Follicular Lymphoma

A TREATMENT GUIDE
FOR PATIENTS AND THEIR FAMILIES

WHERE INFORMATION EQUALS HOPE

CONTENT REVIEWED BY A DISTINGUISHED MEDICAL ADVISORY BOARD
ZYDELIG® AccessConnect™: your partner in therapy.

Now that your doctor has prescribed ZYDELIG for you, we want to help you access, afford and adhere to your therapy. And that’s precisely what ZYDELIG AccessConnect was designed to do. This support program can help:

- Evaluate your insurance coverage options for ZYDELIG
- Match the right financial assistance to your situation
- Ensure you receive ZYDELIG in a timely manner
- You adhere to ZYDELIG, as prescribed, through useful tips provided by a Patient Support nurse

You can register for this important program at your doctor’s office, or by visiting the AccessConnect website, at www.zydeligaccessconnect.com.

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FOLLICULAR LYMPHOMA SURVIVOR

“...We couldn’t have asked for better care. I had fantastic doctors.”
– Faye Janes
Stage I Follicular Lymphoma survivor

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STAGING
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• Evaluate your insurance coverage options for ZYDELIG
• You adhere to ZYDELIG, as prescribed, through useful tips provided by a Patient Support nurse
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Cancers fall into two general categories: solid cancers and hematologic (blood) cancers. When most people think of cancer, they think of solid cancer, which involves a tumor that grows and sometimes spreads to other places in the body. In contrast, blood cancers affect blood, bone marrow and lymph nodes and may not create an actual tumor.

Lymphoma is a type of blood cancer that arises in the lymphatic system, which is part of the immune system. It is the most common blood cancer in the United States, accounting for approximately five percent of all cancer diagnoses. It is estimated that nearly 81,000 people will be diagnosed with lymphoma in 2015.

Lymphoma develops when normal lymphocytes (a type of white blood cell) transform into abnormal cancer cells that reproduce uncontrollably. As these cancer cells multiply, they collect in the lymph nodes, bone marrow, spleen, tonsils, adenoids or thymus, where they can form tumors. These cells eventually begin to outnumber normal cells, causing an enlargement of the lymph nodes, spleen or other organs.

### ABOUT THE LYMPHATIC SYSTEM

To fully understand lymphoma, it's important to first gain a general understanding of the lymphatic system. The lymphatic system is a network of tissues and vessels that carry fluid, called lymph, throughout the body. Lymph contains lymphocytes that attack infectious agents.

The two main types of lymphocytes that can develop into lymphomas are B lymphocytes (B cells) and T lymphocytes (T cells).
- **B cells** produce protein antibodies that attach to infectious organisms, such as bacteria and viruses, marking them for destruction.
- **T cells** attack infectious organisms directly and play a part in controlling the immune system.

Both B cells and T cells can transform into lymphoma cells. However, in the United States, B cell lymphomas are much more common.

### TYPES OF LYMPHOMA

Lymphoma represents more than 60 different cancer subtypes that involve lymphocytes, and it can occur in adults and children of any age. The two main types of lymphoma are Hodgkin lymphoma and non-Hodgkin lymphoma.

**Hodgkin lymphoma**

With an estimated 9,000 new cases of Hodgkin lymphoma in the United States in 2015, it is not as common as non-Hodgkin lymphoma.

Hodgkin lymphoma is characterized by the presence of abnormal B cells (called Reed-Sternberg [R-S] cells), although other abnormal cell types may be present. Hodgkin lymphoma usually starts in the lymph nodes and often spreads from one lymph node to another. It can also spread to other organs.

**Non-Hodgkin lymphoma**

Non-Hodgkin lymphoma (NHL) is the most common cancer of the lymphatic system. Approximately 71,850 new cases of NHL are diagnosed annually in the United States.

NHL is not a single disease but rather a group of several closely related cancers. The World Health Organization estimates that there are more than 60 types of NHL, some of which are more common than others. Although the various types of NHL share some common features, they differ in their microscopic appearance, molecular features, growth patterns, impact on the body and treatment options.

NHLs are broadly divided into two major groups: B cell lymphomas and T cell lymphomas. B cell lymphomas develop from abnormal B lymphocytes and account for 85 percent of all NHLs, and T cell lymphomas develop from abnormal T lymphocytes and account for the remaining 15 percent of all NHLs. NHLs may also be classified as indolent (slow-growing) or aggressive (fast-growing).

**Follicular lymphoma**

Follicular lymphoma is the second most common form of low-grade NHL and the second most common type of lymphoma overall diagnosed in the United States. Approximately 25 to 30 percent of people with NHL in the United States have this type. Most follicular lymphoma diagnoses occur in adults over the age of 60, with equal rates of occurrence in male and female individuals; this specific lymphoma is rare in young people.

Follicular lymphoma affects B cell lymphocytes and is indolent, which means it grows very slowly. Like most lymphomas, follicular lymphoma usually begins in the lymph nodes. The cells can spread into the blood and bone marrow. Other internal organs, including the liver and spleen, may also be affected.

Because follicular lymphoma grows so slowly, doctors may decide not to treat it right away and instead adopt a “watchful waiting” approach. Several treatment options are avail-
able, though. (Learn more about treatment options on page 12.) Over time, some follicular lymphomas transform into an aggressive (fast-growing) diffuse B cell type of lymphoma, so it’s important for people with follicular lymphoma to be monitored closely.

