**
- **Nausea and appetite loss**

- **Abdominal pain with nausea and vomiting**
- **Trouble breathing**
- **Trouble with your vision**
- **Trouble sleeping at night**

This summary does not include all possible side effects of combination therapy. You should talk to your health care provider, if you do not feel well while taking REBETOL and INTRON A. Your health care provider can give you more information about managing your side effects.

What should I know about the hepatitis C virus?

Hepatitis C infection is a disease caused by a virus that infects the liver. This liver infection becomes a continuing (chronic) condition in most patients. Patients with chronic hepatitis C infection may develop cirrhosis, liver cancer, and liver failure. The virus is spread from one person to another by contact with the infected person's blood. You should talk to your health care provider about ways to prevent you from infecting others.

How do I Inject INTRON A?

- When you have been trained to do it properly. If you have any questions, contact your health care provider before injecting INTRON A.
- Use the sterile technique taught by your health care provider. Use disposable needles after each use, and throw them away properly as directed by your health care provider, nurse, or pharmacist.
- If someone else gives you your injection, that person should be trained in the use of sterile technique and how to avoid an accidental needle stick.

Preparing the INTRON A Dose

IMPORTANT: Before each use, the liquid in the vial (small bottle) should be clear, colorless to light yellow, and without particles. **Do not use the medicine if you see particles or the color is not correct.** Call your doctor, nurse, or pharmacist to find out what to do if this happens.

1. Check the date printed on the INTRON A carton to make sure that the expiration date has not passed.
2. Wash your hands well and remove the protective plastic cap from the top of the INTRON A vial.
3. Remove the protective plastic wrapper from the syringe provided (Figure A). The safety sleeve should be tight against the flange for use and moved over the needle only when ready for disposal, as instructed in step 6.

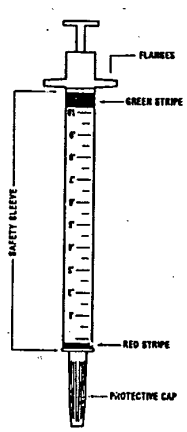


Figure A

4. Clean the rubber stopper on the top of the INTRON A vial with an alcohol swab.
5. Remove the protective cap from the syringe needle. Ensure safety sleeve is pushed firmly against the syringe flange so that the needle is fully exposed. Fill the syringe with air by pulling the plunger to the level that represents your correct dose. **(Figure B)**.

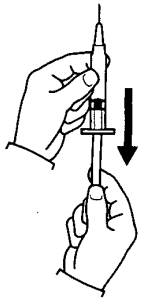


Figure B

6. Hold the INTRON A vial upright without touching the cleaned top of the vial with your hands **(Figure C).**

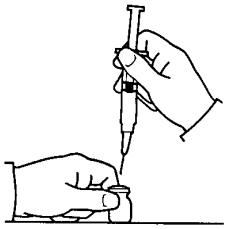


Figure C

7. Insert the needle into the vial containing the INTRON A solution and inject the air into the vial **(Figure D).**

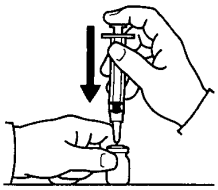


Figure D

8. Turn vial and syringe upside down in one hand. Be sure tip of needle is in the INTRON A solution. Your other hand will be free to move the plunger. Pull back on plunger slowly to draw the correct dose into syringe **(Figure E).**

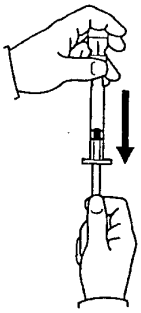


Figure E

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

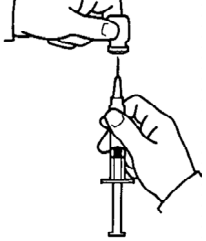


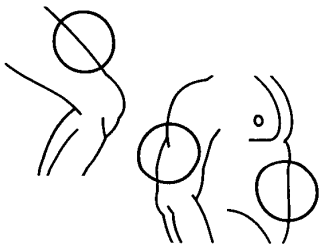
Figure F

10. Replace the needle cap. If the solution is cold, warm the syringe between your hands. Lay the syringe down on a flat surface so that needle does not touch anything.

Subcutaneous (under the skin) Injection

1. Select the site for injection

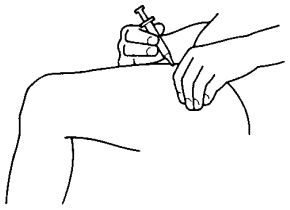
- The best sites for injection are tissues with a layer of fat between skin and muscle, such as the
    - thigh
    - outer surface of the upper arm
    - abdomen (stomach area), except the navel (belly button) or waistline
- If you are very thin, use only the thigh or outer surface of the arm for injection.
- Do not inject INTRON A solution in the same place repeatedly. Change your injection site in a regular pattern.



