Busilvex

Scientific conclusions and grounds recommending the variation to the terms of the marketing authorisation

International non-proprietary name: busulfan

Procedure No. EMEA/H/C/000472/PSUSA/0464

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Scientific conclusions

Taking into account the PRAC Assessment Report on the PSURs for busulfan (intravenous use), the scientific conclusions of the CHMP are as follows:

In the PSUR, the MAH of Busilvex conducted a review of "Interstitial lung disease" in clinical and post-marketing experience. Eighty-nine (89) events were retrieved from the MAH's safety database using the SMQ "Interstitial lung disease" in the cumulative post-marketing experience. Twenty-two (22) out of those 89 events were reported as "Interstitial lung disease". It is to be noted also that 14 "Acute respiratory distress syndromes" were reported. Regarding the cumulative safety data collected within the clinical trials sponsored by the Busilvex MAH, no interstitial lung disease were reported.

Clinical and radiographic features of diffuse drug-induced interstitial lung disease are often difficult to distinguish from other causes of diffuse lung disease (e.g. infections, lung involvement of an underlying malignancy, pulmonary oedema, connective tissue disease), and there no signs, symptoms, laboratory or radiological data that could be considered as pathognomonic.

Patients may still die from interstitial lung disease notably transplant patients. Even if transplant patients are particularly at high risk of interstitial lung disease because they had many risk factors and that Busilvex administration seems to be only one of them, better information of physicians and consequently an earlier diagnosis may reduce the number of interstitial lung diseases. Consequently, the MAH proposed to add in the table of adverse reactions in the section 4.8 "Undesirable effects", the event "Interstitial lung disease" with a frequency unknown. No changes to the package leaflet were deemed necessary as the main symptoms, shortness of breath / breathlessness and cough are already presented as very common respiratory events. Interstitial lung disease is already included in section 4.8 of the SmPC of busulfan for oral use.

Therefore, in view of available data regarding interstitial lung disease, the PRAC considered that changes to the product information were warranted for busulfan for intravenous use.

The CHMP agrees with the scientific conclusions made by the PRAC

Grounds recommending the variation to the terms of the Marketing Authorisation(s)

On the basis of the scientific conclusions for busulfan for intravenous use the CHMP is of the opinion that the benefit-risk balance of the medicinal products containing the active substance busulfan for intravenous use is favourable subject to the proposed changes to the product information.

The CHMP recommends that the terms of the Marketing Authorisation(s) should be varied.