An introduction to
Clinically Isolated Syndrome (CIS)

If you’re facing a diagnosis of clinically isolated syndrome (or early multiple sclerosis), you probably have questions and want to know as much as you can.

Your doctor is your primary resource for information, but this brochure can help you get the conversation started.

INDICATIONS

BETASERON® (interferon beta-1b) is a prescription medicine used to treat relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.

IMPORTANT SAFETY INFORMATION

Do not take BETASERON (interferon beta-1b) if you are allergic to interferon beta-1b, to another interferon beta, to human albumin, or mannitol.

Please see Important Safety Information throughout and Important Facts About BETASERON® on pages 14 and 15. For BETACONNECT™ Instructions for Use, please visit www.betaconnectifu.com, and for myBETAapp™ Instructions for Use, please visit www.mybetaappifu.com.
Understanding Clinically Isolated Syndrome

What is clinically isolated syndrome (CIS)?

CIS is a first episode of neurologic symptoms caused by inflammation in the central nervous system. The episode must last for at least 24 hours and is considered a relapsing form of multiple sclerosis (MS). In fact, CIS is often referred to as early MS.

Inflammation in the central nervous system happens when your body’s immune system mistakenly attacks and damages the protective coating around your nerves, which is called myelin. This damage prevents your nerves from sending signals to your brain, spinal cord, and other parts of your body the way they should.

How is CIS diagnosed?

To make a diagnosis of CIS, your doctor—most likely a neurologist—will perform a magnetic resonance imaging (MRI) scan to look for signs of inflammation and loss of myelin in the central nervous system.

Your doctor may also perform:

- A physical examination, including a neurologic examination
- A complete medical history with specific questions about your symptoms and how long you have had them
- Lab tests to rule out other possible causes of your symptoms

Occasionally, your doctor may perform a spinal tap to look at the fluid that surrounds your brain and spinal cord.

What happens during a CIS episode?

The location where the damage to the myelin occurs in the central nervous system will determine what symptoms you might experience during a CIS episode. Damage can be in the spinal cord, optic nerve, or brain.

When damage to the myelin occurs in the spinal cord, the onset of symptoms may be sudden, developing over 1 to 2 hours, or more gradual, happening over a week or more. Symptoms can include muscle weakness; abnormal sensations in the toes and feet; numbness or tingling in the arms, legs, or face; bladder and bowel problems; or Lhermitte's sign (an electric shock-like sensation when the neck is moved that is felt down the spine, and often into the arms and legs).

When damage to the myelin occurs in the optic nerve, the onset of symptoms may be sudden or develop over a few hours. Symptoms can include blurred vision or loss of sight, pain behind the eyeball, impaired color or blind spots surrounded by an area of normal vision, or other eye problems.

When damage to the myelin occurs in the brain, the symptoms may include nausea, vomiting, double vision, dizziness, hearing loss, or problems with balance or walking.

Abbreviations used in this brochure

CIS—clinically isolated syndrome
DMT—disease-modifying therapy
IV—intravenous
MRI—magnetic resonance imaging
MS—multiple sclerosis
RRMS—relapsing-remitting multiple sclerosis

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IMPORTANT SAFETY INFORMATION (continued)

BETASERON can cause serious side effects, including:

- Liver Problems Including Liver Failure: Symptoms of liver problems may include yellowing of your eyes, itchy skin, feeling very tired, flu-like symptoms, nausea or vomiting, bruising easily or bleeding problems. Your healthcare provider will do blood tests to check for these problems while you take BETASERON.

- Serious Allergic Reactions: Serious allergic reactions can happen quickly and may happen after your first dose of BETASERON or after you have taken BETASERON many times. Symptoms may include difficulty breathing or swallowing, swelling of the mouth or tongue, rash, itching, or skin bumps.
Understanding Clinically Isolated Syndrome

How is CIS treated?
In some cases, treatment with a high-dose oral or intravenous (IV) steroid is recommended to reduce symptoms caused by inflammation. Disease-modifying therapy (DMT) is recommended when CIS is considered more likely to progress. The goal of using DMT is to delay a second episode.

Is DMT effective at delaying another episode?
Many large clinical studies have been conducted to prove that early treatment with DMT can delay another episode. Based on the results of these studies, the FDA has approved several medicines to treat patients in the CIS stage.

Early treatment with DMT may lessen the chance of the disease progressing because of additional damage to nerve cells.

What is the difference between CIS and RRMS?
Patients who experience CIS may or may not progress to other forms of relapsing MS. Relapsing-remitting multiple sclerosis (RRMS) is the most common form of relapsing MS (85% of patients).

In both CIS and RRMS, damage to the myelin interferes with the way the nerves send signals, which causes similar neurologic symptoms. The main difference, however, is that a person with CIS has only experienced a first episode, while someone with RRMS has had more than one.