RISK FACTORS FOR FOLLICULAR LYMPHOMA
Although the exact cause of follicular lymphoma is unknown, mutations in DNA (the hereditary genetic material found in cells) lead to the development of the disease. What triggers these mutations is also largely unknown, but research suggests that certain risk factors may play a role in the development of all NHLs:

- **Age** – The risk of NHL increases with age, with most cases occurring in people 60 years or older.
- **Autoimmune disorders** – Certain autoimmune disorders and some drugs used to treat them increase the risk of NHL.
- **Body weight** – Some studies show that the risk of NHL is greater for people who are overweight or who consume a high-fat diet.
- **Chemical exposure** – Long-term exposure to chemicals such as pesticides and fertilizers may increase the risk of NHL.
- **Chronic infections** – People who experience chronic infections have an increased risk of NHL, likely because their immune systems are constantly producing new lymphocytes to fight the infection.
- **Family history** – The children and siblings of people with NHL are at an increased risk for developing the disease.
- **Immune deficiency disorders** – People with certain immune deficiency disorders have a greater chance of developing NHL.

- **Organ transplantation** – Recipients of organ transplants often have a higher risk of developing NHL because they must take drugs to lower their immune system function.
- **Previous cancer treatment** – People who have previously been treated for cancer may be at an increased risk for the development of NHL.
- **Race** – In the United States, NHL is more likely to occur in white individuals than in African and Asian Americans.
- **Radiation exposure** – People who have been exposed to radiation have an increased risk of NHL.

SYMPTOMS OF FOLLICULAR LYMPHOMA
Some people with NHL do not experience any symptoms. When symptoms do occur, they generally include swelling or enlargement of the lymph nodes (which is often but not always painless), fatigue, fever, night sweats, unexplained weight loss, easy bruising or bleeding and frequent infections.

Other symptoms, such as abdominal pain, chest pain and difficulty breathing, may also be present, depending on the area of the body in which the lymphocytes collect.

TAKE CONTROL
If you have follicular lymphoma, you can help yourself feel more in control by learning as much as you can about the specific characteristics of your disease, your treatment options and ways you can help make yourself healthier, both physically and emotionally. Numerous survivors have credited a balance of regular exercise and plenty of rest to feeling better during and after follicular lymphoma treatment. Healthy eating habits also help, as they can help people achieve — and maintain — a healthy weight. Spending time with family and friends, getting involved in support groups and/or participating in religion or spirituality are also credited by survivors as helping them thrive during treatment for follicular lymphoma.

**BY THE NUMBERS**
**DIAGNOSING LYMPHOMA**
Breakdown of estimated lymphoma diagnoses per year in the United States

<table>
<thead>
<tr>
<th>Total Lymphoma Diagnoses</th>
<th>Lymphoma Diagnoses</th>
<th>Non-Hodgkin Lymphoma Diagnoses</th>
</tr>
</thead>
<tbody>
<tr>
<td>81,000</td>
<td>12%</td>
<td>25-30%</td>
</tr>
<tr>
<td>88% non-Hodgkin lymphoma</td>
<td>12%</td>
<td>25-30%</td>
</tr>
<tr>
<td>88% non-Hodgkin lymphoma</td>
<td>12%</td>
<td>25-30%</td>
</tr>
</tbody>
</table>
Several tests are available to help your doctors learn more about your follicular lymphoma. These tests provide details that help your doctors make a specific diagnosis and assign a stage to the cancer. (See page 6 for staging information.) An accurate diagnosis and stage are essential for determining the best treatment options, which may spare you from treatment that is unlikely to be effective.

**BIOPSY PROCEDURES**

A biopsy is the only way to accurately diagnose follicular lymphoma. The type of biopsy your doctor chooses to perform is based on your specific situation.

- **Excisional or incisional biopsy** – These are the most common types of biopsy if follicular lymphoma is suspected. The doctor removes either an entire lymph node through a cut in the skin (excisional biopsy) or a small section of a suspected tumor (incisional biopsy). For both types, local or general anesthesia is used as necessary.

- **Fine- or core-needle biopsy** – During a fine-needle procedure, computed tomography (CT) or ultrasound is used to guide the insertion of a fine, thin needle into the lymph node or other organ that’s suspected to have follicular lymphoma cells. Fluid or small pieces of tissue are then removed. In core-needle biopsy procedures, the needle is larger and a small cylinder of tissue is removed. For both types, the needle insertion site is first numbed with a local anesthetic.

- **Bone marrow biopsy** – Bone marrow biopsy samples are typically taken from the back of the pelvic bone. During a bone marrow biopsy, a needle is inserted into the bone, and a small piece of bone and marrow is removed. Local anesthesia is used, so most patients feel only pressure and brief pain during the procedure.

Samples of tissue obtained during these procedures are examined by a pathologist to see if follicular lymphoma cancer cells are present. The pathologist will also document the number of lymph nodes that contain cancer cells and other important facts about the cancer. In some instances, the pathologist may not be able to identify all the necessary information because the tissue sample is too small. When this happens, another biopsy may be necessary. The pathologic evaluation of biopsy samples offers the most valuable information for the diagnosing and staging of follicular lymphoma.

**BLOOD TESTS**

Further laboratory evaluation may include blood tests. A complete blood count (CBC) measures the number of red and white blood cells and platelets in the blood. Low blood cell counts can indicate that the cancer has spread to the bone marrow and is affecting the formation of new blood cells.

Blood chemistry tests to examine kidney and liver function may also be ordered, and your doctor might request a lactate dehydrogenase (LDH) blood test as well, as LDH levels are often high in people with follicular lymphoma. Lastly, your blood might be tested for infections such as hepatitis or HIV because these viruses can affect your treatment.

