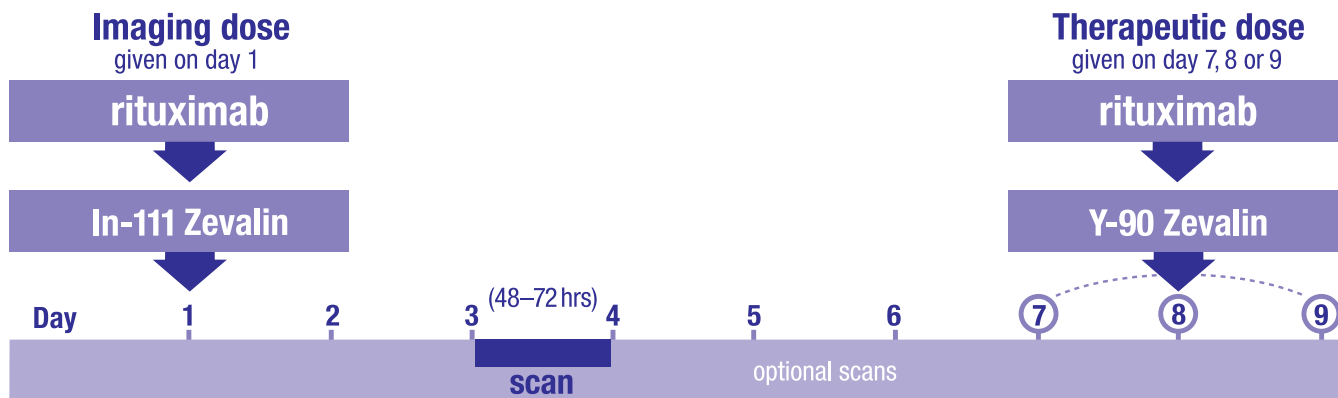


Patient Name: \_\_\_\_\_

Patient ID: \_\_\_\_\_

Primary Oncologist: \_\_\_\_\_

## The Zevalin<sup>®</sup> (Ibritumomab Tiuxetan) therapeutic regimen treatment timeline



*You should not be given Y-90 Zevalin if a scan performed after you receive In-111 Zevalin shows an altered pattern of distribution in your body.*

### Appointment Schedule

	Date	Time	Location	Physician	Phone
<b>Rituximab Infusion</b>	_____	_____	_____	_____	_____
<b>In-111 Zevalin Injection</b>	_____	_____	_____	_____	_____
<b>Required Scan</b>	_____	_____	_____	_____	_____
<b>Optional Scans</b>	_____	_____	_____	_____	_____
<b>Rituximab Infusion</b>	_____	_____	_____	_____	_____
<b>Y-90 Zevalin Injection</b>	_____	_____	_____	_____	_____

#### Questions?

If you have any questions about the Zevalin therapeutic regimen or rituximab, be sure to ask your doctor or nurse.

To be completed by a healthcare professional

**Patient information:** Date \_\_\_\_\_ Weight \_\_\_\_\_ kg Platelet count \_\_\_\_\_

**Special instructions/Follow-up:** \_\_\_\_\_



# Zevalin® Therapeutic Regimen Information

## General information

- The Zevalin therapeutic regimen is indicated for the treatment of patients with relapsed or refractory low-grade or follicular B-cell non-Hodgkin's lymphoma (NHL), including patients with rituximab refractory follicular NHL.
- The Zevalin therapeutic regimen has been given accelerated approval for the treatment of relapsed or refractory, rituximab-naïve, low-grade and follicular NHL based on studies that have shown durable objective overall response rates, a surrogate endpoint for progression-free survival. Studies to determine whether the Zevalin therapeutic regimen confers an effect on progression-free survival are ongoing.
- The Zevalin therapeutic regimen consists of 3 components: rituximab, Indium-111 (In-111) Zevalin, and Yttrium-90 (Y-90) Zevalin.
- The entire Zevalin therapeutic regimen is given over a period of 7 to 9 days.
- Your doctor will provide you with a separate patient brochure explaining the rituximab portion of your treatment.

