

**Initial REMS approval: 07/23/2014**  
**Most recent modification: 03/2018**

**NDA 205858**

**ZYDELIG® (idelalisib) tablets**

**Drug Class: Phosphoinositide-3 Kinase-Delta Inhibitor**

Gilead Sciences, Inc.  
333 Lakeside Drive  
Foster City, CA 94404  
Phone: (800) 445-3235

**RISK EVALUATION AND MITIGATION STRATEGY (REMS)**

**I. GOAL:**

The goal of the Zydelig REMS is to mitigate the risks of fatal and /or serious hepatotoxicity; fatal and/or serious and severe diarrhea or colitis; fatal and/or serious pneumonitis; fatal and/or serious infections, and fatal and serious intestinal perforation associated with Zydelig treatment by informing healthcare providers of the risks of

- fatal and/or serious hepatotoxicity
- fatal and/or serious and severe diarrhea or colitis
- fatal and/or serious pneumonitis
- fatal and/or serious infections
- fatal and serious intestinal perforation

**II. REMS ELEMENTS**

**A. Communication Plan**

Gilead Sciences, Inc. (Gilead) must implement the following communication plan for healthcare providers who are likely to prescribe Zydelig. The communication plan must consist of the following:

- 1. REMS Letter Healthcare Providers - A *REMS Letter to Healthcare Providers* must be distributed within 30 calendar days of the approval of the REMS modification (01/26/2018). The letter must be distributed electronically to oncologists and hematologists who are likely to prescribe Zydelig. If a targeted healthcare provider's**

email address is not available, or if an email is undeliverable, the provider will receive the letter through the mail. The *REMS Letter to Healthcare Providers* must inform healthcare providers of the risks of fatal and/or serious hepatotoxicity; fatal and/or serious and severe diarrhea or colitis; fatal and/or serious pneumonitis; fatal and/or serious infections; and fatal and serious intestinal perforation associated with Zydelig treatment. The letter must be accompanied by the Prescribing Information (with Medication Guide attached) and the *Zydelig REMS Fact Sheet*. The *REMS Letter to Healthcare Providers* must be available from the *Zydelig REMS Website* at the time of distribution and remain on the website for 12 months after approval of the REMS modification (01/26/2018).

- 2. REMS Letter for Professional Societies** - A *REMS Letter for Professional Societies* must be distributed electronically within 30 calendar days of the approval of the REMS modification (01/26/2018). If a targeted Professional Society's email address is not available, or if an email is undeliverable, the letter must be sent through the mail. The *REMS Letter for Professional Societies* must inform the leadership of the professional societies described below of the risks of fatal and/or serious hepatotoxicity; fatal and/or serious and severe diarrhea or colitis; fatal and/or serious pneumonitis; fatal and/or serious infections; and fatal and serious intestinal perforation associated with Zydelig treatment. Gilead must request the leadership of the professional societies distribute this risk information to their memberships.

The *REMS Letter for Professional Societies* must be distributed to the following organizations:

- American Society of Clinical Oncology (ASCO)
- American Society of Hematology (ASH)
- Oncology Nursing Society (ONS)
- National Comprehensive Cancer Network (NCCN)
- Hematology Oncology Pharmacy Association (HOPA)
- American Pharmacists Association (APhA)
- American Society of Health-System Pharmacists (ASHP)

- 3. REMS Fact Sheet** – A *Zydelig REMS Fact Sheet* must be distributed to Healthcare Providers. The *Zydelig REMS Fact Sheet* must be included in the mailings of the *REMS Letter to Healthcare Providers* and the *REMS Letter for Professional Societies* and must be available on the *Zydelig REMS Website*. Hard copies of the *Zydelig REMS Fact Sheet* must also be distributed by Gilead's sales representatives and medical field-based personnel to healthcare providers during follow-up details/visits with healthcare providers for the first 12 months after the approval of the REMS modification (01/26/2018). Gilead sales representatives and medical field-based personnel must orally review the risk messages contained in the *Zydelig REMS Fact Sheet* during the visit with the healthcare provider.
- 4. Journal Information Piece** - Gilead must publish in the following professional journals an information piece that includes the risks of fatal and/or serious hepatotoxicity, fatal

and/or serious and severe diarrhea or colitis, fatal and serious pneumonitis and serious intestinal perforation associated with Zydelig treatment.