Use an alcohol swab to cleanse the skin where the injection is to be made. Wait for area to dry.

2. Remove the cap from the needle. Ensure the safety sleeve is pushed firmly against the syringe flange so that the needle is fully exposed. Hold the syringe with one hand, as you would hold a pencil. With the other hand, pinch approximately a 2-inch fold of loose skin.

3. With a quick dart-like motion, push the needle about 1/4 inch into the pinched skin at an angle of 45° to 90°.

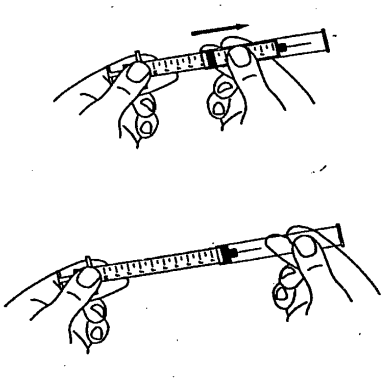


After the needle is in, remove hand used to pinch skin and use it to hold syringe barrel. Pull back the plunger very slightly with one hand. If blood comes into the syringe, the needle has entered a blood vessel. Do not inject. Withdraw and discard needle and syringe as instructed in step 6 below. Prepare a new syringe and inject at a new site. (Follow steps 2 and 3.)

4. If blood does not appear in the syringe, gently push the plunger all the way down.

5. 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 (rub) the injection site. If there is bleeding, cover the area with an adhesive bandage.

6. After use, firmly grasp the safety sleeve and pull over the exposed needle until you hear a click, and the green stripe on the safety sleeve covers the red stripe on the needle.



7. Use disposable syringe only once to ensure sterility of syringe and needle. Dispose of syringe and needle as directed.

   Your health care professional should tell you about the proper handling and disposal of all syringes and needles and the importance of not reusing any syringes or needles.

Your health care professional should give you a container for throwing away used needles and syringes. Throw away the full container according to directions provided by your doctor.

8. After 2 hours, check injection site for signs of inflammation, such as redness, swelling, or tenderness. If there are signs of inflammation, contact your doctor.

Instructional leaflet and video are available through your health care provider.

How do I store my medications?

STORAGE OF REBETOL CAPSULES

REBETOL capsules should be stored in the refrigerator between 36° and 46°F (2° and 8°C) or at room temperature 77°F (25°C).

STORAGE OF INTRON A INJECTION VIAL

INTRON A Injection vial should be stored in the refrigerator between 36° and 46°F (2° and 8°C), not in the freezer.

General advice about prescription medicines

Do not use REBETOL Capsules or INTRON A for conditions for which they were not prescribed. If you have any concern about REBETRON Combination Therapy, ask your health care provider. Your health care provider or pharmacist can give you information about REBETRON Combination Therapy that was written for health care professionals. Do not give these medicines to other people, even if they have the same condition you have.

Ingredients:

REBETOL capsules contain ribavirin and the inactive ingredients microcrystalline cellulose, lactose monohydrate, croscarmellose sodium, and magnesium stearate. The capsule shell consists of gelatin and titanium dioxide. The capsule is printed with edible blue pharmaceutical ink which is made of shellac, anhydrous ethyl alcohol, isopropyl alcohol, n-butyl alcohol, propylene glycol, ammonium hydroxide, and FD&C Blue #2 aluminum lake.
INTRON A contains interferon alfa-2b recombinant, sodium chloride, dibasic sodium phosphate, monobasic sodium phosphate, edetate disodium, polysorbate 80, m-cresol (as a preservative).

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

Manufactured by:

Schering Corporation
Kenilworth, NJ 07033 USA

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Rev. X/01 B-

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REBETOL (ribavirin, USP) Capsules

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  Female sexual partners of male patients being treated with REBETOL must not become pregnant during treatment and for six months after treatment has stopped. Therefore, two forms of birth control must be used during this time.

  If pregnancy occurs, report the pregnancy to your healthcare provider right away.

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(suicide) or hurt themselves or others. If you experience any of these thoughts or symptoms you should tell your health care provider right away. **See "<u>What are the possible side effects of REBETRON Combination Therapy?</u>" for important information on signs of mental problems.**

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Who should not take REBETRON Combination Therapy?