## Warnings

- Rituximab, a key part of the Zevalin therapeutic regimen, is known to cause a severe allergic reaction in some patients. It is called an infusion reaction and it does not happen often. When it does occur, it usually happens during the first rituximab infusion. Some patients who have had this severe infusion reaction have died within 24 hours of receiving rituximab. Symptoms of this reaction include low blood oxygen levels, fluid in the lungs, great difficulty in breathing, changes in heart beat, heart attack, and a condition where the heart is unable to pump enough blood to meet the needs of the body.
- Approximately 80% of fatal infusion reactions occurred in association with the first rituximab infusion. Patients who develop symptoms of this severe type of infusion reaction should have their rituximab or Zevalin infusions stopped and receive medical treatment.
- Treatment with Y-90 Zevalin can result in very low blood cell counts for a prolonged period of time. The Zevalin therapeutic regimen should not be given to patients with 25% or more of their bone marrow cells affected by lymphoma and/or patients whose bone marrow may have difficulty recovering from therapy.
- Some patients who have received the Zevalin therapeutic regimen have had a serious type of skin reaction, with blistering of the skin and the inside of the nose and mouth (mucous membranes) and some of these patients have died from this reaction. Patients who develop this type of severe reaction should not receive treatment with any more components of the Zevalin therapeutic regimen and should seek medical treatment immediately.
- It is very important to tell your doctor if you are pregnant or nursing. Y-90 Zevalin may cause harm to the unborn baby if given to a pregnant woman. Also, it is expected that if Zevalin can pass into breast milk, women with children that are breast fed should stop nursing with breast milk and switch to formula feeding.
- The following guidelines are to ensure safe administration of the Zevalin therapeutic regimen:
  - The dose of Y-90 Zevalin that you receive should not exceed the maximum allowable dose of 32 mCi (1184 MBq) (mCi and MBq are measurements of radiation).
  - You should not be given Y-90 Zevalin if a scan performed after you receive In-111 Zevalin shows an altered pattern of distribution in your body.
- Because In-111 Zevalin and Y-90 Zevalin contain radioisotopes, they are radiopharmaceuticals and should only be used by physicians and other professionals qualified by training and experienced in the safe use and handling of radionuclides.

## Important safety information

- Following treatment with the Zevalin therapeutic regimen, most patients experience a period of low blood cell counts. In some patients, low blood cell counts may be prolonged and severe. Low white blood cell counts can decrease the ability to fight infections. Low red blood cell counts can cause fatigue. Low platelet counts can cause difficulty in forming blood clots, leading to increased bruising or bleeding. Low blood

cell counts can occur up to 7 to 9 weeks following completion of the Zevalin therapeutic regimen. Counts may remain low for 22 to 35 days. Most patients recover, however, in less than 5% of cases patients experienced low blood cell counts which lasted beyond the expected recovery period.

- Very low blood cell counts may lead to serious or life-threatening complications such as severe infections. In studies with the Zevalin therapeutic regimen, 29% of patients developed infections during the first three months after treatment. In a small number of patients (5%), serious or life-threatening infections have occurred such as fever, sepsis (blood infection), cellulitis (skin infection), colitis (intestinal infection), osteomyelitis (bone infection), urinary tract infection, pneumonia, diarrhea, and upper respiratory tract infection.
- Serious bleeding has also occurred, and a small number of patients have died from severe bleeding inside the head.
- Some patients have needed transfusions or have been given medications to help their blood cell counts recover faster. Your doctor may provide you with special instructions if your blood cell counts become very low.
- Some patients who have received the Zevalin therapeutic regimen have experienced a very serious reaction with blistering of the skin and mucous membranes. Some patients have died from this severe reaction. The time frame for developing this type of severe reaction has varied. In some patients it occurred within days, in other patients it occurred 3 to 4 months following treatment with the Zevalin therapeutic regimen. Patients who develop this type of severe reaction should contact their doctor immediately and should not receive further treatment with any component of the Zevalin therapeutic regimen.
- In the month following treatment with the Zevalin therapeutic regimen, some patients have also developed radiation injuries and related problems in tissues that contain or are close by areas of lymphoma involvement.
- Following treatment with the Zevalin therapeutic regimen, development of a second type of cancer involving blood cells has occurred, with a total of 19 cases reported among 746 patients (2.6%). This second cancer occurred on average 1.9 years after patients received the Zevalin therapeutic regimen. The number of cases with this second type of cancer continues to increase.
- Zevalin contains albumin that has been obtained from human blood. Because of effective blood donor screening and the Zevalin manufacturing process, the risk of transmitting a viral disease is extremely remote. A risk of transmission of Creutzfeldt-Jakob Disease (CJD) is also considered extremely remote. No cases of transmission of viral diseases or CJD have ever been identified for albumin.