- Journal of Clinical Oncology
- Blood
- New England Journal of Medicine
- Hematology Oncology Today
- Oncology & Hematology Review
- Leukemia and Lymphoma

The information piece will be published quarterly in each publication for one year following the REMS modification (01/26/2018).

- 5. Dissemination of REMS information at scientific meetings** – The *Zydelig REMS Fact Sheet* and the Prescribing Information must be prominently displayed at scientific meetings where Gilead has a presence (e.g., booth) through the end of January 2019.
- 6. REMS Program Website** –The *Zydelig REMS Program Website* ([www.zydeligrems.com](http://www.zydeligrems.com)) will continue for 12 months after the approval of this REMS modification (01/26/2018). The *Zydelig REMS Program Website* must include the option to print the currently approved Prescribing Information, Medication Guide, *REMS Letter for Healthcare Providers*, *REMS Factsheet*, and *Patient Safety Information Card*. The Zydelig product website must include a prominent REMS-specific link to the *Zydelig REMS Program Website*. All website information must be updated within 60 calendar days of approval of the REMS modification (01/26/2018).
- 7. Zydelig Patient Safety Information Card** - A Patient Safety Information Card highlights the risks of Zydelig and includes information on the management of these risks. Gilead’s sales representatives or medical field based personnel must distribute the *Patient Safety Information Cards* to prescribers within the first 12 months of approval of the REMS modification (01/26/2018). The *Patient Safety Information Card* must also be available on the Zydelig REMS Program Website for 12 months after the approval of the REMS modification (01/26/2018).

The following are part of the REMS and are appended.

- *REMS Letter to Healthcare Providers*
- *REMS Letter for Professional Societies*
- *REMS Fact Sheet*
- *Journal Information Piece*
- *Zydelig REMS Website*
- *Zydelig Patient Safety Information Card*

**B. Timetable for Submission of Assessments**

Gilead must submit REMS assessments to the FDA 18 months, 4 years, and 7 years from the date of the initial approval of the REMS (07/23/2014). To facilitate inclusion of as much information as possible while allowing reasonable time to prepare the submission, the reporting interval covered by each assessment should conclude no earlier than 60 calendar days before the submission date for that assessment so that it will be received by the FDA on or before the due date.

## Zydelig REMS

### FDA REQUIRED UPDATED REMS SAFETY INFORMATION

**Boxed Warning Risk of:**

- **Fatal and/or serious hepatotoxicity - *updated***
- **Fatal and/or serious and severe diarrhea or colitis - *updated***
- **Fatal and/or serious pneumonitis**
- **Fatal and/or serious infections - *updated***
- **Fatal and serious intestinal perforation**

January 2018

Dear Healthcare Provider:

The FDA has required this safety notice as part of the Zydelig REMS (**R**isk **E**valuation and **M**itigation **S**trategy) to inform you about the recent **update to the incidence rates of fatal and serious toxicities in the Zydelig Boxed Warning** as follows:

**WARNING: FATAL AND SERIOUS TOXICITIES: HEPATIC, SEVERE DIARRHEA, COLITIS, PNEUMONITIS, INFECTIONS and INTESTINAL PERFORATION**

- Fatal and/or serious hepatotoxicity occurred in 16% to 18% of ZYDELIG-treated patients. Monitor hepatic function prior to and during treatment. Interrupt and then reduce or discontinue ZYDELIG.
- Fatal and/or serious and severe diarrhea or colitis occurred in 14% to 20% of ZYDELIG-treated patients. Monitor for the development of severe diarrhea or colitis. Interrupt and then reduce or discontinue ZYDELIG.
- Fatal and/or serious pneumonitis occurred in 4% of ZYDELIG-treated patients. Monitor for pulmonary symptoms and interstitial infiltrates. Interrupt or discontinue ZYDELIG.
- Fatal and/or serious infections occurred in 21% to 48% of ZYDELIG-treated patients. Monitor for signs and symptoms of infection. Interrupt ZYDELIG if infection is suspected.
- Fatal and serious intestinal perforation can occur in ZYDELIG-treated patients across clinical trials. Discontinue ZYDELIG if intestinal perforation is suspected.

