20 September 2018
EMA/CHMP/778348/2018
Human Medicines Evaluation Division

Assessment report for paediatric studies submitted according to Article 46 of the Regulation (EC) No 1901/2006

Galvus

vildagliptin

Procedure no: EMEA/H/C/771/P46/044-046

Note

Assessment report as adopted by the CHMP with all information of a commercially confidential nature deleted.

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

An agency of the European Union

© European Medicines Agency, 2018. Reproduction is authorised provided the source is acknowledged.

Table of contents

1. Introduction

European Medicines Agency decision 'P/177/2011' of 26 August 2011 granted product specific waiver for vildagliptin (Galvus), (EMEA-000700-PIP02-10) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council.

However, in accordance with Article 46 of Regulation (EC) No1901/2006 the MAH submitted three post authorisation MAH sponsored observational studies performed in Japan which involved use in the pediatric population.

Article 46 of Regulation (EC) No 1901/2006 (the 'Paediatric Regulation') sets out the obligation for marketing-authorisation holders (MAHs) to submit any MAH-sponsored studies involving the use of an authorised medicinal product in the paediatric population to the competent authority, whether or not they are part of a paediatric investigation plan (PIP). For centrally authorised medicinal products, the studies should be submitted to the European Medicines Agency

In Japan the definition of pediatric age group is < 15 years while according to the EU's criterion, pediatric age group is defined as <18 years. The studies performed in Japan included adults with T2DM and as consequence patients between 15 and 18 years of age were also included. This trigger the need for submission of any MAH-sponsored studies involving the use of an authorised medicinal product in the paediatric population in accordance with Article 46 of Regulation (EC) No1901/2006.

A critical expert statement has also been submitted.

2. Scientific discussion

2.1. Information on the development program

Not applicable

2.2. Information on the pharmaceutical formulation used in the studies

Not applicable, same as for adults

2.3. Clinical aspects

2.3.1. Introduction

The MAH submitted clinical safety reports for the following observational studies conducted in patients with T2DM in Japan:

- CLAF237AJP04 - Assessment of relationship between diabetic complications/patient characteristics and clinical course
- CLAF237AJP01 - Evaluation of safety of Equa in early stages of use, and the relationship between changes in HbA1c and patient characteristics
- CLAF237A1401 - Evaluation of long-term safety and cardiovascular events etc.

2.3.2. Clinical studies

Study CLAF237AJP01

Objective

The objective of this study was to evaluate the safety of vildagliptin in early stages of use (6 months) and the relationship between changes in HbA1c and patient characteristics (BMI, age [elderly or nonelderly] etc.) and concomitant drugs (use of sulfonylurea etc.) during 6 months of use.

Study design

A 6-months observational study without control group conducted in Japan.

Study population

Patients with type 2 diabetes mellitus who have never received vildagliptin, and are not responding adequately to either of the following therapies which is a requirement in the package insert of vildagliptin at the first approval:

1. Diet therapy, exercise therapy only

2. Use of a sulfonylurea product in addition to diet therapy, exercise therapy

Sample size

A total of 10,832 patients were enrolled, and 10,498 and 10,491 patients were included in the safety and efficacy analysis sets, respectively.

Treatments

Vildagliptin 50 mg

Results

Among the 10 498 patients enrolled there was one patient below 18 years (i.e 16 years), at the time of enrolment.

There was no AE, SAE or death reported for this patient during the study.

Study CLAF237AJP04

Objective

- Evaluation of the long-term (2-year) safety and efficacy of vildagliptin 50 mg
- Assessment of the relationship between the incidence of the onset/aggravation of diabetic complications and clinical course (changes over time in HbA1c, absolute changes in HbA1c) in long-term (2-year) treatment with vildagliptin

Study design

A 2-year post marketing surveillance study.

Study population

Patients with type 2 diabetes mellitus who have never received vildagliptin

Sample size

There were 20,902 patients with confirmed registration, of which 19,501 patients database is locked. For safety analysis 19,218 patients were included in the safety analysis population.

Treatments

Vildagliptin 50 mg

Results

At time of the enrolment there were four patients with age 16, 17, 15, and 17 years in study CLAF237AJP04 study.

There was no AE, SAE or death reported for these patients during the study.

CLAF237A1401

Objective

The objective was to evaluate the long-term clinical safety and efficacy of EQUA and the occurrence of CV events for the purpose of using these data to prepare the re-examination dossier.

Study design

A multicenter post-marketing surveillance

Study population

Patients with type 2 diabetes mellitus without a history of treatment with EQUA

Only patients who are not responding adequately to either of the following therapies, which is a requirement in the package insert of EQUA at the start of this investigation:

1) Diet therapy, exercise therapy only

2) Use of a SU product in addition to diet therapy/exercise therapy

Sample size

Overall there were 3,905 patients with confirmed registration, of which 3,831 patients database is locked. In the safety analysis population 3,768 patients were included.

Treatments

Vildagliptin 50 mg

Results

At time of enrolment in study CLAF237A1401 there was one patient with an age of 16 years. There was no AE, SAE or death reported for this patient during the study.

2.3.3. Discussion on clinical aspects

In total, six subjects in the ages between 15 and 17 years have been enrolled in three MAH sponsored observational studies in Japan in patients with Type 2 diabetes treated with vildagliptin. In total, there were approximately 37 000 subjects with confirmed registration in the three studies. No new safety concerns were identified, i.e no AE, SAE or deaths were reported for any of the patients in the paediatric population.

The MAH has not provided any data regarding efficacy or exposure time of the drug in the enrolled paediatric patients. However, in this case this is acceptable since the number of patients was low and no conclusions of clinical relevance are expected.

3. CHMP overall conclusion and recommendation

No safety concern was identified among the six paediatric patients with T2DM aged between 15-17 years enrolled in the three Japanese observational studies (CLAF237AJP04, CLAF237AJP01 and CLAF237A1401).

☒ Fulfilled:

No regulatory action required.