

Idelalisib (Zydelig®)**Criteria for Use****June 2015**

VA Pharmacy Benefits Management Services, Medical Advisory Panel, and VISN Pharmacist Executives

The following recommendations are based on medical evidence, clinician input, and expert opinion. The content of the document is dynamic and will be revised as new information becomes available. The purpose of this document is to assist practitioners in clinical decision-making, to standardize and improve the quality of patient care, and to promote cost-effective drug prescribing. THE CLINICIAN SHOULD UTILIZE THIS GUIDANCE AND INTERPRET IT IN THE CLINICAL CONTEXT OF THE INDIVIDUAL PATIENT. INDIVIDUAL CASES THAT ARE EXCEPTIONS TO THE EXCLUSION AND INCLUSION CRITERIA SHOULD BE ADJUDICATED AT THE LOCAL FACILITY ACCORDING TO THE POLICY AND PROCEDURES OF ITS P&T COMMITTEE AND PHARMACY SERVICES.

The Product Information should be consulted for detailed prescribing information.

See the VA National PBM-MAP-VPE Monograph on this drug at www.pbm.va.gov or <http://vaww.pbm.va.gov> for further information.

Exclusion Criteria *If the answer to ANY item below is met, then the patient should NOT receive idelalisib.*

- Care not provided by a VA or VA purchased care (e.g. Choice Program, Fee Basis) hematology/oncology provider.
- Unable to swallow oral capsules whole and intact
- Patient with history of non-adherence with oral medication, follow-up appointments or laboratory visits
- Co-administration with CYP3A substrates if an increase in their AUC would be expected to have a clinically relevant effect, such as substrates with narrow therapeutic indices, as their AUC may increase significantly.
- Co-administration with strong CYP3A4 inducer (e.g. carbamazepine, rifampin, phenytoin, St. John's Wort)
- History of serious allergic reactions including anaphylaxis and toxic epidermal necrolysis.
- Gastrointestinal condition that may interfere with idelalisib absorption.
- Chronic or unresolved infection
- Pregnancy
- Severe renal impairment defined as CrCl \leq 15 ml/min (drug has not been studied in this setting)
- AST (SGOT) or ALT (SGPT) \geq 2.5x ULN, bilirubin $>$ 1.5x ULN, or with moderate-severe hepatic impairment (Child-Pugh B or C). (see Issues for Consideration)
- Absolute Neutrophil Count (ANC) $<$ 1000 cells/ μ L, and/or platelet count $<$ 50,000 cells/ μ L unless bone marrow involvement

Inclusion Criteria *The following must be fulfilled in order to meet criteria.*

- Diagnosis of Chronic Lymphocytic Leukemia (CLL) meeting initiation of therapy criteria[#], in combination with rituximab With RELAPSED disease [patient achieved CR* or PR* on initial therapy (e.g. fludarabine, bendamustine, chlorambucil)] AND progressed on retreatment with initial therapy OR is not a candidate for retreatment with initial therapy

AND

- Goals of care and role of Palliative Care consult have been discussed and documented.
- ECOG Performance Status 0 – 2* ^

For women of childbearing potential

- Pregnancy should be excluded prior to receiving idelalisib and the patient provided contraceptive counseling on potential risk vs. benefit of taking idelalisib if patient were to become pregnant; effective contraception should be used during treatment and for at least 1 month after the last dose of idelalisib

Dosage and Administration

- Dose is 150 mg orally twice daily with or without food. Swallow tablets whole.
- If a dose is missed by less than 6 hours, take the dose right away and the next dose as usual; if a dose is missed by more than 6 hours, wait and take the next dose at the usual time.
- Refer to Prescribing Information for recommended Dose Modifications for toxicities.

June 2015

Updated versions may be found at <http://www.pbm.va.gov> or <https://vaww.cmopnational.va.gov/cmop/PBM/default.aspx>

Monitoring

- Symptomatic pneumonitis (i.e. cough, dyspnea, hypoxia, interstitial infiltrates on radiologic exam or decline O₂ sat'n \geq 5%)
- CBC with differential at baseline and at least every 2 weeks for first 3 months of therapy and at least weekly in patients with ANC < 1000/mm³
- AST and ALT every 2 weeks for first 3 months; every 4 weeks for next 3 months; then every 1-3 months thereafter.
Monitor weekly if ALT or AST > 3x ULN until resolved;
Withhold idelalisib if ALT or AST > 5x ULN, monitor ALT, AST and Tbili weekly until resolved
- Unusual bleeding and/or bruising
- Fever and signs/symptoms of infection
- Severity and duration of diarrhea or colitis
- Severe cutaneous reactions
- Triglycerides and blood glucose at baseline and as clinically indicated
- Evidence of disease response or progression (via radiographic scan or symptomatology)

Issues for Consideration

- Accelerated approval for FL and SLL was based upon the endpoint of overall response rate. Improvement in survival or disease-related symptoms has not been established. Use of idelalisib for the treatment of FL or SLL should be adjudicated on a case-by-case basis.
- There is a lack of evidence regarding the use of idelalisib as monotherapy in relapsed CLL. Therapy in the relapsed setting should include both idelalisib and rituximab.
- Avoid concurrent use of idelalisib with other drugs that may cause diarrhea.
- Avoid concurrent use of idelalisib with other drugs that may cause liver toxicity.

Discontinuation Recommendations

- Non-adherence with therapy, laboratory or follow-up requests
- Decline in ECOG performance status to level unacceptable for patient to maintain quality of life
- Recurrence of severe or life-threatening toxicity upon rechallenge with idelalisib
- Evidence of progressive disease (note: lymphocytosis after the start of idelalisib therapy should not be considered as disease progression, as this may be an effect of idelalisib therapy). Clinical trial data reports that the rate of lymphocytosis peaked at week 2 and resolved by week 12.

*CR Complete Response; PR Partial Response; ECOG Eastern Cooperative Oncology Group

Data from: Hallek M, Cheson BD, Catovsky D, et al. Guidelines for the diagnosis and treatment of chronic lymphocytic leukemia: a report from the International Workshop on Chronic Lymphocytic Leukemia updating the National Cancer Institute-Working Group 1996 guidelines. Blood 2008; 111:5446.

^ http://www.ecog.org/general/perf_stat.html

Prepared: June 2015. Contact: Berni Heron, VA Pharmacy Benefits Management Services

June 2015

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