Do not use these medicines if:

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- **liver problems** (other than hepatitis C infection)
- **organ transplant**, and are taking medicine that keeps your body from rejecting your transplant (suppresses your immune system)
- **thyroid disease**. REBETRON Combination Therapy may make your thyroid disease worse or harder to treat. REBETRON Combination Therapy may be stopped if you develop thyroid abnormalities that cannot be controlled by medication.
- **lung problems.** REBETRON Combination Therapy can cause breathing problems or worsen breathing problems you already have.
- **alcoholism or drug abuse or addiction**
- **cancer**
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- You can take your REBETOL Capsules with or without food, but you should take it the same way every day.
- It is important to follow your dosing schedule and your health care provider's instructions on how to take your medicines.
- Take the medicines for as long as they are prescribed, and do not take more than the recommended doses.

- 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.
- If you miss a dose of INTRON A, take the missed dose as soon as possible during the same day or on the next day, and continue your regular dosing schedule. If several days go by without taking INTRON A, check with your health care provider about what to do. Do not double the next dose.
- 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.

Instructions on how to inject INTRON A are at the end of this Medication Guide.

What should I avoid while taking REBETRON Combination Therapy?

- **Pregnancy:** If you or your sexual partner becomes pregnant, tell your health care provider right away. (See "**What is the most important information I should know about therapy with Rebetron Combination Therapy**?" at the beginning of this Medication Guide.)

Talk with your health care provider about how to avoid pregnancy. If you or your sexual partner becomes pregnant while being treated with REBETRON Combination Therapy or during the 6 months after treatment ends, you must report the pregnancy to your health care provider right away. Your *health care provider* should call toll-free 1-800-727-7064. Your health care provider will be asked to give follow-up information about the pregnancy. Any information about your pregnancy that is reported about you will be confidential.

- Breastfeeding. The medicine may pass through your milk and harm the baby.
- Drinking alcohol, including beer, wine and liquor because this may make your liver disease worse.
- Do not inject yourself with Intron A if it is discolored or contains particles.
- Taking any medicines other than those prescribed or approved by your health care provider
- Ask your health care provider if there are other things you should avoid, in addition to alcohol (beer, wine, liquor), prescription and nonprescription drugs, and alternative medications (herbal medicine).

What are the possible side effects of REBETRON Combination Therapy?

Harm to unborn children. REBETRON Combination Therapy can harm your unborn child. It can cause birth defects and may kill your unborn child. (For more details, see "**What is the most important information I should know about REBETRON Combination Therapy?**" at the beginning of this Medication Guide.)

- **Anemia**. REBETRON Combination Therapy causes anemia (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 counts.
- **Infections.** INTRON A therapy may lower your white blood cell count, making it easier for you to get serious infections. You must have your blood tested regularly during

treatment to check for this problem.

- **Mental Problems**. Tell your health care provider if you have ever had any mental illness, including depression, suicidal behavior, or psychosis (loss of contact with reality such as hearing voices or seeing things that are not there). Also, tell your health care provider if you are taking any medications for these problems. **Tell your health care provider right away if you have the following:**

  - Start to feel unusually sad or have crying spells
  - **Lose interest in your usual activities**
  - **Have changes in your normal sleep patterns**
  - **Become more irritable than usual**
  - **Lose your appetite**
  - **Become unusually tired**
  - **Have trouble concentrating**
  - **Withdraw from family and friends**
  - **Have thoughts about hurting yourself or others.**

Tell your health care provider right away if you have any of the following symptoms. They may be signs of a serious side effect:

- trouble breathing, hives or swelling
- chest pain
- severe stomach or lower back pain
- bloody diarrhea or bloody stools (bowel movements). These may appear to be black and tarry.
- high fever
- bruising
- bleeding
- decreased vision

What are the most common side effects of REBETRON Combination Therapy?

- **"Flu-like" symptoms.** These include headache, feeling very tired (fatigue), muscle aches, and fever. These get better as treatment continues. You can reduce some of these flu-like symptoms by injecting your INTRON A about 2 hours before bedtime. Some health care providers suggest taking non-prescription pain and fever reducers, such as acetaminophen or ibuprofen before taking INTRON A. This may be helpful to prevent or relieve the fever and headache.
- **Feeling tired**
- **Hair thinning**
- **Rash and itching**
- **Nausea and appetite loss**
- **Abdominal pain with nausea and vomiting**
- **Trouble breathing**
- **Trouble with your vision**
- **Trouble sleeping at night**

This summary does not include all possible side effects of combination therapy. You should talk to your health care provider, if you do not feel well while taking REBETOL and

INTRON A. Your health care provider can give you more information about managing your side effects.

What should I know about the hepatitis C virus?