Ask your physician for the rituximab patient brochure or package insert for important information on rituximab.

## Common side effects of the Zevalin therapeutic regimen

- The most common side effects from treatment with the Zevalin therapeutic regimen are low white blood cell counts (neutropenia), low platelet counts (thrombocytopenia), low red blood cell counts (anemia), abdominal symptoms (nausea, vomiting, abdominal pain, and diarrhea), increased cough, difficulty breathing, dizziness, joint pain, loss of appetite, nervousness, and bruising.

## For your treatment with the Zevalin therapeutic regimen

- In general, no special preparations are needed.
- Let your doctor or nurse know if you take blood thinners or other medications that interfere with blood clotting.
- You do not need to change your diet or regular activities.
- You may wear your regular clothes to receive your treatments.
- Your doctor or nurse may have specific suggestions or recommendations for you to follow.

## During your treatment with the Zevalin therapeutic regimen

- On Treatment Day 1, you will receive an intravenous infusion of rituximab; this may take several hours. Within 4 hours of receiving the rituximab infusion, an injection of In-111 Zevalin is given at a nuclear medicine or radiation oncology department. This injection will take about

10 minutes and is administered through a free flowing intravenous line (IV).

- A required gamma camera imaging study is taken 48 to 72 hours after the injection of In-111 Zevalin. If your doctors have any questions about what the imaging study shows, additional scans may be done at other timepoints. If your doctors see that your body's distribution pattern of In-111 Zevalin is different from what is expected, you may not be given Y-90 Zevalin.
- On Treatment Day 7, 8, or 9, a second rituximab infusion is given; again, this may take several hours. Within 4 hours of receiving the rituximab infusion, an injection of Y-90 Zevalin is given at a nuclear medicine or radiation oncology department. This injection will take about 10 minutes and is administered through a free flowing intravenous line (IV).
- In some patients, treatment with the Zevalin therapeutic regimen may cause a severe allergic reaction called an infusion reaction. Some patients have died from this severe reaction. When it occurs, it usually happens with the first dose of rituximab. Signs and symptoms of this severe reaction may include low blood pressure, fluid retention, low blood oxygen levels, or difficulty breathing. Such symptoms may require stopping the rituximab infusion or Zevalin injection. The most severe forms of this infusion reaction have resulted in fluid in the lungs, severe difficulty in breathing, itching, changes in heart beat, heart attack, and a condition where the heart is unable to pump enough blood to meet the needs of the body.
- Other side effects that may occur during treatment with the Zevalin therapeutic regimen include weakness (43%), nausea (31%), infection (29%), chills (24%), fever (17%), abdominal pain (16%), general pain (13%), shortness of breath (14%), headache (12%), vomiting (12%), sore throat (10%), cough (10%), and dizziness (10%).
- During the Zevalin injection, should some of the medicine leak in or around the skin at the infusion site, the area may become red and tender and an open wound may develop.
- If you experience any of these side effects, tell a healthcare professional immediately.

## After your treatment with the Zevalin therapeutic regimen

- Typically, there is no need to stay in the hospital.
- There is no need to avoid contact with family, friends, or coworkers.
- The amount of radiation you receive with In-111 Zevalin is very small, and no special precautions are needed following this procedure.
- The effects of Y-90 Zevalin stay mainly within your body and bodily fluids such as urine, saliva, blood, and stool. Observe the following guidelines for 7 days after receiving Y-90 Zevalin. These will minimize potential radiation exposure to other people.
- Wash your hands after using the bathroom.
- Use a condom during sexual intercourse to avoid transfer of bodily fluids.
- Avoid deep kissing.
- Throughout therapy and for up to 12 months following treatment, effective contraception is recommended.

## You should notify your doctor immediately if:

- You develop shortness of breath or difficulty breathing.
- You develop a fever above \_\_\_\_\_°F.
- You develop signs of infection such as sore throat, cough, chills, redness, inflammation, or pain when urinating.
- You develop a rash or soreness in your joints.
- You develop bleeding or bruising.

For additional details regarding the Zevalin therapeutic regimen, please refer to the full prescribing information, including **Boxed Warnings for Zevalin and Rituxan and A Resource Guide for Patients and Their Families**. Both are available through your healthcare provider or for download at [www.Zevalin.com](http://www.Zevalin.com)

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit [www.fda.gov/medwatch](http://www.fda.gov/medwatch), or call 1-800-FDA-1088.