With CIS, MRI results may show damage in the area of the brain that is responsible for the current symptoms. In RRMS, the MRI scan may show multiple lesions (areas of damage) in different areas of the brain. When the MRI scan shows that another episode occurred in the past, the person may be diagnosed with RRMS.

Does CIS always progress?
Not all people who experience CIS will go on to develop RRMS. An MRI scan is one of the most important tools used to identify the risk of the disease progressing.

Studies have shown there is a high risk of developing RRMS when CIS is accompanied by brain lesions that are similar to those seen in other relapsing forms of MS. When this is the case, patients have a 60% to 80% chance of a second episode and diagnosis of RRMS within several years.

Where can I find more information?
Multiple Sclerosis Association of America
myMSAA.org

National Multiple Sclerosis Society
nationalMSsociety.org

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IMPORTANT SAFETY INFORMATION (continued)
• Depression or Suicidal Thoughts: Call your healthcare provider right away if you have any of the following symptoms, especially if they are new, worse or worry you: thoughts about suicide or dying, new or worse depression (sinking feeling or sadness), new or worse anxiety (feeling uneasy, nervous or fearful for no reason), trouble sleeping (insomnia), acting aggressive, being angry, or violent, acting on dangerous impulses, hallucinations, other unusual changes in behavior or mood.

Other possible serious side effects with BETASERON include:
• Heart Problems: BETASERON may worsen heart problems including congestive heart failure. Symptoms of heart problems may include swollen ankles, shortness of breath, decreased ability to exercise, fast heartbeat, tightness in chest, increased need to urinate at night, not being able to lay flat in bed.
About BETASERON® (interferon beta-1b)

What is BETASERON?

BETASERON is a prescription medicine used to treat relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.

BETASERON is similar to certain interferon proteins that are produced in the body and is given by injection under your skin (subcutaneous injection) every other day.

How can BETASERON help?

BETASERON has proven to be effective for patients who have clinically isolated syndrome.

In a 2-year study, 292 patients with clinically isolated syndrome* who started treatment early with BETASERON significantly reduced their likelihood of having a second flare-up compared with 176 patients on placebo.†

How can BETASERON® help? (continued)

MRA data from the same 2-year study showed that BETASERON patients with the first symptoms of MS had fewer newly active lesions at 2 years.

The exact relationship between MRI findings and the clinical status of patients is not known.

†Newly active lesions=nonenhancing new or enlarging T2 lesions; new Gd-enhancing lesions.

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IMPORTANT SAFETY INFORMATION (continued)

• Injection Site Problems: Serious skin reactions can happen in some people including areas of severe damage to skin and the tissue below the skin (necrosis). These reactions can happen anywhere you inject BETASERON. Symptoms of injection site problems may include swelling, redness, or pain at the injection site, fluid drainage from the injection site, breaks in your skin or blue-black skin discoloration. Change your injection site each time you inject BETASERON as it will lessen the chance of you having a serious skin reaction. Avoid injecting BETASERON into an area of the skin that is sore, reddened, infected or has other problems.

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Your BETASERON® (interferon beta-1b) Journey

When you become a BETASERON patient, you get all the benefits of the BETAPLUS® Patient Support Program. BETAPLUS provides you with personalized one-on-one support throughout your treatment.

1. Your BETAPLUS coverage specialist will determine if you qualify for $0 copay assistance
2. A BETA Nurse will schedule an appointment for your in-home injection training*
3. Your BETASERON and BETACONNECT™ autoinjector will be delivered to your home
4. You will receive your comprehensive injection training kit and in-home training from an MS-trained BETA Nurse. Your BETA Nurse will show you how to prepare your medication, inject BETASERON properly, and manage your injection site rotations. He or she will also provide you with tools to help you manage your therapy and help pair your BETACONNECT™ with myBETAapp™

After your one-on-one injection training, your BETA Nurse will stay in touch to:
- Guide you to the resources you need
- Answer questions about BETASERON
- Support and help you stay motivated—on the phone, in person, via webcam, or by email

And, when you share your injection data with myBETAapp, your BETA Nurse can follow your progress and provide you with proactive support.† He or she can help to:
- See if you have missed any injections
- Remind you to rotate injection sites properly
- Identify your typical injection patterns

*Where state laws and insurance allow.
†Healthcare professionals must have BETACONNECT Navigator access, and a patient must enable sharing in myBETAapp for HCPs to obtain this information.

Financial Support

A BETAPLUS® coverage specialist will help you understand your insurance benefits and navigate any issues. They can also help if you experience insurance changes. One-on-one support is always there when you need it.

