2 December, 2013

Iclusig▼ (ponatinib): updated advice on the risk of vascular occlusive events

Dear Healthcare Professional,

ARIAD Pharma Ltd., in agreement with the European Medicines Agency (EMA) and the Irish Medicines Board (IMB) would like to inform you of strengthened warnings on the risk of vascular occlusive events associated with ponatinib and give guidance on how this risk can be managed.

Summary:

- **The number of arterial and venous thrombotic events seen in ponatinib-treated patients has increased with longer-term follow-up of ongoing phase 1 and phase 2 clinical trials. These include cardiovascular, cerebrovascular, and peripheral vascular adverse events, and venous thrombotic events.**
- **Healthcare professionals may continue to use ponatinib, with increased caution, in line with the authorised indication (see below).**
- **Ponatinib should not be used in patients with a history of myocardial infarction or stroke, unless the potential benefit of treatment outweighs the potential risk.**
- **Cardiovascular status of patients should be assessed and cardiovascular risk factors should be actively managed before starting treatment with ponatinib. Cardiovascular status should continue to be monitored and optimised during treatment.**
- **Hypertension should be medically controlled during ponatinib therapy and treatment interruption should be considered if hypertension is not controlled.**
- **Patients should be monitored for evidence of vascular occlusion or thromboembolism, and treatment should be interrupted immediately if this occurs.**

The Summary of Product Characteristics (SmPC) will be updated to include these strengthened warnings.

Further information

Iclusig® is indicated in the European Union in adult patients with:

- chronic phase, accelerated phase, or blast phase chronic myeloid leukaemia (CML) who are resistant to dasatinib or nilotinib; who are intolerant to dasatinib or nilotinib and for whom subsequent treatment with imatinib is not clinically appropriate; or who have the T315I mutation.
- Philadelphia chromosome positive acute lymphoblastic leukaemia (Ph+ ALL) who are resistant to dasatinib; who are intolerant to dasatinib and for whom subsequent treatment with imatinib is not clinically appropriate; or who have the T315I mutation.

A review of available data has been performed following new information suggesting that vascular occlusive events occur at a higher cumulative incidence than initially observed at the time of marketing authorisation.

The review shows that the cumulative number of arterial and venous thrombotic events has increased with longer-term follow-up of Iclusig treated patients in ongoing phase 1 and phase 2 clinical trials. These include cardiovascular, cerebrovascular, and peripheral vascular adverse events, and venous thrombotic events.

Patients with and without cardiovascular risk factors, including patients 50 years of age or younger, experienced these events. Vascular occlusive adverse events were more frequent with increasing age and in patients with prior history of ischemia, hypertension, diabetes, or hyperlipidaemia.

The product information will now be updated with this new information together with recommendations of how to minimise the risk

A benefit-risk consideration should always be undertaken before and during Iclusig therapy.

Healthcare professionals are recommended to monitor cardiac function and evidence of thromboembolism, vascular occlusion and ischaemia.

ARIAD will continue to monitor the safety of Iclusig through established reporting mechanisms.

Call for reporting of adverse reactions.
Please report suspected adverse reactions in patients treated with Iclusig to the Irish Medicines Board, preferably through the online reporting option at www.imb.ie, or alternatively via the downloadable or Yellow Card report form. Adverse reactions can also be reported to the IMB by calling on (01) 676 4971.

When reporting please provide as much information as possible, including information about medical history, any concomitant medication, onset and treatment dates.

As Iclusig is a newly approved product (as of 1 July 2013), this medicine is subject to additional monitoring.

Company contact point:
Please feel free to contact 00800 000 27423 if you need further information.

Or send a letter to the Marketing Authorisation Holder: ARIAD Pharma Ltd., Brooklands Business Park, Wellington Way, Weybridge, KT13 0TT, United Kingdom.

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions.

Yours faithfully

Dr Kai Chan
Head of Medical Affairs, Europe