The updated incidence rates of fatal and serious toxicities in the Zydelig Boxed Warning reflect data from patients treated with Zydelig in combination with rituximab or with unapproved combination therapies.

Please see the enclosed **Zydelig REMS Fact Sheet**, a non-promotional fact sheet reviewed by the FDA, for more detailed safety information. Be sure to give the **Zydelig Patient Safety Information Card** to all patients. This card, additional copies of the fact sheet, and other important information are available at: [www.ZydeligREMS.com](http://www.ZydeligREMS.com).

Zydelig is a kinase inhibitor indicated for the treatment of patients with:

- Relapsed chronic lymphocytic leukemia (CLL) in combination with rituximab, in patients for whom rituximab alone would be considered appropriate therapy due to other co-morbidities.
- Relapsed follicular B-cell non-Hodgkin lymphoma (FL) in patients who have received at least two prior systemic therapies
- Relapsed small lymphocytic lymphoma (SLL) in patients who have received at least two prior systemic therapies



## Zydelig REMS

### Limitation of use:

Zydelig is not indicated and is not recommended for first-line treatment of any patient. Zydelig is not indicated and is not recommended in combination with bendamustine and/or rituximab for the treatment of FL.

This letter does not contain the complete safety profile for Zydelig. Please review the enclosed Prescribing Information.

### **Reporting Adverse Events**

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. Healthcare Providers should report all suspected adverse events associated with Zydelig to the FDA or to Gilead at 1-800-445-3235.

Sincerely,

William Guyer, Pharm.D.  
Senior Vice President, Medical Affairs

**Subject: Revised Boxed Warning for Zydelig: Update to Incidence Rates of Fatal and Serious Toxicities**

## Zydelig® REMS

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### Zydelig REMS

#### **FDA REQUIRED UPDATED REMS SAFETY INFORMATION**

**Boxed Warning includes the Risk of:**

- **Fatal and/or serious hepatotoxicity – updated**
- **Fatal and/or serious and severe diarrhea or colitis – updated**
- **Fatal and/or serious pneumonitis**
- **Fatal and/or serious infections – updated**
- **Fatal and serious intestinal perforation**

January 2018

Dear Healthcare Provider:

The FDA has required this safety notice as part of the Zydelig REMS (Risk Evaluation and Mitigation Strategy) to inform you about the recent update to the incidence rates of fatal and serious toxicities in the Zydelig Boxed Warning as follows:

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The updated incidence rates of fatal and serious toxicities in the Zydelig Boxed Warning reflect data from patients treated with Zydelig in combination with rituximab or with unapproved combination therapies.

Please see the [Zydelig REMS Fact Sheet](#), a non-promotional fact sheet reviewed by the FDA, for more detailed safety information. Please give the [Zydelig Patient Safety Information Card](#) to all patients. The card, the fact sheet, and other important information are available at: [www.ZydeligREMS.com](http://www.ZydeligREMS.com).

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This email does not contain the complete safety profile for Zydelig. To review the Prescribing Information, including complete **BOXED WARNING** and Medication Guide, see links below.

[Prescribing Information](#)

[Medication Guide](#)

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Sincerely,

[signature]

William Guyer, Pharm.D.  
Senior Vice President, Medical Affairs

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Gilead Sciences, Inc. 333 Lakeside Drive Foster City, CA 94404 USA  
[www.ZydeligREMS.com](http://www.ZydeligREMS.com) Phone 650 574 3000 Facsimile 650 578 9264 REMS-ZYD-0035

Back



From: **Gilead Sciences, Inc.** Hide  
To: <Healthcare Provider Name>

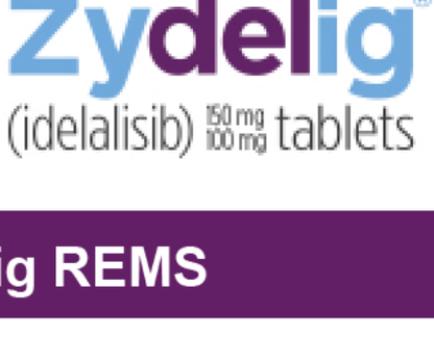
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### Revised Boxed Warning for Zydelig: Update to Incidence Rates of Fatal and Serious Toxicities