Hepatitis C infection is a disease caused by a virus that infects the liver. This liver infection becomes a continuing (chronic) condition in most patients. Patients with chronic hepatitis C infection may develop cirrhosis, liver cancer, and liver failure. The virus is spread from one person to another by contact with the infected person's blood. You should talk to your health care provider about ways to prevent you from infecting others.

How do I Inject INTRON A?

- When you have been trained to do it properly. If you have any questions, contact your health care provider before injecting INTRON A.
- Use the sterile technique taught by your health care provider. Use disposable needles after each use, and throw them away properly as directed by your health care provider, nurse, or pharmacist.
- If someone else gives you your injection, that person should be trained in the use of sterile technique and how to avoid an accidental needle stick.

The INTRON A Injection multidose pen (INTRON A multidose pen) is a pre-filled multidose syringe containing six doses of INTRON A (interferon alfa-2b, recombinant). This multidose pen is specially designed to deliver six doses of 3 MIU of INTRON A. If necessary, it can also be used to deliver different doses (i.e. if your health care provider wants you to increase or decrease your dose). The different doses that it can deliver are 1.5 MIU, 3 MIU, 4.5 MIU and 6 MIU. Six MIU is the maximum dose that this pen can give at one time.

Please note the following important points BEFORE using your INTRON A multidose pen:

- The INTRON A multidose pen should **ONLY** be used with the enclosed **Novofine*** needles. The use of other needles may result in the pen not working properly and/or the wrong dose of INTRON A solution delivered.

- **ALWAYS** discard needles and used pens carefully; **NEVER** discard the pen with a needle attached.

- Use the INTRON A multidose pen **ONLY** in accordance with these instructions. **DO NOT** allow the INTRON A multidose pen to be handled roughly or otherwise misused. To avoid possible transmission of disease, DO NOT share your multidose pen with anyone; it is for you and you alone.

- **KEEP** out of reach of children.
- When not in use you should **STORE** the INTRON A multidose pen in the **REFRIGERATOR at 36°-46°F (2° to 8°C)** (not too near the freezer compartment).

- **ALWAYS** check that INTRON A **IS CLEAR** in appearance prior to use. If it DOES NOT have a clear uniform appearance **DO NOT USE**. Please consult your health care provider or pharmacist.

- ***ALWAYS*** *check the expiration date;* ***NEVER*** *use after the expiration date.*

Description of your INTRON A multidose pen

Diagrams A and B show you all the different parts of the pen and the Novofine* needle. The most important parts to note are as follows:

- The **push button scale** tells you what dose has been set.

- The **color coding** strip and the **push button** are at the bottom of the pen as it is held cap up. (The six doses of 3 MIU multidose pen have a brown coding strip)

- The INTRON A multidose pen can only be fully capped when the **triangle** on the **cap scale** is aligned with the **dosage indicator** on the barrel.

INTRON A Pen

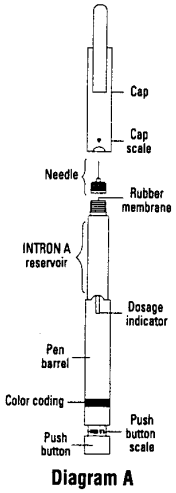

Diagram A

Novofine* Needle Assembly

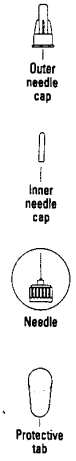

Diagram B

HOW TO USE YOUR INTRON A Multidose Pen

When you are ready to give your injection prepare your pen as follows. ***(NOTE: Boldface print indicates ACTION STEPS):***

1. **First check that you have the correct INTRON A multidose pen as prescribed by your health care provider**, (i.e. the six doses of 3 MIU INTRON A multidose pen which have a **brown** push button and a **brown** color coding strip).

2. **Pull off the cap of the pen and disinfect the rubber membrane** (see Diagram C) **with one alcohol wipe**.

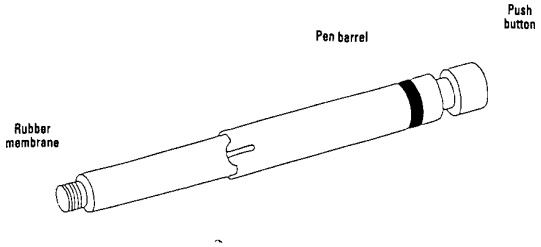

Diagram C

3. **Remove the protective tab from the Novofine* needle.** Note that the rear portion of the needle is revealed once the protective tab is removed (see Diagram D).

