EMA/122219/2010
EMEA/H/C/522

EPAR summary for the public

Avandamet

rosiglitazone and metformin hydrochloride

This document is a summary of the European Public Assessment Report (EPAR) for Avandamet. It explains how the Committee for Medicinal Products for Human Use (CHMP) assessed the medicine to reach its opinion in favour of granting a marketing authorisation and its recommendations on the conditions of use for Avandamet.

What is Avandamet?

Avandamet is a medicine that contains two active substances, rosiglitazone and metformin hydrochloride. It is available as tablets (yellow: 1 mg rosiglitazone and 500 mg metformin hydrochloride, and 2 mg rosiglitazone and 1,000 mg metformin hydrochloride; pale pink: 2 mg rosiglitazone and 500 mg metformin hydrochloride; pink: 4 mg rosiglitazone and 1,000 mg metformin hydrochloride).

What is Avandamet used for?

Avandamet is used in patients who have type 2 diabetes, particularly those who are overweight.

Avandamet is used in patients who are not satisfactorily controlled on metformin (an antidiabetes medicine) used on its own and at the maximum possible dose ('dual therapy').

Avandamet can also be used with a sulphonylurea (another type of antidiabetes medicine) in patients who are not satisfactorily controlled on metformin and a sulphonylurea at their maximum possible doses ('triple therapy').

The medicine can only be obtained with a prescription.

How is Avandamet used?

The recommended starting dose of Avandamet is 4 mg rosiglitazone and 2,000 mg metformin hydrochloride a day. It is given in two divided doses, either as two 1-mg/500-mg tablets or one

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7418 8416
E-mail info@ema.europa.eu **Website** www.ema.europa.eu
An agency of the European Union

2-mg/1,000-mg tablet. The rosiglitazone dose may need to be increased to 8 mg a day after eight weeks if better blood glucose control is needed, but this should be done with caution in patients who are also taking a sulphonylurea, due to the risk of fluid retention. The maximum recommended daily dose is 8 mg/2,000 mg. The dose of rosiglitazone may be added to metformin and adjusted before a patient is switched to Avandamet.

In triple therapy, when starting treatment in patients who are already taking metformin and a sulphonylurea, Avandamet is given so that the patient receives 4 mg of rosiglitazone a day, and the same dose of metformin as before. If the patient is already using triple therapy, then Avandamet is given to provide the same doses of rosiglitazone and metformin as before.

Taking Avandamet with or just after food may reduce any stomach problems caused by metformin.

How does Avandamet work?

Type 2 diabetes is a disease in which the pancreas does not make enough insulin to control the level of glucose in the blood or when the body is unable to use insulin effectively. Avandamet contains two active substances, which have different modes of action:

- rosiglitazone makes cells (fat, muscle and liver) more sensitive to insulin, which means that the body makes better use of the insulin it produces;
- metformin works mainly by inhibiting glucose production and reducing its absorption in the gut.

As a result of the action of both active substances, the blood glucose is reduced and this helps to control type 2 diabetes.

Rosiglitazone has been authorised in the European Union (EU) as Avandia since 2000, to be used with metformin in type 2 diabetes patients who are not satisfactorily controlled on metformin alone.

How has Avandamet been studied?

The studies of Avandia taken with metformin as separate tablets were used to support the use of Avandamet. Another study was also carried out comparing the effects of adding either rosiglitazone or placebo (a dummy treatment) to metformin.

In triple therapy, one study looked at the effect of adding rosiglitazone to a sulphonylurea (glibenclamide) and metformin in 1,202 patients whose blood glucose was not being controlled sufficiently.

The studies measured the level of a substance in the blood called glycosylated haemoglobin (HbA1c), which gives an indication of how well the blood glucose is controlled.

What benefit has Avandamet shown during the studies?

Avandamet was more effective than metformin alone and than placebo in reducing HbA1c. Adding rosiglitazone to treatment with metformin and a sulphonylurea brought about a small but significant extra reduction in HbA1c levels.

What is the risk associated with Avandamet?

The most common side effect with Avandamet (seen in more than 1 patient in 10) is gastrointestinal symptoms (such as feeling sick, vomiting, diarrhoea, stomach ache and loss of appetite). For the full list of all side effects reported with Avandamet, see the Package Leaflet.

Avandamet should not be used in people who may be hypersensitive (allergic) to rosiglitazone, metformin or any of the other ingredients. It must not be used in patients who have heart failure (an inability of the heart to pump enough blood around the body), an 'acute coronary syndrome' such as unstable angina (a severe type of chest pain that changes in intensity) or certain types of heart attack, diseases that could affect the oxygen supply to the tissues (such as lung or heart problems, a recent heart attack or shock), problems with their liver or kidneys, acute alcohol intoxication (excessive alcohol consumption), alcoholism, or complications of diabetes (diabetic ketoacidosis or diabetic coma).

The doses of Avandamet may need to be adjusted when given with certain other medicines such as gemfibrozil or rifampicin. The full list is available in the Package Leaflet.

Why has Avandamet been approved?

The CHMP decided that Avandamet's benefits are greater than its risks and recommended that it be given marketing authorisation.

Other information about Avandamet:

The European Commission granted a marketing authorisation valid throughout the EU for Avandamet to SmithKline Beecham Ltd. on 20 October 2003. After five years, the marketing authorisation was renewed for a further five years.

The full EPAR for Avandamet can be found here. For more information about treatment with Avandamet, read the Package Leaflet (also part of the EPAR).

This summary was last updated in 03-2010.