January 2018 at 5:00 PM

## Zydelig® REMS

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## Zydelig REMS

### FDA REQUIRED UPDATED REMS SAFETY INFORMATION

**Boxed Warning includes the Risk of:**

- **Fatal and/or serious hepatotoxicity – updated**
- **Fatal and/or serious and severe diarrhea or colitis – updated**
- **Fatal and/or serious pneumonitis**
- **Fatal and/or serious infections – updated**
- **Fatal and serious intestinal perforation**

January 2018

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Sincerely,

[Signature]

William Guyer, Pharm.D.  
Senior Vice President, Medical Affairs

## Zydelig REMS

### FDA REQUIRED UPDATED REMS SAFETY INFORMATION

**Boxed Warning Risk of:**

- **Fatal and/or serious hepatotoxicity - updated**
- **Fatal and/or serious and severe diarrhea or colitis - updated**
- **Fatal and/or serious pneumonitis**
- **Fatal and/or serious infections - updated**
- **Fatal and serious intestinal perforation**

January 2018

Dear <Name>:

The FDA has required Gilead Sciences to distribute this safety notice to the [Professional Organization] as part of the Zydelig REMS (**R**isk **E**valuation and **M**itigation **S**trategy). The **incidence rates of fatal and serious toxicities have been updated in the Boxed Warning** for Zydelig. We request that you distribute this information to your members about the following serious risks of Zydelig:

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## Zydelig REMS

- Relapsed follicular B-cell non-Hodgkin lymphoma (FL) in patients who have received at least two prior systemic therapies
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### Limitation of use:

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### **Reporting Adverse Events**

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Sincerely,

William Guyer, Pharm.D.  
Senior Vice President, Medical Affairs

From: Gilead Sciences, Inc.

To: <Name, Professional Society>

**Subject: Revised Boxed Warning for Zydelig: Update to Incidence Rates of Fatal and Serious Toxicities**

## Zydelig® REMS

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### Zydelig REMS

#### **FDA REQUIRED UPDATED REMS SAFETY INFORMATION**

**Boxed Warning includes the Risk of:**

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January 2018

#### **IMPORTANT SAFETY NOTICE**

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[Prescribing Information](#)

[Medication Guide](#)

#### **Reporting Adverse Events**

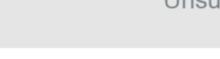
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[signature]

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Senior Vice President, Medical Affairs

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Gilead Sciences, Inc. 333 Lakeside Drive Foster City, CA 94404 USA  
[www.ZydeligREMS.com](http://www.ZydeligREMS.com) Phone 650 574 3000 Facsimile 650 578 9264 REMS-ZYD-0037

Reference ID: 4238482

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From: **Gilead Sciences, Inc.** Hide  
To: <Name, Professional Society>

**Revised Boxed Warning for Zydelig:  
Update to Incidence Rates of Fatal  
and Serious Toxicities**

January 2018 at 5:00 PM

**Zydelig® REMS**

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**Zydelig REMS**

**FDA REQUIRED UPDATED  
REMS SAFETY INFORMATION**

- Boxed Warning includes the Risk of:**
- **Fatal and/or serious hepatotoxicity – updated**
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[Prescribing Information](#)

[Medication Guide](#)

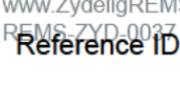
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Sincerely,

[signature]

William Guyor, Pharm.D.