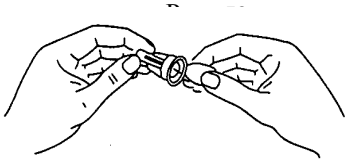

Diagram D

4. **Gently push the Novofine* needle onto the pen as shown in Diagram E**. (Notice that the rear portion of the needle described in Step 3 will pierce through the rubber membrane that you disinfected previously.) **Now screw the needle onto the INTRON A multidose pen securely by turning it in a clockwise direction** (see Diagram F).

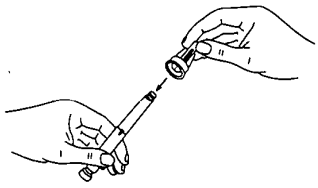

Diagram E

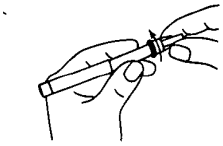

Diagram F

5. **First, pull off the outer needle cap** (Diagram G). **Then, pull off the inner needle cap carefully, bearing in mind that the needle will now be exposed** (Diagram H). Keep the outer needle cap for later use.

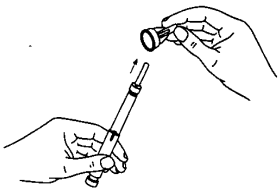

Diagram G

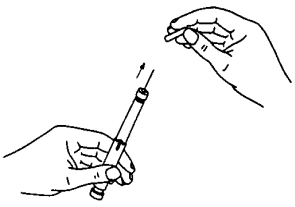

Diagram H

The pen is now ready to use. Since a small amount of air may collect in the needle and reservoir during storage, the next step is to remove any air bubbles.

6. **Hold the INTRON A multidose pen with the needle point upwards**.

7. **Tap the reservoir with your finger so that any air bubbles rise to the top of the reservoir, just below the needle** (Diagram I).

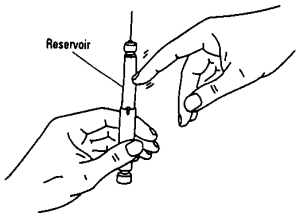

Diagram I

8. **Hold the pen by the barrel and turn the reservoir in the direction as indicated by the arrow in Diagram J (clockwise) until you feel it click.**

Diagram J

9. **Keeping the pen pointing upwards, press the push button up fully and see if a drop of INTRON A solution appears at the needle tip** (notice the drop at the tip of needle in Diagram K).

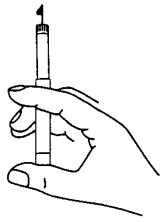

Diagram K

10. **If no drop appears then repeat Steps 7, 8, and 9 until a drop appears at the needle tip.** Note: Some air may still remain in the pen, but this is not important as you have removed the air from the needle and the dose will be accurate.

11. **Replace the INTRON A multidose pen cap with the 'triangle' opposite the dosage indicator as seen in Diagram L.**

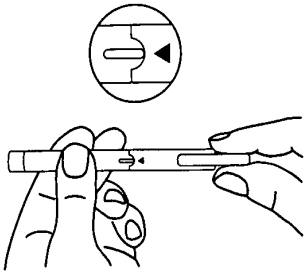

Diagram L

The pen is now ready to set the dose. For the next step hold the pen in the middle of the barrel. This will allow the push button to move freely, ensuring that the correct dose is set.

12. **To set the required dose, hold the pen horizontally by the barrel with one hand. With the other hand, turn the cap in a clockwise direction indicated by the arrow in Diagram M.** You will observe the push button rising, indicating the dose set. To set a 3 MIU dose, turn the cap 2 full turns (10 clicks) = 3.0 MIU.

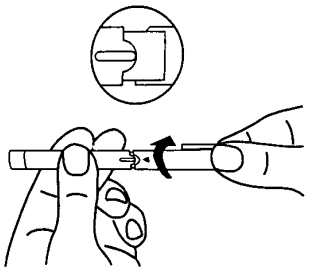

Diagram M

Note: If your health care provider has prescribed a dose other than 3 MIU, the correct dose can be set by turning the cap as many times as indicated as follows:

1 full turn (5 clicks) = 1.5 MIU
3 full turns (15 clicks) = 4.5 MIU
4 full turns (20 clicks) = 6.0 MIU

The push button scale will show you the dose set (see Diagram N). At that point check that you have the correct dose.

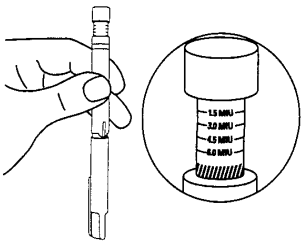

Diagram N

13. **After each complete turn make sure that the triangle is opposite the dosage**

indicator (see Diagram O). If you have set a wrong dose, simply turn the cap back (counter-clockwise) as far as you can until the push button is fully home and start again. Once the correct dose is set, you are ready to give the injection.