**DIAGNOSTIC IMAGING STUDIES**

Imaging studies are primarily used to more closely examine the affected area and to see if the cancer has spread (metastasized), which aids in defining the stage of the disease. You may not need every diagnostic imaging study listed here. Your doctors will consider the results of your physical examination, biopsy findings, blood test results and general health status in deciding which tests will provide the most useful information.

**Positron emission tomography (PET)**

PET images are not as finely detailed as those from CT or MRI, but they can provide useful information, such as whether an enlarged lymph node contains cancer cells and whether an area that looks normal on a CT scan might actually be follicular lymphoma. PET scans are the most sensitive tests for finding follicular lymphoma.

**Chest X-ray**

An X-ray is a photograph of the structures inside your body, particularly your bones. Chest X-rays can help doctors determine whether there are any enlarged lymph nodes in the chest area.

**Computed Tomography (CT)**

CT produces three-dimensional, cross-sectional X-ray images, so it can provide more precise details in soft tissues than a standard X-ray. CT scans provide an excellent assessment of the size of the lymph nodes, confirming whether they’re enlarged. In cases of follicular lymphoma, CT images of the abdomen, pelvis, chest, head and neck can be useful.

**Magnetic resonance imaging (MRI)**

MRI uses strong magnets and radiowaves to produce detailed images of lymph nodes. MRI is not used as often as CT for diagnosing follicular lymphoma, but it can help determine whether the cancer has spread to the spinal cord or brain.

Be sure to talk openly with your health care team to ensure you understand everything involved in the diagnostic phase of your cancer care.

**QUESTIONS TO ASK YOUR MEDICAL TEAM**

**ABOUT YOUR PROGNOSIS**

If you would like to know more about your prognosis (predicted outcome from treatment), do not be afraid to ask your doctor. Learning more can help you better plan for the future.

- Is my follicular lymphoma curable?
- If I go into remission, what does that mean?
- Is there anything I can do to improve my prognosis?

**ADDITIONAL RESOURCES**

- **American Cancer Society:**
  www.cancer.org
  How is non-Hodgkin lymphoma diagnosed?
- **American Society of Clinical Oncology:**
  www.cancer.net
  Lymphoma – Non-Hodgkin: Diagnosis
UNAWARING SUPPORT AND LOVE
GUIDE SURVIVOR THROUGH CANCER JOURNEY

Before I was diagnosed with lymphoma, I had never given any thought to having cancer. I was active, enjoyed working as a nurse, and couldn’t have been happier. After all, at age 60, I met the love of my life.

So when I felt a hard lump at the nape of my neck, I just thought it was part of my neck bone. But I was working for a nurse practitioner at the time, and when she saw it, she told me I needed to have it checked right away.

I had a needle aspiration that didn’t go well, and I was referred to a surgeon. It was a scary time, but because I have an issue with my thyroid, I still didn’t think anything bad was going to happen.

Three weeks later my surgeon removed the hard lymph node, and then the phone call came: they found malignant cells. That’s when I broke out in a cold sweat. I had a moment alone that night and broke down. I called Don (who would later become my husband) and my sister. I quickly learned that Don would be my rock through my journey and beyond. He went to every appointment and was with me every step.

What could have been a very ugly experience in another place actually turned out to be wonderful. We couldn’t have asked for better care, and I had fantastic doctors. The chemotherapy infusion rooms also made a big difference. Each person had an individual room, which provided privacy, and every room was very comforting.

I started the R-CHOP (rituximab — cyclophosphamide, doxorubicin, vincristine and prednisone) chemotherapy regimen and had an infusion every three weeks for six months. I was pleasantly surprised that I never got sick or vomited. My only problems were losing my leg strength as well as being tired, bloated and incontinent. But I continued to work throughout my treatment and could eat almost anything.

My hair, however, did fall out about two weeks after I began the chemo. A friend shaved my head and I bought a sassy blonde wig. I felt so naked with a bald head, but my wig made me look like Carol Channing.

After five treatments, Don and I traveled to my son’s wedding in Tacoma, Wash. My legs were so weak at the time and I wasn’t sure if I could make it in from the car. But to my surprise, Don proposed to me after the wedding. I remember wondering why anyone would want to inherit a wife with a problem like this, but that’s when I knew he was truly the wind beneath my wings.

I completed the chemotherapy, and we began working to get my leg muscles back. We bought bicycles, joined an athletic club and lifted weights. I was determined to reclaim my strength. It took about two years, but I finally recovered.

For the next six years, I had no unusual health issues except consistently low platelet levels. Early in 2012, routine scans indicated that my platelet level was at three — it was supposed to be above 150. A second test confirmed that my antibodies were eating my platelets.

Because of this, I repeated rituximab therapy, but it didn’t help. After reviewing my options, I chose to have my spleen removed. Thankfully, the surgery went so well that my platelets reached a normal level and we were on the road again two weeks later.

In spite of minor neuropathy at the end of my toes, cancer has been a positive life experience for me. It let me know that I could do what I needed to do to survive. I was also so thankful to have Don walking beside me. I couldn’t have made it without him.

Faye Janes is an adventurous woman who was not going to be detoured by a cancer diagnosis. Originally from Kansas, she was 42 when she went back to nursing school. She loved her profession, and the training helped sustain her when she was diagnosed with Stage I follicular lymphoma in 2005. She and her husband, Don, are now retired and are full-time RV travelers, serving as volunteer hosts at various RV sites. They have four grown sons between them and one granddaughter.
After you receive a diagnosis of follicular lymphoma, the next step for doctors is to determine the stage of the disease and develop an appropriate treatment plan.