## FDA REQUIRED Updated Safety Information for Zydelig<sup>®</sup> (idelalisib)

**Safety information updates were made to the Boxed Warning, including incidence rates of fatal and serious toxicities.**

### **BOXED WARNING For Zydelig (Idelalisib)**

**Risk of:**

- **Fatal and/or serious hepatotoxicity - updated**
- **Fatal and/or serious and severe diarrhea or colitis - updated**
- **Fatal and/or serious pneumonitis**
- **Fatal and/or serious infections - updated**
- **Fatal and serious intestinal perforation**

### **Fatal and/or Serious Hepatotoxicity**

- Fatal and/or serious hepatotoxicity occurred in 18% of patients treated with Zydelig monotherapy and 16% of patients treated with Zydelig in combination with rituximab or with unapproved combination therapies.
- Elevations in ALT or AST greater than 5 times the upper limit of normal have occurred. These findings were generally observed within the first 12 weeks of treatment and were reversible with dose interruption. After resumption of treatment at a lower dose, 26% of patients had recurrence of ALT and AST elevations. Discontinue Zydelig for recurrent hepatotoxicity.
- Avoid concurrent use of Zydelig with other drugs that may cause liver toxicity.
- Monitor ALT and AST in all patients every 2 weeks for the first 3 months of treatment, every 4 weeks for the next 3 months, then every 1 to 3 months thereafter. Monitor weekly for liver toxicity if the ALT or AST rises above 3 times the upper limit of normal until resolved. Withhold Zydelig if the ALT or AST is greater than 5 times the upper limit of normal, and continue to monitor AST, ALT and total bilirubin weekly until the abnormality is resolved.

### **Fatal and/or Serious and Severe Diarrhea or Colitis**

- Severe diarrhea or colitis (Grade 3 or higher) occurred in 14% of patients treated with Zydelig monotherapy and 20% of patients treated with Zydelig in combination with rituximab or with unapproved combination therapies. Diarrhea can occur at any time.
- Avoid concurrent use of Zydelig and other drugs that cause diarrhea. Diarrhea due to Zydelig responds poorly to antimotility agents. Median time to resolution ranged between one week and one month across trials, following interruption of Zydelig therapy and in some instances, use of corticosteroids.

### **Fatal and/or Serious Pneumonitis**

- Fatal and serious pneumonitis occurred in patients treated with Zydelig. Clinical manifestations included interstitial infiltrates and organizing pneumonia.
- In randomized clinical trials of combination therapies, pneumonitis occurred in 4% of patients treated with Zydelig compared to 1% on the comparator arms. Time to onset of pneumonitis ranged from <1 to 15 months. Monitor patients on Zydelig for pulmonary symptoms.
- In patients taking Zydelig who present with pulmonary symptoms such as cough, dyspnea, hypoxia, interstitial infiltrates on a radiologic exam, or a decline by more than 5% in oxygen saturation, interrupt Zydelig until the etiology has been determined.
- If symptomatic pneumonitis or organizing pneumonia is diagnosed, initiate appropriate treatment with corticosteroids and permanently discontinue Zydelig.

## FDA REQUIRED Updated Safety Information for Zydelig<sup>®</sup> (idelalisib)

### Fatal and/or Serious Infections

- Fatal and/or serious infections occurred in 21% of patients treated with Zydelig monotherapy and 48% of patients treated with Zydelig in combination with rituximab or with unapproved combination therapies. The most common infections were pneumonia, sepsis, and febrile neutropenia. Treat infections prior to initiation of Zydelig therapy.
- Monitor patients on Zydelig for signs and symptoms of infection and interrupt Zydelig for Grade 3 or higher infection.
- Serious or fatal *Pneumocystis jirovecii* pneumonia (PJP) or cytomegalovirus (CMV) occurred in <1% of patients treated with Zydelig. Provide PJP prophylaxis during treatment with Zydelig. Interrupt Zydelig in patients with suspected PJP infection of any grade, and permanently discontinue Zydelig if PJP infection of any grade is confirmed. Regular clinical and laboratory monitoring for CMV infection is recommended in patients with history of CMV infection or positive CMV serology at the start of treatment with Zydelig. Interrupt Zydelig in the setting of positive CMV PCR or antigen test until the viremia has resolved. If Zydelig is subsequently resumed, patients should be monitored by PCR or antigen test for CMV reactivation at least monthly.