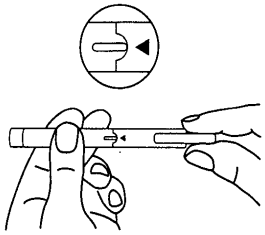

Diagram O

14. To give the injection, remove the pen cap from the needle. With one hand, pinch a 2-inch fold of loose skin.

15. With your other hand, pick up the pen and hold it as you would a pencil. Insert the needle into the pinched skin at an angle of approximately 45° (see Diagram P) **then press the push button down fully.**

If blood comes into the pen, do not inject. Withdraw the needle and consult your physician or pharmacist.

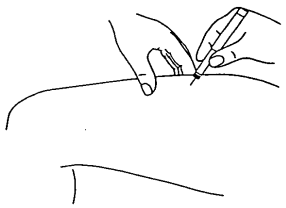

Diagram P

16. **Leave the needle in place for a few seconds, while holding down the push button, to allow the INTRON A Solution to distribute under the skin.**

17. **Slowly release the push button, then remove the needle.**

18. **Carefully replace the *outer* needle cap using a scooping motion** (See Diagram Q).

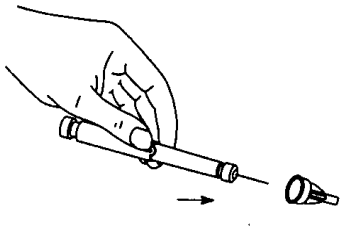

Diagram Q

19. **Completely unscrew the needle assembly using a counter-clockwise turning motion as show in Diagram R. Then carefully lift it off the pen and discard the capped needle** (see Diagram S).

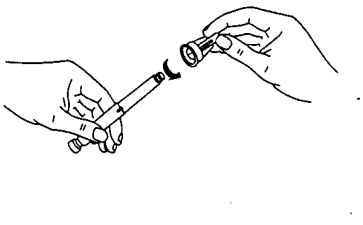

Diagram R

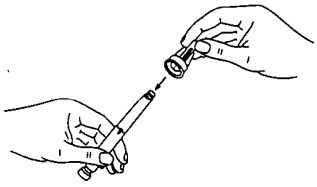

Diagram S

20. **Replace the pen cap with the triangle once again opposite the dosage indicator as shown in Diagram T.**

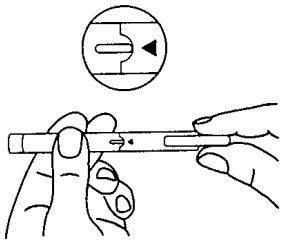

Diagram T

Instructional leaflet and video are available through your health care provider.

How do I store my medications?
STORAGE OF REBETOL CAPSULES
REBETOL capsules should be stored in the refrigerator between 36° and 46°F (2° and 8°C) or at room temperature 77°F (25°C).

STORAGE OF INTRON A INJECTION MULTIDOSE PEN
INTRON A Injection multidose pen should be stored in the refrigerator between 36° and 46°F (2° and 8°C), not in the freezer.

*** Novofine is a registered trademark of Novo Nordisk.**

General advice about prescription medicines
Do not use REBETOL Capsules or INTRON A for conditions for which they were not prescribed. If you have any concern about REBETRON Combination Therapy, ask your health care provider. Your health care provider or pharmacist can give you information about REBETRON Combination Therapy that was written for health care professionals. Do not give these medicines to other people, even if they have the same condition you have.

Ingredients:
REBETOL capsules contain ribavirin and the inactive ingredients microcrystalline cellulose, lactose monohydrate, croscarmellose sodium, and magnesium stearate. The capsule shell consists of gelatin and titanium dioxide. The capsule is printed with edible blue pharmaceutical ink which is made of shellac, anhydrous ethyl alcohol, isopropyl alcohol, n-butyl alcohol, propylene glycol, ammonium hydroxide, and FD&C Blue #2 aluminum lake. INTRON A contains interferon alfa-2b recombinant, sodium chloride, dibasic sodium phosphate, monobasic sodium phosphate, edetate disodium, polysorbate 80, m-cresol (as a preservative).

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

Manufactured by:

Schering Corporation
Kenilworth, NJ 07033 USA

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Rev. X/01 B-

F-XXXXXXXX

MEDICATION GUIDE

REBETOL (ribavirin, USP) Capsules

Read this medication guide carefully before you begin taking REBETOL [REB-eh-tol] Capsules, and each time you refill your prescription in case new information has been included. This summary does not tell you everything about REBETOL Capsules. Your health care provider is the best source of information about this medicine. After reading this medication guide, talk with your health care provider if you have any questions about REBETOL.