To stage follicular lymphoma, doctors will order tests to find out how far the disease has spread and which areas of the body it’s affecting. (See page 4 for more information about diagnostic tests.) Based on the results of these diagnostic tests, the doctor will assign a stage to the disease. The Ann Arbor staging system for follicular lymphoma is the most commonly used system (see Table 1). The higher the stage number, the more advanced the disease.

In addition to this staging system, oncologists also use the Follicular Lymphoma International Prognostic Index (FLIPI) to predict the risk of disease recurrence and overall survival. The FLIPI takes into account the age and general health of the patient, the stage of the disease, the hemoglobin level, the number of involved lymph nodes, and the presence or absence of elevated levels of an enzyme called lactate dehydrogenase (LDH) in the blood.

The FLIPI assigns one point for each of the following risk factors:
- age older than 60 years
- late-stage disease (Stage III or IV)
- hemoglobin level less than 12 g/dL
- four or more involved lymph node areas
- high LDH level

The lower the score, the better the prognosis (predicted outcome from treatment).

Lastly, the World Health Organization recommends that follicular lymphoma be assigned a histologic grade, which is determined by the number of centroblasts (a special kind of B lymphocyte) found when examining a sample with a microscope (see Table 2). The grade defines how aggressive the cancer cells are likely to be and helps doctors make various treatment decisions, including when treatment should start. The higher the grade, the more likely the disease is to progress.

To determine a patient’s prognosis, the doctor may also test how well a patient is able to function and carry out daily activities by using a functional assessment scale.
STAGES OF FOLLICULAR LYMPHOMA

Follicular lymphoma is staged according to how many lymph nodes are affected and where they are in the body. The dotted line below indicates on which side of the diaphragm the affected lymph nodes are.

Stage I:
One lymph node area

Stage II:
Two or more lymph node areas, same side of the diaphragm

Stage III:
Lymph node areas on both sides of the diaphragm

Stage IV:
Spread outside the lymph system to an organ that is not directly next to the involved lymph node area(s)

QUESTIONS TO ASK YOUR MEDICAL TEAM

DISCUSSING
TREATMENT OPTIONS

- What is the goal of each of my treatment options?
- How do the benefits of the recommended cancer treatment compare with the risks?
- Are there any clinical trials open to me?
- Will I need to be hospitalized for the treatment, or can it be done in an outpatient clinic?
- What is the expected timeline of each treatment plan?
- How will each treatment affect my daily life?
- What are the possible side effects of each of my treatment options?
- How long will the side effects probably last?
- Is there a way to decrease the possibility that these side effects will occur?
- Are there medications available to relieve or prevent these side effects?
- How can I keep myself as healthy as possible during treatment?

MOBILE APP

MEDICATION REMINDERS

Proper medication adherence is critical to your care. This means taking the right dose of your medication at the right time, as prescribed by your doctor. To get the full benefit of your medication, you must take it as prescribed. As more oral anti-cancer drugs become available for patients to take at home, medication adherence becomes even more important. Many mobile apps can remind you to take your medication on time.

- MediSafe Meds & Pill Reminder / free (Android, iOS)
- Dosecast – Medication Reminder / free (Android, iOS)
- Med Helper Pill Reminder / free (Android, iOS)
- Drugs.com Medication Guide / free (Android)
- Pill Reminder by Drugs.com / free (iOS)
- Pill Reminder AnyTimer / free (Android)
- MedCoach Medication Reminder / free (Android, iOS)
- PocketNurse / free (Android)
- Pill Monitor Free – Medication Reminders and Logs / free (iOS)
- RXmindMe Prescription / free (iOS)

Visit the App Store on iTunes (iPhone, iPod, iPad) or the Google Play Store on Android devices to find more complete information on these and other medication reminders. (Use “medication reminder” as your search term.)
Ask your doctor about ZYDELIG, an oral treatment option for people with relapsed Follicular Lymphoma (FL) who have received at least 2 prior medicines.

ZYDELIG is first in a new class of drugs for patients with returning or relapsed FL who have received at least 2 prior medicines. In a clinical trial of 72 patients with relapsed FL, 54% responded to treatment with ZYDELIG, with 8% experiencing remission and 46% experiencing a partial response. ZYDELIG was approved based on response rates. Continued approval of ZYDELIG for FL is based on additional studies to determine if it improves symptoms or survival.

IMPORTANT SAFETY INFORMATION

What is the most important information I should know about ZYDELIG?

ZYDELIG can cause serious side effects that can lead to death, including:

- **Liver problems.** Your doctor will do blood tests before and during your treatment with ZYDELIG to check for liver problems. Tell your doctor right away if you get yellowing of your skin or the white part of your eyes (jaundice), dark or brown (tea colored) urine, pain in the upper right side of your stomach area (abdomen), or bleeding or bruising more easily than normal.

- **Severe diarrhea.** Diarrhea is common with ZYDELIG and can sometimes be severe. Tell your doctor right away if the number of bowel movements you have in a day increases by 6 or more. Ask your doctor about medicines you can take to treat your diarrhea.

- **Lung or breathing problems.** Your doctor may do tests to check your lungs if you have breathing problems during treatment with ZYDELIG. Tell your doctor right away if you get new or worsening cough, shortness of breath, difficulty breathing, or wheezing.

(continued on next page)
I’m living with Relapsed FL.

P.S.

Brought our grandkids here last weekend. Bought more tickets on Wednesday.

Guess where tonight’s date night was?

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Important Safety Information for ZYDELIG (cont’d)

- **Tear in intestinal wall (perforation).** Tell your doctor or get medical help right away if you get new or worsening stomach area (abdomen) pain, chills, fever, nausea, or vomiting.