### Fatal and Serious Intestinal Perforation

- Fatal and serious intestinal perforation occurred in Zydelig-treated patients.
- At the time of perforation, some patients had moderate to severe diarrhea.
- Advise patients to promptly report any new or worsening abdominal pain, chills, fever, nausea, or vomiting.
- Discontinue Zydelig permanently in patients who experience intestinal perforation.

### INDICATION

Zydelig is a kinase inhibitor indicated for the treatment of patients with:

- Relapsed chronic lymphocytic leukemia (CLL) in combination with rituximab, in patients for whom rituximab alone would be considered appropriate therapy due to other co-morbidities.
- Relapsed follicular B-cell non-Hodgkin lymphoma (FL) in patients who have received at least two prior systemic therapies.
- Relapsed small lymphocytic lymphoma (SLL) in patients who have received at least two prior systemic therapies.

Limitations of use:

Zydelig is not indicated and is not recommended for first-line treatment of any patient. Zydelig is not indicated and is not recommended in combination with bendamustine and/or rituximab for the treatment of FL.

**You are encouraged to report negative side effects of Zydelig to Gilead at 1-800-445-3235 and/or the FDA at [www.fda.gov/medwatch](http://www.fda.gov/medwatch) or call 1-800-FDA-1088.**

*This journal piece is part of the FDA-required Zydelig REMS. Visit [www.ZydeligREMS.com](http://www.ZydeligREMS.com) for more information.*

*For complete safety information, see the Prescribing Information available at [www.ZydeligREMS.com](http://www.ZydeligREMS.com).*

## **FDA REQUIRED Zydelig (idelalisib) UPDATED REMS SAFETY INFORMATION**

### **Boxed Warning for the Risk of:**

- **Fatal and/or serious hepatotoxicity - updated**
- **Fatal and/or serious and severe diarrhea or colitis - updated**
- **Fatal and/or serious pneumonitis**
- **Fatal and/or serious infections - updated**
- **Fatal and serious intestinal perforation**

### **Fatal and/or Serious Hepatotoxicity**

- Fatal and/or serious hepatotoxicity occurred in 18% of patients treated with Zydelig monotherapy and 16% of patients treated with Zydelig in combination with rituximab or with unapproved combination therapies.
- Elevations in ALT or AST greater than 5 times the upper limit of normal have occurred. These findings were generally observed within the first 12 weeks of treatment and were reversible with dose interruption. After resumption of treatment at a lower dose, 26% of patients had recurrence of ALT and AST elevations. Discontinue Zydelig for recurrent hepatotoxicity.
- Avoid concurrent use of Zydelig with other drugs that may cause liver toxicity.
- Monitor ALT and AST in all patients every 2 weeks for the first 3 months of treatment, every 4 weeks for the next 3 months, then every 1 to 3 months thereafter. Monitor weekly for liver toxicity if the ALT or AST rises above 3 times the upper limit of normal until resolved. Withhold Zydelig if the ALT or AST is greater than 5 times the upper limit of normal, and continue to monitor AST, ALT and total bilirubin weekly until the abnormality is resolved.

### **Fatal and/or Serious and Severe Diarrhea or Colitis**

- Severe diarrhea or colitis (Grade 3 or higher) occurred in 14% of patients treated with Zydelig monotherapy and 20% of patients treated with Zydelig in combination with rituximab or with unapproved combination therapies. Diarrhea can occur at any time.
- Avoid concurrent use of Zydelig and other drugs that cause diarrhea. Diarrhea due to Zydelig responds poorly to antimotility agents. Median time to resolution ranged between one week and one month across trials following interruption of Zydelig therapy and in some instances, use of corticosteroids.

### **Fatal and/or Serious Pneumonitis**

- Fatal and serious pneumonitis occurred in patients treated with Zydelig. Clinical manifestations included interstitial infiltrates and organizing pneumonia. In randomized clinical trials of combination therapies, pneumonitis occurred in 4% of patients treated with Zydelig compared to 1% on the comparator arms. Time to onset of pneumonitis ranged from <1 to 15 months. Monitor patients on Zydelig for pulmonary symptoms.
- In patients taking Zydelig who present with pulmonary symptoms such as cough, dyspnea, hypoxia, interstitial infiltrates on a radiologic exam, or a decline by more than 5% in oxygen saturation, interrupt Zydelig until the etiology has been determined. If symptomatic pneumonitis or organizing pneumonia is diagnosed, initiate appropriate treatment with corticosteroids and permanently discontinue Zydelig.