What is the most important information I should know about therapy with REBETOL Capsules?

- **REBETOL Capsules may cause birth defects or death of an unborn child. Therefore, if you are pregnant or your sexual partner is pregnant, do not take REBETOL.** If you could become pregnant, you must not become pregnant during therapy and for 6 months after you have stopped therapy. During this time you must use 2 forms of birth control, and you must have pregnancy tests that show that you are not pregnant.

  Female sexual partners of male patients being treated with REBETOL must not become pregnant during treatment and for 6months after treatment has stopped. Therefore, you must use 2 forms of birth control during this time.

  If pregnancy occurs, report the pregnancy to your health care provider right away. (See **"What should I avoid while taking REBETOL?")**

- **REBETOL Capsules can cause a dangerous drop in your red blood cell count**. REBETOL Capsules can cause anemia, which is a decrease in the number of red blood cells. This can be dangerous, especially if you have heart or breathing problems. Tell your health care provider before taking REBETOL if you have ever had any of these 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 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 (PEG-INTRON) for treating chronic hepatitis C infection. . REBETOL Capsules and INTRON A when used together are called REBETRON Combination Therapy. Your health care provider or pharmacist should give you a copy of the REBETRON Combination Therapy or PEG-INTRON Medication Guide. They have additional important information about combination therapy not covered in this guide.

What is REBETOL (ribavirin)?

"REBETOL" is the antiviral drug ribavirin. It is used in combination with interferon alfa-2b to treat some patients with chronic hepatitis C infection. It is not known how REBETOL and interferon alfa-2b work

together to fight hepatitis C infection.(**see the REBETRON Combination Therapy or PEG-INTRON Medication Guide).**

It is not known if treatment with REBETOL and interferon alfa-2b will cure hepatitis C virus infections or prevent cirrhosis, liver failure, or liver cancer that can be caused by hepatitis C virus infections. It is not known if treatment with REBETOL and interferon alfa-2b will prevent an infected person from infecting another person with the hepatitis C virus.

Who should not take REBETOL Capsules?

Do not use these medicines if:

- You are a female and you are pregnant or plan to become pregnant at any time during your treatment with REBETOL or during the 6 months after your treatment has ended.
- You 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. (See **"What is the most important information I should know about therapy with REBETOL Capsules?"** and "**What should I avoid while taking REBETOL Capsules?")**
- You are breast-feeding. REBETOL may pass through your milk and harm your baby. Talk with your provider about whether you should stop breast-feeding.
- You are allergic to any of the ingredients in REBETOL Capsules. See the ingredients listed at the end of this Medication Guide.

Tell your health care provider before starting treatment with REBETOL Capsules in combination with interferon alfa-2b if you have any of the following medical conditions:

- **mental health problems, such as depression or anxiety**. REBETOL/interferon alfa-2btherapy may make them worse. Tell your health care provider if you are being treated or had treatment in the past for any mental problems, including depression, suicidal behavior, or a feeling of loss of contact with reality, such as hearing voices or seeing things that are not there (psychosis). Tell your health care provider if you take any medicines for these problems.
- **high blood pressure, heart problems, or have had a heart attack.** REBETOL Capsules may worsen heart problems. Patients who have had certain heart problems should not take REBETOL Capsules.
- **blood disorders,** including anemia (low red blood cell count), thalassemia (Mediterranean anemia), and sickle-cell anemia. REBETOL Capsules can reduce the number of red blood cells you have. This may make you feel dizzy or weak and could worsen any heart problems you might have.
- **kidney problems.** If your kidneys do not work properly, you may experience worse side effects from REBETOL therapy and require a lower dose.
- **liver problems** (other than hepatitis C infection)
- **organ transplant**, and are taking medicine that keeps your body from rejecting your transplant (suppresses your immune system).
- **thyroid disease**. REBETOL/interferon alfa-2b therapy may make your thyroid disease worse or harder to treat. REBETOL/interferon alfa-2b therapy may be stopped if you develop thyroid problems that cannot be controlled by medicine.
- **lung problems.** REBETOL/interferon alfa-2b Therapy can cause breathing problems or worsen breathing problems you already have.
- **alcoholism or drug abuse or addiction**

- **cancer**
- **infection with hepatitis B virus and/or human immunodeficiency virus** (the virus that causes AIDS).
- **diabetes.** REBETOL/interferon alfa-2b therapy may make your diabetes worse or harder to treat.
- **past interferon treatment for hepatitis C virus infection that did not work for you.**

For more information see the Rebetron Combination Therapy or PEG-INTRON Medication Guides.