   If you have any of the above serious side effects during treatment with ZYDELIG, your doctor may completely stop your treatment, stop your treatment for a period of time, or change your dose of ZYDELIG.

Who should not take ZYDELIG?

- If your doctor determines you have a history of serious allergic or skin reactions.

What are the other possible side effects of ZYDELIG?

ZYDELIG can cause serious side effects, including:

- **Severe skin reactions.** Tell your doctor if you get painful sores or ulcers on your skin, lips, or in your mouth, or severe rash with blisters or peeling skin.

- **Serious allergic reactions (anaphylaxis).** Tell your doctor or get medical help right away if you have a serious allergic reaction.

- **Low white blood cell count (neutropenia).** Your doctor will check your blood counts regularly during treatment with ZYDELIG. Tell your doctor right away if you have a fever or any signs of an infection.

   The most common side effects of ZYDELIG include fever, feeling tired, nausea, cough, stomach area (abdomen) pain, and chills.

What should I tell my doctor before taking ZYDELIG?

- All of your medical conditions, including if you have liver, lung, or breathing problems.

- If you are pregnant or plan to become pregnant. ZYDELIG may harm your unborn baby. Women who are able to become pregnant should use effective birth control (contraception) during treatment with ZYDELIG and for 1 month after stopping treatment. Talk to your doctor about birth control methods. Tell your doctor right away if you become pregnant during treatment with ZYDELIG.

- If you are breastfeeding or plan to breastfeed. You and your doctor should decide if you will take ZYDELIG or breastfeed. You should not do both.

- All the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. ZYDELIG and certain other medicines may affect each other.

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

For more information please see the Brief Summary of full Prescribing Information with important warnings on the next pages.
What is the most important information I should know about ZYDELIG?

ZYDELIG can cause serious side effects that can lead to death, including:

• **Liver problems.** Your doctor will do blood tests before and during your treatment with ZYDELIG to check for liver problems. Tell your doctor right away if you get any of the following symptoms of liver problems:
  - Yellowing of your skin or the white part of your eyes (jaundice)
  - Dark or brown (tea colored) urine
  - Pain in the upper right side of your stomach area (abdomen)
  - Bleeding or bruising more easily than normal

• **Severe diarrhea.** Diarrhea is common with ZYDELIG and can sometimes be severe. Tell your doctor right away if the number of bowel movements you have in a day increases by six or more. Ask your doctor about medicines you can take to treat your diarrhea.

• **Lung or breathing problems.** Your doctor may do tests to check your lungs if you have breathing problems during treatment with ZYDELIG. Tell your doctor right away if you get new or worsening cough, shortness of breath, difficulty breathing, or wheezing.

• **Tear in intestinal wall (perforation).** Tell your doctor or get medical help right away if you get new or worsening stomach area (abdomen) pain, chills, fever, nausea, or vomiting.

If you have any of the above serious side effects during treatment with ZYDELIG, your doctor may completely stop your treatment, stop your treatment for a period of time, or change your dose of ZYDELIG.

See “What are the possible side effects of ZYDELIG?” for more information about side effects.

What should I tell my doctor before taking ZYDELIG?

Before taking ZYDELIG, tell your doctor about all of your medical conditions, including if you:

• Have liver problems.
• Have lung or breathing problems.
• Are pregnant or plan to become pregnant. ZYDELIG may harm your unborn baby. Females who are able to become pregnant should use effective birth control (contraception) during treatment with ZYDELIG and for 1 month after stopping treatment. Talk to your doctor about birth control methods that may be right for you. Tell your doctor right away if you become pregnant during treatment with ZYDELIG.
• Are breastfeeding or plan to breastfeed. It is not known if ZYDELIG passes into your breast milk. You and your doctor should decide if you will take ZYDELIG or breastfeed. You should not do both.

Tell your doctor about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. ZYDELIG and certain other medicines may affect each other. Know the medicines you take. Keep a list of your medicines and show it to your doctor and pharmacist when you get a new medicine.

(continued on next page)
What is ZYDELIG?
ZYDELIG is a prescription medicine used to treat people with
- Follicular B-cell non-Hodgkin Lymphoma (FL) when the disease has come back after treatment with at least two prior medicines. ZYDELIG was approved based on response rates. Continued approval of ZYDELIG for FL is based on additional studies to determine if it improves symptoms or survival.

It is not known if ZYDELIG is safe and effective in children less than 18 years of age.

Who should not take ZYDELIG?
- If your doctor determines you have a history of serious allergic or skin reactions.

How should I take ZYDELIG?
- Take ZYDELIG exactly as your doctor tells you to take it.
- Your doctor may change your dose of ZYDELIG or tell you to stop taking ZYDELIG. Do not change your dose or stop taking ZYDELIG without first talking to your doctor.
- Take ZYDELIG 2 times a day.
- You may take ZYDELIG with or without food.
- Take ZYDELIG tablets whole.
- Do not miss a dose of ZYDELIG. If you miss a dose of ZYDELIG by less than 6 hours, take the missed dose right away. Then take your next dose as usual. If you miss a dose of ZYDELIG by more than 6 hours, wait and take the next dose of ZYDELIG at your usual time.

What are the possible side effects of ZYDELIG?
ZYDELIG can cause serious side effects, including:
- See “What is the most important information I should know about ZYDELIG?”
- Severe skin reactions. Tell your doctor if you get any of the following symptoms during treatment with ZYDELIG:
  - Painful sores or ulcers on your skin, lips, or in your mouth.
  - Severe rash with blisters or peeling skin.
- Anaphylaxis. Tell your doctor or get medical help right away if you have a serious allergic reaction while taking ZYDELIG.
- Low white blood cell count (neutropenia). Your doctor will check your blood counts regularly during treatment with ZYDELIG. Tell your doctor right away if you have a fever or any signs of an infection while taking ZYDELIG.

