HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use ZYDELIG safely and effectively. See full prescribing information for ZYDELIG.

ZYDELIG® (idelalisib) tablets, for oral use
Initial U.S. Approval: 2014

WARNING: FATAL AND SERIOUS TOXICITIES: HEPATIC, SEVERE DIARRHEA, COLITIS, PNEUMONITIS, and INTESTINAL PERFORATION
See full prescribing information for complete boxed warning.

- **Fatal and/or serious hepatotoxicity occurred in 14% of Zydelig-treated patients. Monitor hepatic function prior to and during treatment. Interrupt and then reduce or discontinue Zydelig. (5.1)**
- **Fatal and/or serious and severe diarrhea or colitis occurred in 14% of Zydelig-treated patients. Monitor for the development of severe diarrhea or colitis. Interrupt and then reduce or discontinue Zydelig. (5.2)**
- **Fatal and serious pneumonitis can occur in Zydelig-treated patients. Monitor for pulmonary symptoms and bilateral interstitial infiltrates. Interrupt or discontinue Zydelig. (5.3)**
- **Fatal and serious intestinal perforation can occur in Zydelig-treated patients across clinical trials. Discontinue Zydelig if intestinal perforation is suspected. (5.4)**

----------INDICATIONS AND USAGE----------

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. (1.1)
- Relapsed follicular B-cell non-Hodgkin lymphoma (FL) in patients who have received at least two prior systemic therapies. (1.2)
- Relapsed small lymphocytic lymphoma (SLL) in patients who have received at least two prior systemic therapies. (1.3)

Accelerated approval was granted for FL and SLL based on overall response rate. Improvement in patient survival or disease related symptoms has not been established. Continued approval for these indications may be contingent upon verification of clinical benefit in confirmatory trials.

----------DOSAGE AND ADMINISTRATION----------

Recommended starting dose: 150 mg orally, twice daily. (2.1)

----------DOSAGE FORMS AND STRENGTHS----------

Tablets: 150 mg, 100 mg. (3)

----------CONTRAINDICATIONS----------

History of serious allergic reactions including anaphylaxis and toxic epidermal necrolysis. (4)

----------WARNINGS AND PRECAUTIONS----------

- Severe cutaneous reactions: Monitor patients for the development of severe cutaneous reactions and discontinue Zydelig. (5.5)
- Anaphylaxis: Monitor patients for anaphylaxis and discontinue Zydelig. (5.6)
- Neutropenia: monitor blood counts. (5.7)
- Embryo-fetal toxicity: may cause fetal harm. Advise women of potential risk to a fetus and to avoid pregnancy while taking Zydelig. (5.8)

----------ADVERSE REACTIONS----------

The most common adverse reactions (incidence ≥20%) are diarrhea, pyrexia, fatigue, nausea, cough, pneumonia, abdominal pain, chills, and rash (6.1).

The most common laboratory abnormalities (incidence ≥30%) are neutropenia, hypertriglyceridemia, hyperglycemia, ALT elevations, and AST elevations (6.1).

To report SUSPECTED ADVERSE REACTIONS, contact Gilead Sciences, Inc. at 1-800-GILEAD-5 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch

----------DRUG INTERACTIONS----------

- CYP3A inducers: Avoid coadministration of strong CYP3A inducers with Zydelig. (7.1)
- CYP3A substrates: Avoid coadministration of CYP3A substrates with Zydelig. (7.2)

----------USE IN SPECIFIC POPULATIONS----------

Nursing mothers: Discontinue drug or nursing. (8.3)

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.

Revised: 7/2014

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

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

- **Fatal and/or serious hepatotoxicity occurred in 14% of Zydelig-treated patients. Monitor hepatic function prior to and during treatment. Interrupt and then reduce or discontinue Zydelig as recommended *[see Dosage and Administration (2.2), Warnings and Precautions (5.1)].***
- **Fatal and/or serious and severe diarrhea or colitis occurred in 14% of Zydelig-treated patients. Monitor for the development of severe diarrhea or colitis. Interrupt and then reduce or discontinue Zydelig as recommended *[see Dosage and Administration (2.2), Warnings and Precautions (5.2)].***
- **Fatal and serious pneumonitis can occur in Zydelig-treated patients. Monitor for pulmonary symptoms and bilateral interstitial infiltrates. Interrupt or discontinue Zydelig as recommended *[see Dosage and Administration (2.2), Warnings and Precautions (5.3)].***
- **Fatal and serious intestinal perforation can occur in Zydelig-treated patients across clinical trials. Discontinue Zydelig for intestinal perforation *[see Warnings and Precautions (5.4)].***

1 INDICATIONS AND USAGE

1.1 Relapsed Chronic Lymphocytic Leukemia

Zydelig is indicated, in combination with rituximab, for the treatment of patients with relapsed chronic lymphocytic leukemia (CLL) for whom rituximab alone would be considered appropriate therapy due to other co-morbidities.

1.2 Relapsed Follicular B-cell non-Hodgkin Lymphoma

Zydelig is indicated for the treatment of patients with relapsed follicular B-cell non-Hodgkin lymphoma (FL) who have received at least two prior systemic therapies.

