EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Committee for Medicinal Products for Human Use (CHMP)

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

International non-proprietary name: regadenoson

Procedure No. EMEA/H/C/PSUSA/00002616/201410

Period covered by the PSUR: 10 April 2014 – 9 October 2014

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Send a question via our website www.ema.europa.eu/contact

Scientific conclusions

Taking into account the PRAC Assessment Report on the PSUR for regadenoson, the scientific conclusions of CHMP are as follows:

The Marketing Authorisation Holder (MAH) conducted a review of all cases of respiratory arrest to determine if this adverse reaction occurred independently of hypersensitivity reaction or cardiac arrest (known risks of regadenoson). A cumulative review of bronchoconstriction was also conducted.

There are seven cases where respiratory arrest occurred without features of cardiac arrest or hypersensitivity reaction; in 5 of those cases the patients had a history of chronic obstructive pulmonary disease (COPD) or asthma. There was one fatal case, although it was poorly documented.

Based on this data, the PRAC considers that it is necessary to update the current warning in section 4.4 of the Summary of Product Characteristics (SmPC) to clarify that respiratory arrest can occur and to add the event to section 4.8 of the SmPC with a frequency of “not known” as there were no cases detected in clinical trials.

The cumulative review of bronchoconstriction identified 45 evaluable cases following regadenoson administration that did not have features of a hypersensitivity reaction. Of the 35 cases where medical history was provided, in 25 there was a history of bronchoconstrictive disease (asthma, COPD or bronchospasm) and in 10 there was no documented history of bronchoconstrictive disease, including 3 cases where the reporter explicitly stated that there was no history of asthma/bronchospasm/COPD.

Given the findings of the cumulative review, the PRAC considered that the current warning in section 4.4 regarding bronchoconstriction should be updated so that it is clear that bronchoconstriction can occur with regadenoson. In addition, section 4.8 of the SmPC is to be updated to include preferred terms that reflect bronchoconstriction i.e. “bronchospasm” with a frequency of “not known”, “wheezing with a frequency of “uncommon”.

The warning in section 4.4 of the SmPC regarding bronchoconstriction is also be amended to clarify that that appropriate bronchodilator therapy and resuscitative measures are available for all patients prior to regadenoson administration (not just those with a history of bronchoconstrictive disease).

Therefore, in view of available data regarding regadenoson, the PRAC considered that changes to the product information were warranted.

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

Grounds recommending the variation to the terms of the Marketing Authorisation

On the basis of the scientific conclusions for regadenoson the CHMP is of the opinion that the benefit-risk balance of the medicinal product containing regadenoson is favourable subject to the proposed changes to the product information.

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