The most common side effects of ZYDELIG include fever, feeling tired, nausea, cough, stomach area (abdomen) pain, and chills.

Tell your doctor if you have any side effect that bothers you or that does not go away. These are not all the possible side effects of ZYDELIG. Call your doctor for medical advice about side effects.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.
Many treatment options exist to help you with your battle with follicular lymphoma. In general, follicular lymphoma responds well to treatment but is difficult to cure. Your specific treatment plan will be selected according to several factors, including your overall health and the stage of your disease. Some of the most common options to treat follicular lymphoma are outlined here.

Remember that as research evolves and new treatments are discovered, current options may change. New treatments are evaluated in studies known as clinical trials (see sidebar on page 13).

**WATCHFUL WAITING**
With watchful waiting, your doctor will closely monitor your follicular lymphoma and begin active treatment when the disease causes symptoms other than mildly swollen lymph nodes. This approach tends to be common because follicular lymphoma develops slowly. Watchful waiting allows patients to safely avoid treatment and its side effects until it is absolutely necessary. Some patients may never need active treatment; however, if disease progresses, your doctor may opt to start treatment with chemotherapy, immunotherapy, targeted therapy, radiation therapy or stem cell transplantation.

**CHEMOTHERAPY**
Chemotherapy is the use of strong drugs, also called cytotoxic drugs, to stop the growth of cancer cells either by killing them or preventing them from dividing and growing. Chemotherapy is sometimes referred to as conventional chemotherapy to distinguish it from targeted therapy, which also involves the use of drugs that travel throughout the body.

Chemotherapy is a treatment option for all stages of follicular lymphoma. A single chemotherapy drug may be used, or your doctor may instead prescribe a combination of chemotherapy drugs or a chemotherapy drug plus rituximab (Rituxan), which is a monoclonal antibody. (See the section “Immunotherapy” for more information.) The chemotherapy drugs used most often to treat follicular lymphoma include bendamustine (Treanda), chlorambucil (Leukeran), cyclophosphamide (Cytoxan, Neosar), doxorubicin (Adriamycin), lenalidomide (Revlimid) and vincristine (Oncovin). For patients who are unable to tolerate intensive chemotherapy regimens, cyclophosphamide and chlorambucil are often the preferred options because they are milder.

Another drug, prednisone, is a corticosteroid, not a chemotherapy drug, but it is included in many chemotherapy combination regimens. Prednisone is an anti-inflammatory drug and can help reduce swelling around tumors, and it also appears to help cause the death of cancerous white blood cells.

Combination chemotherapy regimens are often used to treat many types of cancer, including follicular lymphoma. The regimens used to treat follicular lymphoma include one or more chemotherapy drugs in combination with rituximab.

- **R-CVP**: rituximab combined with cyclophosphamide, vincristine and prednisone
- **R-CHOP**: rituximab combined with cyclophosphamide, doxorubicin, vincristine and prednisone
- **R-Bendamustine**: rituximab combined with bendamustine

In addition, there is a notable clinical trial underway that is referred to as Revlimid(R).
In this trial, treatment is with a combination of lenalidomide with rituximab.

**IMMUNOTHERAPY**

Immunotherapy uses the body’s own immune system to help fight follicular lymphoma. The main types of immunotherapies used to treat this particular cancer are monoclonal antibodies, which are laboratory-made versions of immune system proteins designed to attack cancer cells.

The monoclonal antibody rituximab is commonly used to treat follicular lymphoma. It attaches to a specific protein found on B cells, the cells from which follicular lymphoma arise. Rituximab makes the B cells more visible to your immune system, which helps it attack them more efficiently. Rituximab may be used to treat follicular lymphomas of all stages, either alone or in combination with chemotherapy.

A somewhat similar treatment option involves the use of the radioactive monoclonal antibody drug ibritumomab tiuxetan (Zevalin). This drug combines a radioactive particle with a monoclonal antibody, allowing it to deliver radiation directly to the cancer cells. This approach leaves most of the surrounding healthy cells undamaged. Ibritumomab tiuxetan may be used to treat advanced Stage II, Stage III and Stage IV follicular lymphomas. It may also be used as a follow-up treatment if the lymphoma shrinks or goes away with the initial treatment; this type of use can help lower the chance that the lymphoma will relapse (come back).

**TARGETED THERAPY**

Researchers have learned about the cell pathways that can lead to many types of cancers, including follicular lymphoma, and have also learned how to develop drugs that block those pathways. These drugs are known as targeted drugs (or agents), and treatment is known as targeted therapy. Targeted therapy drugs block the signals that proteins and other molecules send along signaling pathways, which are systems in the body that direct basic cell functions like cell growth, division and death.

Effective targeted therapy depends on two factors: identifying targets that play an important role in the growth and survival of cancer cells, and developing agents that can attack those targets. The targeted therapy drug used to treat follicular lymphoma is idelalisib (Zydelig). This targeted drug blocks one of the proteins that helps follicular lymphoma cells grow and survive; it is approved to treat follicular lymphoma that has relapsed after treatment with at least two previous chemotherapy drugs.

One concern associated with both chemotherapy and targeted therapy is that cancer cells can become resistant to the drugs, which may make therapy less effective over time. Researchers continue to explore ways to overcome resistance and identify new pathways to target and develop agents to interrupt the growth of follicular lymphoma cells.

