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EMA/CHMP/310041/2013
Committee for Medicinal Products for Human Use (CHMP)

Signifor

pasireotide

Procedure No.: EMEA/H/C/002052/PSU 008

Scientific conclusions and grounds recommending the variation to the terms of the Marketing Authorisation

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The scientific conclusions of PRAC are as follows:

The MAH proposed the following changes to the product information as part of the PSUR procedure:

Update of section 4.8 of the SmPC to correct the frequency allocated to the adverse reaction 'anaemia' to 'uncommon' and section 4.4 of the SmPC with a minor change to the wording for the existing warning on hyperglycaemia. The Package leaflet has been updated accordingly.

Hyperglycaemia

Clinical data suggest a higher potential of pasireotide to induce hyperglycaemia as compared to octreotide. The MAH believes that spelling out "ketoacidosis" as a potential complication of severe hyperglycaemia in section 4.4 Special warnings and precautions for use (Glucose metabolism) would further enhance guidance to health care professionals.

The observation of cases with ketoacidosis is already mentioned in section 4.8 of the SmPC. Since the current wording in section 4.4 is considered imprecise in this regard, the proposed amendment to add ketoacidosis as an example of a potential complication associated with hyperglycaemia is acceptable to the PRAC. As information on hyperglycaemia is not given at this level of detail in the Package Leaflet, no consequential changes to the Package Leaflet are needed.

Anaemia

Anaemia is already included as an ADR in section 4.8 of the SmPC. However, the frequency allocated for the term "anemia", inadvertently labelled during table formatting as "common", was proposed by the MAH to be corrected to "uncommon" in the context of this PSUR procedure. The MAH also proposed to amend the Package Leaflet to reflect the change in the SmPC.

Anaemia is included in the submitted Core Data Sheet (CDS) with an overall frequency of 0.6 % (uncommon) based on the AEs suspected to be drug related.

The ADRs table included in the SmPC lists all adverse reactions with causal relationship between the medicinal product and the event demonstrated in line with the SmPC guideline. These data were provided in the Clinical Study Report for Study B2305. In this report, anaemia has a frequency of 0% for pasireotide 600 ug bid and 1.3 % for pasireotide 900 ug bid with an overall frequency of 0.6%. Thus the frequency "uncommon" would apply.

The proposed change of frequency for anaemia is accepted by the PRAC.

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

In addition, the MAH took the opportunity to implement some editorial changes in the annexes in line with the latest QRD template and to update section 6 of the Package Leaflet to add the contact details for the local representative in Croatia, which is acceptable.

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 Signifor the CHMP is of the opinion that the benefit-risk balance of the medicinal product containing the active substance pasireotide is favourable subject to the proposed changes to the product information.

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