### **Fatal and/or Serious Infections**

- Fatal and/or serious infections occurred in 21% of patients treated with Zydelig monotherapy and 48% of patients treated with Zydelig in combination with rituximab or with unapproved combination therapies. The most common infections were pneumonia, sepsis, and febrile neutropenia. Treat infections prior to initiation of Zydelig therapy.
- Monitor patients on Zydelig for signs and symptoms of infection and interrupt Zydelig for Grade 3 or higher infection.

### Fatal and/or Serious Infections (cont'd)

- Serious or fatal *Pneumocystis jirovecii* pneumonia (PJP) or cytomegalovirus (CMV) occurred in <1% of patients treated with Zydelig. Provide PJP prophylaxis during treatment with Zydelig. Interrupt Zydelig in patients with suspected PJP infection of any grade, and permanently discontinue Zydelig if PJP infection of any grade is confirmed. Regular clinical and laboratory monitoring for CMV infection is recommended in patients with history of CMV infection or positive CMV serology at the start of treatment with Zydelig. Interrupt Zydelig in the setting of positive CMV PCR or antigen test until the viremia has resolved. If Zydelig is subsequently resumed, patients should be monitored by PCR or antigen test for CMV reactivation at least monthly.

### Fatal and Serious Intestinal Perforation

- Fatal and serious intestinal perforation occurred in Zydelig-treated patients. At the time of perforation, some patients had moderate to severe diarrhea.
- Advise patients to promptly report any new or worsening abdominal pain, chills, fever, nausea, or vomiting.
- Discontinue Zydelig permanently in patients who experience intestinal perforation.

### INDICATION:

Zydelig is a kinase inhibitor indicated for the treatment of patients with:

- Relapsed chronic lymphocytic leukemia (CLL) in combination with rituximab, in patients for whom rituximab alone would be considered appropriate therapy due to other co-morbidities.
- Relapsed follicular B-cell non-Hodgkin lymphoma (FL) in patients who have received at least two prior systemic therapies.
- Relapsed small lymphocytic lymphoma (SLL) in patients who have received at least two prior systemic therapies.

#### Limitation of use:

Zydelig is not indicated and is not recommended for first-line treatment of any patient. Zydelig is not indicated and is not recommended in combination with bendamustine and/or rituximab for the treatment of FL.

## WHAT IS THE ZYDELIG REMS?

A REMS (**R**isk **E**valuation and **M**itigation **S**trategy) is a program required by the FDA to manage known or potential serious risks associated with a drug product. FDA has determined that a REMS is necessary to ensure that the benefits of Zydelig outweigh its risks. The purpose of the Zydelig REMS is to inform Healthcare Providers of fatal and serious risks of hepatotoxicity, severe diarrhea or colitis, pneumonitis, infections, and intestinal perforation. This fact sheet is required by the FDA as part of the Zydelig REMS program.

A **Patient Safety Information Card** is also available for you to provide to your patients. The card reminds patients of the symptoms of the serious risks of Zydelig and should be shown to any healthcare provider involved in your patient's care. The card and other information and resources are available at [www.ZydeligREMS.com](http://www.ZydeligREMS.com).

This fact sheet does not contain the complete safety profile for Zydelig. Please see the Prescribing Information, including the **BOXED WARNING** and Medication Guide.

## REPORTING ADVERSE EVENTS

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. Healthcare Providers should report all suspected adverse events associated with Zydelig to the FDA or to Gilead at 1-800-445-3235.

  
Zydelig<sup>®</sup>  
(idelalisib) 150 mg  
100 mg tablets

## Patient Safety Information Card

Reference ID: 4238482



## Important Safety Information for Patients Taking Zydelig<sup>®</sup>

There are serious risks to understand when taking Zydelig.

Be certain to get regular blood tests as scheduled by your doctor.

Also, if you experience any of the following symptoms, you should immediately call your doctor and seek emergency medical care.

