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**EPAR summary for the public**

# Glubrava

Pioglitazone / metformin hydrochloride

This is a summary of the European public assessment report (EPAR) for Glubrava. 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 Glubrava.



## What is Glubrava?

Glubrava is a medicine that is available as tablets containing two active substances, pioglitazone (15 mg) and metformin hydrochloride (850 mg).

## What is Glubrava used for?

Glubrava is used in adults (particularly those who are overweight) who have type 2 diabetes. Glubrava is used in patients who are not satisfactorily controlled on metformin (a diabetes medicine) used on its own and at the maximum possible dose.

The medicine can only be obtained with a prescription.

## How is Glubrava used?

The usual dose of Glubrava is one tablet taken twice a day. Patients changing from metformin only to Glubrava may need to introduce pioglitazone slowly until a dose of 30 mg per day is reached. It is possible to change to Glubrava directly from metformin if appropriate. Taking Glubrava with or just after food may reduce any stomach problems caused by metformin. Elderly patients should have their kidney function monitored regularly.

Treatment with Glubrava should be reviewed after three to six months, and discontinued in patients who are not deriving sufficient benefit. At subsequent reviews, prescribers should confirm that benefits to patients are maintained.

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## How does Glubrava 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. Glubrava contains two active substances which each have a different mode of action. Pioglitazone 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.

## How has Glubrava been studied?

Pioglitazone on its own has been approved in the EU under the name Actos and can be used with metformin in type 2 diabetes patients who are not satisfactorily controlled on metformin alone. Three studies of Actos used with metformin as separate tablets were used to support the use of Glubrava in the same indication. The studies lasted from four months to two years and involved 1,305 patients who took the combination. They measured the level in the blood of a substance (HbA1c), which gives an indication of how well the blood glucose is controlled.

## What benefit has Glubrava shown during the studies?

In all studies, adding pioglitazone 30 mg to metformin led to an improvement in the control of blood glucose, with levels of HbA1c which further decreasing by 0.64 to 0.89% compared with the levels on metformin alone.

## What is the risk associated with Glubrava?

At the start of treatment, abdominal pain (stomach ache), diarrhoea, loss of appetite, nausea (feeling sick) and vomiting may occur. These side effects are very common but disappear on their own in most cases. Lactic acidosis (a build-up of lactic acid in the body) is a side effect which may occur in less than 1 in 10,000 patients. Other side effects such as bone fracture, increased weight and oedema (swelling) may occur in less than 1 in 10 patients. For the full list of all side effects reported with Glubrava, see the package leaflet.

Glubrava must not be used in patients who have heart failure, or problems with their liver or their kidneys. Glubrava must not be used in patients who have a disease that causes lack of oxygen to the tissues such as a recent heart attack or shock. Glubrava must not be used where there is alcohol intoxication, diabetic ketoacidosis (high levels of ketones), conditions that may affect the kidneys, and during breast-feeding. It must also not be used in patients who have or have had bladder cancer or those with blood in the urine that has not yet been investigated. For the full list of restrictions, see the package leaflet.

## Why has Glubrava been approved?

The CHMP concluded that the effectiveness of pioglitazone and metformin in type 2 diabetes had been shown, and that Glubrava simplifies treatment and improves compliance when a combination of the active substances is required. The Committee decided that Glubrava's benefits are greater than its risks and recommended that it be given marketing authorisation.

## What measures are being taken to ensure the safe and effective use of Glubrava?

The company that markets Glubrava will produce educational material for doctors prescribing the medicine, which will cover the possible risk of heart failure and bladder cancer with treatments that contain pioglitazone, the criteria for selecting patients and the need to review treatment regularly and stop treatment if patients are no longer benefiting.

Recommendations and precautions to be followed by healthcare professionals and patients for the safe and effective use of Glubrava have also been included in the summary of product characteristics and the package leaflet.

## Other information about Glubrava

The European Commission granted a marketing authorisation valid throughout the European Union, for Glubrava on 11 December 2007. This authorisation was based on the authorisation granted to Competat on 28 July 2006 ('informed consent').

The full EPAR for Glubrava can be found on the Agency's website: ema.europa.eu/Find medicine/Human medicines/European Public Assessment Reports. For more information about treatment with Glubrava, read the package leaflet (also part of the EPAR) or contact your doctor or pharmacist.

This summary was last updated in 05-2016.