**RADIATION THERAPY**

Radiation therapy is the use of high-energy X-rays to kill cancer cells or keep them from growing. External-beam radiation therapy is given with the use of a radiation machine and is similar to a conventional X-ray, except the radiation beams are strong enough to kill cancer cells.

Radiation therapy may be used to treat Stage I and early Stage II follicular lymphomas, targeting the lymph node areas affected by the cancer. In later stage lymphomas, radiation therapy may be used to reduce symptoms or to treat patients who are too sick to tolerate chemotherapy.

If your doctor includes radiation therapy in your treatment plan, a radiation oncologist will carefully plan and oversee your treatment.

**STEM CELL TRANSPLANTATION**

Stem cell transplantation helps the body produce new blood cells. Stem cells are found in the bone marrow, and they have a special feature that enables them to develop into any one of the three types of blood cells—red blood cells, white blood cells (cells that fight infection) and platelets (clotting cells). There are two types of stem cell transplantation: autologous and allogeneic.

With autologous stem cell transplantation, a person’s own stem cells are removed and preserved so that very high doses of chemotherapy and/or radiation therapy can be given to attack cancer cells without destroying the stem cells. After the conclusion of the intensive chemotherapy or radiation therapy, the person’s stem cells are infused back into the body.

An allogeneic stem cell transplantation is the use of stem cells obtained from a donor with healthy bone marrow whose stem cells are a close match to those of the person to be treated. Allogeneic stem cell transplantation also is considered to be a form of immuno-therapy, because it establishes a new immune system for a person.

In cases of follicular lymphoma, stem cell transplants are most commonly used when the cancer is in remission but likely to come back or when the cancer doesn’t respond to the initial treatment plan.
**Fears about the side effects of treatment** can increase the stress of a follicular lymphoma diagnosis. These fears grow from a belief that the discomfort of side effects cannot be relieved. However, it is now possible to prevent or manage many common side effects of cancer treatment. Managing side effects is important because if you feel better, you are more likely to complete your treatment, which offers a greater chance for a successful outcome.

**MANAGING THE SIDE EFFECTS OF CANCER DRUGS**

While the side effects from targeted therapy and chemotherapy drugs have some differences, several of their most common side effects are the same (see Figure 1). It is extremely important to talk openly with your doctor about any side effects you experience and to call your doctor’s office immediately if a side effect occurs suddenly.

**Fatigue**

Treatment-related fatigue occurs primarily because the body needs extra energy to repair the healthy tissue damaged by cancer treatment. Additionally, other side effects of treatment, such as pain, nausea and vomiting, can cause or worsen fatigue. Although most people think more rest will help relieve fatigue, increasing activity and performing regular exercise (such as walking or bike riding) are the best ways to combat it. If your fatigue is severe, your doctor may prescribe a short-term psychostimulant drug to improve alertness.

**Nausea and vomiting**

Nausea is the unpleasant sensation of feeling the need to vomit, and vomiting occurs when the stomach muscles contract and push the stomach contents up through the mouth. Nausea and vomiting occur as the result of a series of reactions between your stomach and your brain, which start when cancer drugs damage the cells lining the inside of the stomach.

Recent advances have led to the development of new prescription drugs called antiemetics, which can prevent and control nausea and vomiting. To further protect yourself, you may want to try some nondrug approaches, including progressive muscle relaxation, biofeedback, guided imagery, self-hypnosis and acupuncture. Eating several small meals rather than a few big meals, staying hydrated and avoiding unpleasant odors can also help.

**Diarrhea**

Diarrhea is the passing of loose or watery stools three or more times a day, which may cause cramps in the abdomen and pain or discomfort in the rectum. When mild, diarrhea is an inconvenience, but if it’s left untreated it can lead to serious problems, such as dehydration, loss of important nutrients, weight loss and fatigue.

Once diarrhea occurs, consuming only clear liquids may help the lining of your intestines heal. As diarrhea improves, you can slowly add solid foods to your diet, starting with low-fiber foods like white rice or potatoes. Some foods can worsen diarrhea, including dairy products; spicy, greasy or fried foods; raw fruits or vegetables; or foods that are high in fiber. Over-the-counter medicines and fiber supplements are available to control diarrhea, but ask your doctor before taking anything. If diarrhea is severe, your doctor may prescribe other medications or choose to stop your cancer treatment temporarily until your diarrhea is controlled.

**Mouth sores**

Mouth sores, known as oral mucositis, are small cuts or ulcers that can affect the gums, tongue, roof of the mouth or lips. Mouth sores sometimes begin as mild pain or burning, followed by white patches that may become large red lesions. Pain may range from mild to severe, making it difficult to talk, eat or swallow. Taking good care of your teeth and gums is essential to managing mouth sores, and you should brush and floss several times a day. Your doctor may suggest rinsing your mouth with special solutions and may prescribe a medication that coats the lining of your mouth, or pain medications that can be topically applied.

To manage mouth sores, keep your mouth and lips moist by using lip balm, sipping on water, sucking on ice chips and drinking through a straw. Choose soft, moist foods that are easy to swallow, and always let your food cool down to room temperature before you eat. It is also a good idea to avoid alcoholic beverages and tobacco products, as well as hot, spicy, citric, greasy, fried, coarse or rough-textured foods.

**Skin reactions**

Skin reactions can include redness and irritation (similar to sunburn), skin rash or dry, flaky skin. These reactions often cause itchiness and discomfort, and although most are mild to moderate, some can become severe if not treated early. If a rash develops and causes itchiness or pain, your doctor may prescribe a mild corticosteroid cream (hydrocortisone) or an antibiotic gel (clindamycin gel). Severe rashes are usually treated with an oral antibiotic and perhaps an oral corticosteroid, such as methylprednisolone (Medrol) or prednisone. When a rash is severe, the dose of the cancer drug(s) is often reduced or temporarily stopped until the rash improves.