Accelerated approval was granted for this indication based on Overall Response Rate *[see Clinical Studies (14.2)].* An improvement in patient survival or disease related symptoms has not been established. Continued approval for this indication may be contingent upon verification of clinical benefit in confirmatory trials.

1.3 Relapsed Small Lymphocytic Lymphoma

Zydelig is indicated for the treatment of patients with relapsed small lymphocytic lymphoma (SLL) who have received at least two prior systemic therapies.

Accelerated approval was granted for this indication based on Overall Response Rate *[see Clinical Studies (14.3)].* An improvement in patient survival or disease related symptoms has not been established. Continued approval for this indication may be contingent upon verification of clinical benefit in confirmatory trials.

2 DOSAGE AND ADMINISTRATION

2.1 Recommended Dose

The recommended maximum starting dose of Zydelig is 150 mg administered orally twice daily.

Zydelig can be taken with or without food. Tablets should be swallowed whole.

Continue treatment until disease progression or unacceptable toxicity. The optimal and safe dosing regimen for patients who receive treatment longer than several months is unknown.

2.2 Dose Modification

See the table below for dose modification instructions for specific toxicities related to Zydelig. For other severe or life-threatening toxicities related to Zydelig, withhold drug until toxicity is resolved. If resuming Zydelig after interruption for other severe or life-threatening toxicities, reduce the dose to 100 mg twice daily. Recurrence of other severe or life-threatening Zydelig-related toxicity upon rechallenge should result in permanent discontinuation of Zydelig.

Table 1 Dose Modifications for Toxicities Due to Zydelig

Pneumonitis	**Any symptomatic pneumonitis**		
	Discontinue Zydelig in patients with any severity of symptomatic pneumonitis		
ALT/AST	**>3-5 x ULN**	**>5-20 x ULN**	**>20 x ULN**
	Maintain Zydelig dose. Monitor at least weekly until ≤1 x ULN.	Withhold Zydelig. Monitor at least weekly until ALT/AST are ≤1 x ULN, then may resume Zydelig at 100 mg BID.	Discontinue Zydelig permanently.
Bilirubin	**>1.5-3 x ULN**	**>3-10 x ULN**	**>10 x ULN**
	Maintain Zydelig dose. Monitor at least weekly until ≤1 x ULN.	Withhold Zydelig. Monitor at least weekly until bilirubin is ≤1 x ULN, then may resume Zydelig at 100 mg BID.	Discontinue Zydelig permanently.
Diarrhea*	**Moderate diarrhea**	**Severe diarrhea or hospitalization**	**Life-threatening diarrhea**
	Maintain Zydelig dose. Monitor at least weekly until resolved.	Withhold Zydelig. Monitor at least weekly until resolved, then may resume Zydelig at 100 mg BID.	Discontinue Zydelig permanently.
Neutropenia	**ANC 1.0 to <1.5 Gi/L**	**ANC 0.5 to <1.0 Gi/L**	**ANC <0.5 Gi/L**
	Maintain Zydelig dose.	Maintain Zydelig dose. Monitor ANC at least weekly.	Interrupt Zydelig. Monitor ANC at least weekly until ANC ≥0.5 Gi/L, then may resume Zydelig at 100 mg BID.
Thrombocytopenia	**Platelets 50 to <75 Gi/L**	**Platelets 25 to <50 Gi/L**	**Platelets <25 Gi/L**
	Maintain Zydelig dose.	Maintain Zydelig dose. Monitor platelet counts at least weekly.	Interrupt Zydelig. Monitor platelet count at least weekly. May resume Zydelig at 100 mg BID when platelets ≥25 Gi/L.

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; BID, twice daily; ULN, upper limit of normal

*Moderate diarrhea: increase of 4–6 stools per day over baseline; severe diarrhea: increase of ≥7 stools per day over baseline.

3 DOSAGE FORMS AND STRENGTHS

150 mg tablets: pink, oval-shaped, film-coated tablet debossed with “GSI” on one side and “150” on the other side.

100 mg tablets: orange, oval-shaped, film-coated tablet debossed with “GSI” on one side and “100” on the other side.

4 CONTRAINDICATIONS

History of serious allergic reactions including anaphylaxis and toxic epidermal necrolysis.

5 WARNINGS AND PRECAUTIONS

5.1 Hepatotoxicity

Fatal and/or serious hepatotoxicity occurred in 14% of patients treated with Zydelig. Elevations in ALT or AST greater than 5 times the upper limit of normal have occurred *[see Adverse Reactions (6.1)].* 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 *[see Dosage and Administration (2.2)].*

5.2 Severe Diarrhea or Colitis

Severe diarrhea or colitis (Grade 3 or higher) occurred in 14% of Zydelig-treated patients across clinical trials *[see Adverse Reactions (6.1)].* 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 1 week and 1 month across trials, following interruption of Zydelig therapy and in some instances, use of corticosteroids *[see Dosage and Administration (2.2)].*

5.3 Pneumonitis

Fatal and serious pneumonitis occurred in patients treated with Zydelig. Patients taking Zydelig who present with pulmonary symptoms such as cough, dyspnea, hypoxia,

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