22 February 2018
EMA/254102/2018
Committee for Medicinal Products for Human Use (CHMP)

Scientific conclusions and grounds for the variation to the terms of the marketing authorisation(s)

Active substance(s): carfilzomib

Procedure No. EMEA/H/C/PSUSA/00010448/201707

Period covered by the PSUR: 20 January 2017 – 19 July 2017

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5520
Send a question via our website www.ema.europa.eu/contact

Scientific conclusions

Taking into account the PRAC Assessment Report on the PSUR(s) for carfilzomib, the scientific conclusions of CHMP are as follows:

Analysis of all available data indicates 39 events of confusional state (of which 1 was fatal) reported in clinical trials (CT) and 70 events of confusional state (19 serious [of which 1 was fatal]) reported in Post Marketing (PM). Based on the data provided there is notable time to onset (TTO), both from CT and PM data case of dechallenge and rechallenge have been reported, as well as of dose reduction. Data indicating that Health Care Professionals (HCP) have decided to interrupt/modify/stop treatment with Kyprolis in this life-threatening indication due to occurrence of this adverse drug reaction (ADR) is additional evidence to a reasonable possibility of carfilzomib causal role. Based on this, the adverse drug reaction "confusional state" is being added to section 4.8. of the SmPC. The package leaflet is updated accordingly.

Cumulatively, 37 cases of herpes zoster infections were reported in PM setting, while High Level Term (HLT) herpes viral infections were reported in 86/2944 subjects in Clinical Trials (CT). Herpes infection cases occurred in both monotherapy studies, as well as in studies where carfilzomib was combined with dexamethasone and other products (such as lenalidomide-dexamethasone, cyclophosphamide-dexamethasone, melphalan-prednisone, or carboplatin-etoposide). The most frequently reported preferred term (PTs) were herpes zoster, oral herpes and herpes simplex and majority of patients recovered. Taking into account clinical relevance of the herpes zoster condition, as well as information provided in the SmPCs of other similar agents (bortezomib, ixazomib) i.e. class effect and plausible mechanism, the PRAC proposes to include herpes zoster in section 4.8 of the SmPC with frequency common based on CT data. It should be also clearly stated that incidence is based on CT data in which most of patients received prophylaxis. The section 4.2 of the SmPC is also aligned with this new information included in section 4.8.

The CHMP agrees with the scientific conclusions made by the PRAC.

Grounds for the variation to the terms of the marketing authorisation(s)

On the basis of the scientific conclusions for carfilzomib the CHMP is of the opinion that the benefit-risk balance of the medicinal product(s) containing carfilzomib is unchanged subject to the proposed changes to the product information

The CHMP recommends that the terms of the marketing authorisation(s) should be varied.