$0 copay
Get up to $14,500 in copay assistance each calendar year, for as long as you’re on treatment.¹

BETA Bridge
At the start of your treatment, while your insurance benefits are being determined, BETA Bridge gets your therapy started right away. If you face an insurance gap, BETA Bridge can also keep your treatment going for up to 12 months at no cost.²

¹Some limitations apply. Please visit betaseron.com/affordability or call 1-800-788-1467 for more information.
²If you have commercial insurance, you’re eligible.

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IMPORTANT SAFETY INFORMATION (continued)

• Flu-like Symptoms: BETASERON can cause flu-like symptoms including fever, chills, tiredness, sweating, muscle aches when you first start to use it. These symptoms may decrease over time. Taking medicines for fever and pain relief on the days you are using BETASERON may help decrease these symptoms.
• Seizures: Some people have had seizures while taking BETASERON, including people who have never had seizures before. It is not known if the seizures were related to MS, to BETASERON, or to a combination of both. If you have a seizure after taking BETASERON call your healthcare provider right away.
Medication Meets Communication

Your doctor makes treatment decisions based on the best information available. Give them the most accurate information you can—automatically.* Share your injection data with your BETA Nurse and healthcare team every time you inject.* By providing an in-depth view of your injection information, you can have more meaningful discussions with your healthcare team.

Treat using the BETACONNECT™ autoinjector

Exclusively for BETASERON patients, the autoinjector provides:

- Automatic needle insertion and retraction (once the injection is complete), so you never need to see a needle during the injection process
- Built-in injection reminders, so you know when to take your next dose†
- Customizable injection speed and depth‡

†Use the built-in reminder only as a backup. You still must take BETASERON on schedule and follow the instructions from your healthcare provider, even if you use the built-in reminder.

‡Before you change your injection speed or depth settings, talk with your healthcare provider or BETA Nurse.

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Track with myBETAapp™

By keeping track of your injection information, you can go back and review important aspects of your treatment. With myBETAapp, you can see a snapshot of:

- Your injection calendar (view past and future injections)
- Injection sites (to help plan your rotation schedule)

And, when you use the Wellness Tracker in myBETAapp, you can track your everyday health by recording how you feel—whenever, wherever—by answering a few questions on your phone.

Share with your BETA Nurse and healthcare team§

Keep the communication going by sharing your injection information with myBETAapp. Your BETA Nurse can track your progress and help you when needed by:

- Seeing if you’ve missed any injections
- Reminding you to rotate your injection sites
- Identifying your typical injection patterns

If you share your information, your doctor also has the ability to follow your progress and provide you with support if needed.§

§Healthcare professionals must have BETACONNECT Navigator access, and a patient must enable sharing in myBETAapp for HCPs to obtain this information.

IMPORTANT SAFETY INFORMATION (continued)

- Blood Problems: You may have a drop in the levels of infection-fighting white blood cells, red blood cells, or cells that help you form blood clots. If drops in levels are severe, they can lessen your ability to fight infections, make you feel tired or sluggish or cause you to bruise or bleed easily.
- Pregnancy: Tell your doctor if you are pregnant or plan to become pregnant.
How is CIS diagnosed?
Your doctor will take a complete medical history and perform a physical examination and tests, including MRI.

If I have CIS will it definitely progress?
Patients who experience CIS may or may not progress to other forms of relapsing MS. An MRI scan is one of the most important tools used to identify the risk of disease progression.

Why should I begin treatment for CIS if I don’t know that it will progress?
Studies have shown there is a high risk of developing RRMS when CIS is accompanied by brain lesions that are similar to those seen in other relapsing forms of MS. Disease-modifying therapy is recommended in this situation, with the goal of delaying a second episode. Early treatment may lessen the chance of the disease progressing because of additional damage to nerve cells.

Where can I find more information?
To learn more, visit betaseron.com or ask your healthcare provider. You can also find information on the following websites: the Multiple Sclerosis Association of America (myMSAA.org) and the National Multiple Sclerosis Society (nationalMSsociety.org).

What type of symptoms can I track in myBETAapp™?
With the Wellness Tracker, the symptoms you can track include ability to walk, memory, coordination, bowel and bladder control, eating habits, and more.

If I share my injection data in myBETAapp, who will see it?
When you enable sharing, your BETA Nurse can see your information; however, you can also choose to share with your doctor.* If you do share your data with your BETA Nurse or doctor, your personal information will never be shared or sold.

*Healthcare professionals must have BETACONNECT Navigator access, and a patient must enable sharing in myBETAapp for HCPs to obtain this information.

Does BETASERON® require refrigeration?
No. BETASERON can be stored at room temperature.

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IMPORTANT SAFETY INFORMATION (continued)
Most Common Side Effects:
The most common side effects of BETASERON include low white blood cell count, increases in your liver enzymes, headache, increase in your muscle tension, pain, rash, problems sleeping, stomach pain, weakness. These are not all the possible side effects of BETASERON.

Tell your healthcare provider if you have any side effect that bothers you or that does not go away. Tell your healthcare provider about all the medicines you take and your medical conditions.

