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30 January 2018

Dr Tomas Salmonson
Chair of Committee for Medicinal Products for Human Use
European Medicines Agency
30 Churchill Place
Canary Wharf
London E14 5EU
UK

Re: Withdrawal of application for a new indication for Zydelig in combination with bendamustine and rituximab for the treatment of relapsed chronic lymphocytic leukemia

Product: Zydelig (idelalisib), film-coated tablets, 100 mg and 150 mg

Procedure ref.: EMEA/H/C/003843/II/0032/G

Dear Dr Salmonson,

A group of type II variations (EMEA/H/C/003843/II/0032/G) was submitted on 31 January 2017 to request an extension to the approved chronic lymphocytic leukemia (CLL) indication for Zydelig to include its use in combination with bendamustine and rituximab based on the results of the primary analysis of pivotal Study GS-US-312-0115, entitled "A Phase 3, Randomized, Double-Blind, Placebo-Controlled Study Evaluating the Efficacy and Safety of Idelalisib (GS-1101) in Combination with Bendamustine and Rituximab for Previously Treated Chronic Lymphocytic Leukemia". The final clinical study reports for Studies GS-US-312-0123 and 101-08 were also included within this submission to provide supportive safety information for subjects with CLL.

These variations were submitted under Article 7(2)(c) of Regulation (EC) No 1234/2008 as follows:

- Variation C.I.6[a] – submission of the primary analysis of Study GS-US-312-0115 to request an extension to the approved CLL indication to include the combination of idelalisib with bendamustine and rituximab
- Variation C.I.13 – submission of the final clinical study report for Study 101-08 to provide supportive information for the first variation. Submission of this report was also made in fulfilment of PAM008
- Variation C.I.13 - submission of the final clinical study report for Study GS-US-312-0123 to provide supportive information for the first variation

Following the adoption of a second request for supplementary information by CHMP, Gilead Sciences took the decision to withdraw the application for the extended indication. This is based on the CHMP consideration that, whilst the study met the primary endpoint for progression-free survival and demonstrated a clinically meaningful benefit in overall

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survival, longer term data are required to allow the committee to conclude on a positive benefit-risk evaluation for the requested indication.

As agreed with the EMA Procedure Manager, Gilead Sciences would like to request withdrawal of the variation C.I.6[a] for an extension of indication from this group of variations, and for the current procedure to be finalized without changes to the Annexes. A response to the outstanding issues is not required as these are related to the request for an extension of indication. The procedure will conclude the assessment of the final clinical study reports for Studies GS-US-312-0123 and 101-08, the latter in fulfilment of PAM008.

The benefit-risk profile of Zydelig in combination with an anti-CD20 monoclonal antibody (rituximab or ofatumumab) for the treatment of adult patients with relapsed CLL, and of Zydelig monotherapy for the treatment of adult patients with refractory follicular lymphoma (FL), are not impacted by this withdrawal.

This withdrawal does not impact ongoing clinical trials with idelalisib or any future plans for the development of the product. Gilead reserves the right to make further submissions at a future date in this or other therapeutic indication(s).

Gilead would like to sincerely thank the rapporteur, co-rapporteur, PRAC and CHMP members for the time and support dedicated to this application.

I agree for this letter to be published on the EMA website.

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