**RECOVERING FROM RADIATION THERAPY**

Because radiation therapy is delivered from the outside of the body, the skin and underlying tissues in the area being treated may develop redness, dryness, peeling or itchiness. This sensitivity is short-term and usually resolves gradually within two months after treatment stops. Other side effects include fatigue, anemia, hair loss in the area treated, nausea and vomiting. Management techniques for these side effects are very similar to those for managing the side effects from cancer drugs.
In some cases, follicular lymphoma may relapse (come back) after initial treatment has sent the disease into remission. For this reason, follow-up care and healthy living is extremely important.

**MONITORING YOUR HEALTH**

After your initial treatment for follicular lymphoma has been completed, your doctor will design a follow-up care plan to monitor your health and check for a potential relapse. For this plan to be useful, you must understand and follow it exactly. If you have any questions or concerns as your follow-up care plan is being developed, don’t hesitate to talk to your doctor.

Your follow-up care plan will likely include regular physical examinations, blood tests and/or computed tomography (CT). (See page 4 for more information about these procedures.) If signs of relapse are detected, then your doctor will talk to you about new treatment options.

While follow-up care is important for survivors of all types of cancer, it’s especially important for people who have had follicular lymphoma because multiple relapses often occur.

**MANAGING LATE EFFECTS**

In addition to watching for signs of disease relapse, your doctor will use your follow-up care visits to check for long-term side effects, which are also called late effects. These can begin weeks, months or even years after your treatment ends, and they vary based on your overall health and the type of treatment you received.

Some of the more common late effects of follicular lymphoma treatments include reduced fertility, fatigue, peripheral neuropathy, heart problems, stroke, lung damage, shortness of breath, thyroid problems and increased risk for infection.

If you stay on top of your follow-up care plan, these side effects can often be managed, allowing you to maintain a high quality of life.

**LIVING A HEALTHY LIFESTYLE**

Perhaps as important as sticking to your follow-up care schedule and managing late effects is staying healthy and active. It’s important to maintain good nutrition, be as active as you can, get enough rest and be emotionally healthy. Taking these actions can help you feel better both physically and psychologically, allowing you to better cope with the day-to-day challenges of living with follicular lymphoma.

**Maintain good nutrition**

It’s important to make healthy choices when it comes to nutrition before, during and after treatment. This can be a challenge if you have side effects such as loss of appetite, nausea or vomiting. But a healthy diet rich in protein can help you gain strength, which is especially needed during treatment cycles. In general, try to eat a wide variety of nutrient-rich foods and drink plenty of liquids. Because some cancer treatments can cause loss of bone mass, it is helpful to eat dairy foods and other foods high in calcium.

Talk to your doctor or a registered dietitian about the need for calcium and vitamin D, either in your diet or as supplements.

**Be active**

Participating in physical activities or regular exercise can help you feel better overall. Although it may not seem to make sense, physical exercise is actually the best treatment for fatigue. Studies have shown that people with cancer who exercise regularly feel less tired and have more energy. Weight-bearing activities, such as walking, can help strengthen bones, which is important if you have bone metastasis. Think about what type of physical activity you enjoy most, and engage in it daily, or as often as you can tolerate. Try to modify your favorite form of exercise if you experience any pain or discomfort, rather than discontinuing it.

**Get enough rest**

Sleep disturbances are common among people with cancer. One reason is that fatigue related to cancer and its treatment leads people to take frequent naps during the day, which then makes it difficult to sleep at night. You can still set aside time in your day to rest or take naps, but limit them to 20 to 30 minutes each, and avoid napping in the late afternoon or early evening. Your doctor may review the medications you are taking and change them if he or she thinks that drug interactions or side effects are contributing to your sleep problems. Your doctor may also recommend a medication to help you sleep.

**Stay emotionally healthy**

People with cancer often live on an emotional rollercoaster. Allowing yourself to express your emotions freely is vital to remaining emotionally healthy. Finding ways to reduce and manage stress will strengthen your coping abilities. Some possibilities are meditation, guided imagery, muscle relaxation and yoga. Ordinary “escapes,” like reading, television and games can also help you relax. You also must be alert to depression and seek help if you’re experiencing a depressed mood and a loss of interest or pleasure in normal activities. Lastly, maintaining relationships and participating in support groups—either in person or online—can also go a long way toward helping you stay emotionally healthy.

**ADDITIONAL RESOURCES**

- American Cancer Society: [www.cancer.org](http://www.cancer.org)
  - Cancer and Depression
  - Getting a Good Night’s Sleep May Be Challenging for a Cancer Patient
  - Nutrition for People With Cancer
- American Society of Clinical Oncology: [www.cancer.net](http://www.cancer.net)
  - Emotional and Physical Matters
  - Lymphoma – Non-Hodgkin: Late Effects of Treatment
  - Strategies for a Better Night’s Sleep
- National Cancer Institute: [www.cancer.gov](http://www.cancer.gov)
  - Managing Emotional Effects
This medical journal will help you keep track of all of the medications that you're taking. Note the name and contact information for the doctor who prescribed each drug, and give this list to your cancer care team so they can help you manage your medications and avoid drug interactions.

For additional copies of this form, go to www.PatientResource.com/FLMedicalJournal.pdf

### MY DOCTOR APPOINTMENTS

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### MY MEDICATIONS

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### MY MEDICAL TEAM CONTACTS

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