How should I take REBETOL Capsules?

Your health care provider has determined the correct dose of REBETOL Capsules based on your weight. Your health care provider may lower your dose of REBETOL if you have side effects.

The recommended dose of REBETOL Capsules when used with INTRON A is shown in the table below. You can take REBETOL Capsules with or without food, but you should take them the same way every day.

If your weight is:	**Take this many REBETOL Capsules each day:**
165 pounds or less	2 capsules in the AM 3 capsules in the PM
More than 165 pounds	3 capsules in the AM 3 capsules in the PM

The recommended dose of REBETOL Capsules when used in combination with PEG-INTRON is 800 mg per day. That is 400 mg (2 capsules) in the AM and 400 mg (2 capsules) in the PM. When taking REBETOL Capsules with PEG-INTRON, take your REBETOL Capsules with food.

-
- It is important to follow your dosing schedule and your health care provider's instructions on how to take your medicines.
- Take the medicine for as long as prescribed and do not take more than the recommended dose.
- 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.
- 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.
- Tell your provider before taking REBETOL Capsules if you have ever had any heart or breathing problems. Your provider should check your red blood cell count before starting therapy and often during the first 4 weeks of therapy. Your red blood cell count may be checked more frequently if you have had heart or breathing problems.
- Females taking REBETOL Capsules or female sexual partners of male patients taking REBETOL Capsules must have a pregnancy test before treatment begins, every month during treatment, and for 6 months after treatment ends to make sure there is no pregnancy.

What should I avoid while taking REBETOL Capsules?

Avoid the following during REBETOL Capsule treatment:

- **Pregnancy:** If you or your sexual partner gets pregnant during treatment with REBETOL Capsules or in the 6 months after treatment ends, tell your health care provider right away. (See "**What is the most important information I should know about therapy with REBETOL Capsules?**")

  Talk with your health care provider about how to avoid pregnancy. If you or your sexual partner gets pregnant while on REBETOL or during the 6 months after your treatment ends, you must report the pregnancy to your health care provider right away. Your health care provider should call Schering, the company that makes REBETOL at 1-800-727-7064. Your health care provider will be asked to give follow-up information about the pregnancy. Any information about your pregnancy that is reported about you will be 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 non-prescription medicines and herbal supplements.
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What are the most common side effects of REBETOL Capsules?

The most serious possible side effects of REBETOL Capsules are:

- **Harm to unborn children.** REBETOL Capsules 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?**")
- **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.

Tell your provider right away if you have any of the following symptoms. They may be signs of a serious side effect:

- **trouble breathing**
- **hives or swelling**
- **chest pain**
- **severe stomach or low back pain**
- **bloody diarrhea or bloody stools (bowel movements). These may appear black and tarry.**
- **bruising**
- **other bleeding**

The most common side effects of REBETOL Capsules are:

- **feeling tired**
- **nausea and appetite loss**
- **rash and itching**
- **cough**

This summary does not include all possible side effects of REBETOL therapy. Talk to your health care provider, if you do not feel well while taking REBETOL. Your health care

provider can give you more information about managing your side effects.

What should I know about hepatitis C infection?

Hepatitis C infection is a disease caused by a virus that infects the liver. This liver infection becomes a continuing (chronic) condition in most patients. Patients with chronic hepatitis C infection may develop cirrhosis, liver cancer, and liver failure. The virus is spread from one person to another by contact with the infected person's blood. You should talk to your health care provider about ways to prevent you from infecting others.

How do I store my REBETOL Capsules?

Store REBETOL Capsules at room temperature 77°F (25°C).

General advice about prescription medicines
Do not use REBETOL Capsules for conditions for which they were not prescribed. If you have any concern about REBETOL Capsules, ask your health care provider. Your health care provider or pharmacist can give you information about REBETOL Capsules that was written for health care professionals. Do not give this medicine to other people, even if they have the same condition you have.

Ingredients:
REBETOL Capsules contain ribavirin and the inactive ingredients microcrystalline cellulose, lactose monohydrate, croscarmellose sodium, and magnesium stearate. The capsule shell consists of gelatin and titanium dioxide. The capsule is printed with edible blue pharmaceutical ink which is made of shellac, anhydrous ethyl alcohol, isopropyl alcohol, n-butyl alcohol, propylene glycol, ammonium hydroxide, and FD&C Blue #2 aluminum lake.

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

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