These symptoms include:

- Stomach (abdominal) pain or swelling
- Persistent or worsening nausea or vomiting
- Severe diarrhea
- Dark urine color
- Bloody or tar-colored stool
- Shortness of breath, difficulty breathing, or wheezing
- New or worsening cough
- Persistent fever (temperature over 101°F)



Remember! Call your doctor and get emergency medical care right away if you have any of these symptoms and **show this card** to any doctor involved in your care.

**Zydelig**<sup>®</sup>  
(idelalisib) 150 mg  
100 mg tablets

**Patient Safety  
Information Card**

Patient Name

Zydelig Prescriber Name

Prescriber's Phone Number

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its related companies.

Reference ID: A238482



**Important Safety Information for Healthcare Providers**



This patient is taking Zydelig<sup>®</sup> (idelalisib) therapy for the treatment of leukemia or lymphoma.

These are some of the serious risks associated with Zydelig:

- Fatal and/or serious hepatotoxicity
- Fatal and/or serious and severe diarrhea or colitis
- Fatal and/or serious pneumonitis
- Fatal and/or serious infections
- Fatal and serious intestinal perforation

Healthcare Providers:

- Evaluate urgently
- Provide all supportive care
- Contact the prescribing physician (see contact information at left) as soon as possible to coordinate care if a patient presents with signs and symptoms of the risks noted here

For more information about Zydelig, please refer to the full Prescribing Information. In case of safety concerns, call Gilead at 1-800-445-3235.



**Patients receiving Zydelig should carry this card at all times. Show this card to any doctor involved in your healthcare.**

## Zydelig (idelalisib) REMS (Risk Evaluation and Mitigation Strategy)

### What is the Zydelig REMS?

A REMS (Risk Evaluation and Mitigation Strategy) is a program required by the Food and Drug Administration (FDA) to manage known or potential serious risks associated with a drug product.

The purpose of the Zydelig REMS is to inform healthcare providers about the following serious risks of Zydelig:

### Fatal and/or Serious Hepatotoxicity

- Fatal and/or serious hepatotoxicity occurred in 18% of patients treated with Zydelig monotherapy and 18% of patients treated with Zydelig in combination with rituximab or with unapproved combination therapies.

### Fatal and/or Serious and Severe Diarrhea or Colitis

- Fatal and/or serious and severe diarrhea or colitis (Grade 3 or higher) occurred in 14% of patients treated with Zydelig monotherapy and 20% of patients treated with Zydelig in combination with rituximab or with unapproved combination therapies. Diarrhea can occur at any time.

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### Fatal and Serious Intestinal Perforation

- Fatal and serious intestinal perforation occurred in Zydelig-treated patients.
- At the time of perforation, some patients had moderate to severe diarrhea.

**Zydelig Fact Sheet:** A non-promotional fact sheet, reviewed by the FDA, with more detailed safety information on these risks is available. (See link in the box labeled "Materials for Healthcare Providers")

**Zydelig Patient Safety Information Card:** This card should be given to all patients by Zydelig prescribers and should be carried by patients on Zydelig at all times. Patients should show this card to any healthcare professional that sees them in a health-related encounter. (See link in the box labeled "Materials for Patients")

### INDICATION:

Zydelig is a kinase inhibitor indicated for the treatment of patients with

- Relapsed chronic lymphocytic leukemia (CLL) in combination with rituximab, in patients for whom rituximab alone would be considered appropriate therapy due to other co-morbidities.
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#### Limitations of use:

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You are encouraged to report negative side effects of Zydelig to Gilead at 1-800-445-3235 and/or the FDA at [www.fda.gov/medwatch](http://www.fda.gov/medwatch) or call 1-800-FDA-1088.

This site is intended for US Healthcare Professionals.

### Materials for Healthcare Providers

Zydelig REMS Letter  
to Healthcare Providers

[Download PDF](#)

Zydelig REMS Fact Sheet

[Download PDF](#)

### Materials for Patients

Medication Guide

[Download PDF](#)

Zydelig Patient Safety  
Information Card

[Download PDF](#)

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**This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.**  
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/s/  
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BARRY W MILLER  
03/22/2018