NATIONAL PBM BULLETIN

MARCH 29, 2016

DEPARTMENT OF VETERANS AFFAIRS
PHARMACY BENEFITS MANAGEMENT SERVICES (PBM), MEDICAL ADVISORY PANEL (MAP),
VISN PHARMACIST EXECUTIVES (VPEs), AND THE CENTER FOR MEDICAL SAFETY (VA MedSAFE)

IDELALISIB (ZYDELIG®) SAFETY

I. ISSUE

The FDA is alerting health care professionals about the increase in serious adverse events and deaths reported among patients enrolled in clinical trials receiving idelalisib (Zydelig®) in combination with other anticancer therapies.

II. BACKGROUND

Idelalisib is currently FDA-approved for the treatment of:

- 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 (NHL) 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.

III. DISCUSSION

Gilead Sciences, Inc. halted six clinical trials that involve patients with CLL, small lymphocytic lymphoma (SLL) and indolent non-Hodgkin Lymphoma (NHL). Reported findings include a reduction in overall survival and increase in rates of serious adverse events in the idelalisib vs. control arms in three active Phase 3 trials. These trials each evaluate the addition of idelalisib to standard therapies in the first-line CLL and relapsed indolent NHL/SLL settings. Infections, including sepsis and pneumonia, were among the majority of those events.

Combined Studies 123/124/125	Idelalisib (n=664)	Control (n=402)
All deaths	49 (7.4%)	14 (3.5%)
Hazard Ratio (95% CI[1])	2.29 (1.26, 4.18)	

1 Stratified by study

The FDA is reviewing these study findings and will communicate new information as needed. Idelalisib (Zydelig®) prescribing information and REMS will be updated with current information.

IV. PROVIDER CONSIDERATIONS/RECOMMENDATIONS

- Idelalisib should NOT be used as first-line treatment of CLL.
- Educate patients about the risk of serious and/or fatal infections.
- Provide prophylaxis for Pneumocystis pneumonia (PCP/PJP) to all patients throughout their course of idelalisib therapy. Monitor for cytomegalovirus (CMV) and permanently discontinue idelalisib in those with evidence of infection or viremia (positive PCR or antigen test).
- Monitor blood counts at least every 2 weeks for the first 6 months of idelalisib treatment; increase monitoring frequency to at least weekly while absolute neutrophil count (ANC) is less than 1000/mm^3.

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- Providers should continue to report any adverse reactions with the use of idelalisib (Zydelig®) by entering the information into CPRS' Allergies/ Adverse Reactions field and/or via local reporting mechanisms. Adverse events should also be reported, as appropriate, to the VA ADERS program and FDA MedWatch (1-800-FDA-1088, fax 1-800-FDA-0178, online at https://www.accessdata.fda.gov/scripts/medwatch/medwatch-online.htm, or by mail).

V. REFERENCES

FDA Drug Safety and Availability: FDA Alerts Healthcare Professionals about Clinical Trials with Zydelig (idelalisib) in Combination with other Cancer Medicines. (Accessed March 14, 2016).

ACTIONS

- ***Facility Director*** *(or physician designee): Forward this document to the Facility Chief of Staff (COS).*
- ***Facility COS and Chief Nurse Executives:*** *Forward this document to all appropriate providers and health care staff (e.g.,* ***primary care providers, oncology staff, including contract providers, etc****.). In addition, forward to the Associate Chief of Staff (ACOS) for Research and Development (R&D). Forward to other VA employees as deemed appropriate.*
- ***ACOS for R&D:*** *Forward this document to Principal Investigators (PIs) who have authority to practice at the facility and to your respective Institutional Review Board (IRB).*