You are encouraged to report side effects or quality complaints of prescription drugs to the FDA by visiting www.fda.gov/medwatch or calling 1-800-FDA-1088.
Important Facts About BETASERON® (interferon beta-1b)

What is BETASERON?
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Who should not take BETASERON?
Do not take BETASERON if you are allergic to interferon beta-1b, to another interferon beta, to human albumin, or mannitol.

What Warnings and Precautions should I know about BETASERON?
BETASERON can cause serious side effects, including:
• liver problems including liver failure.
Symptoms of liver problems may include:
- yellowing of your eyes, itchy skin, feeling very tired, flu-like symptoms, nausea or vomiting, bruising easily or bleeding problems.
Your healthcare provider will do blood tests to check for these problems while you take BETASERON.
• serious allergic reactions. Serious allergic reactions can happen quickly and may happen after your first dose of BETASERON or after you have taken BETASERON many times. Symptoms may include:
  – difficulty breathing or swallowing
  – swelling of the mouth or tongue
  – rash, itching, or skin bumps
• depression or suicidal thoughts. Call your healthcare provider right away if you have any of the following symptoms, especially if they are new, worse, or worry you:
  – thoughts about suicide or dying
  – new or worse depression
  – new or worse anxiety
  – trouble sleeping (insomnia)
  – acting aggressive, being angry, or violent
  – acting on dangerous impulses
  – hallucinations
  – other unusual changes in behavior or mood
• heart problems. BETASERON may worsen heart problems including congestive heart failure. Symptoms of heart problems may include:
  – swollen ankles, shortness of breath, decreased ability to exercise, fast heartbeat, tightness in chest, increased need to urinate at night, not being able to lay flat in bed.
• injection site problems. Serious skin reactions can happen in some people including areas of severe damage to skin and the tissue below the skin (necrosis). These reactions can happen anywhere you inject BETASERON.

Tell your healthcare provider if you have any side effect that bothers you or does not go away.

Please see Important Safety Information throughout.

Symptoms of injection site problems may include:
  – swelling, redness, or pain at the injection site
  – fluid drainage from the injection site
  – breaks in your skin or blue-black skin discoloration
It is important for you to change your injection site each time you inject BETASERON. This will lessen the chance of you having a serious skin reaction at the site where you inject BETASERON.
Avoid injecting BETASERON into an area of skin that is sore, reddened, infected or has other problems.
• flu-like symptoms. BETASERON can cause flu-like symptoms including:
  – fever, chills, tiredness, sweating, muscle aches when you first start to use it.
These symptoms may decrease over time. Taking medicines for fever and pain relief on the days you are using BETASERON may help decrease these symptoms.
• seizures. Some people have had seizures while taking BETASERON, including people who have never had seizures before. It is not known if the seizures were related to their MS, to BETASERON, or to a combination of both. If you have a seizure after taking BETASERON call your healthcare provider right away.

What should I know before starting BETASERON?
Before you take BETASERON, tell your healthcare provider if you:
• have or have had depression (sinking feeling or sadness), anxiety (feeling uneasy, nervous, or fearful for no reason) or trouble sleeping
• have or have had liver problems
• have or have had blood problems such as bleeding or bruising easily, low red blood cells (anemia) or low white blood cells
• have or have had heart problems
• are pregnant or plan to become pregnant
• are breastfeeding or plan to breastfeed. It is not known if BETASERON passes into your breast milk.
Tell your healthcare provider about all the medicines you take, including prescription and nonprescription medicines, vitamins, and herbal supplements. Know the medicines you take. Keep a list of them to show your healthcare provider and pharmacist when you get a new medicine.

What are the possible side effects of BETASERON?
The most common side effects of BETASERON include:
• low white blood cell count, increases in your liver enzymes, headache, increases in your muscle tension, pain, rash, problems sleeping, stomach pain, and weakness.

These are not all the possible side effects of BETASERON. For more information, ask your healthcare provider or pharmacist.
Tell your healthcare provider if you have any side effect that bothers you or does not go away.
For important risk and use information about BETASERON, please see the enclosed Full Prescribing Information.
The risk information provided here is not comprehensive. To learn more about BETASERON, talk with your healthcare provider or pharmacist. Visit www.betaseron.com to obtain the FDA-approved product labeling or call 1-888-842-2937.
You are encouraged to report side effects or quality complaints of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.
Committed to Supporting Patients, Every Step of the Way

BETASERON®, an effective therapy

24/7 BETA Nurse support

Innovative financial support

BETACONNECT™, a fully electronic autoinjector

myBETAapp™, for on-the-go tracking

Models used for illustrative purposes only.

To learn more about CIS or RRMS and treatment with BETASERON, visit betaseron.com/efficacy and talk with your healthcare provider today.

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