EMA/521799/2019
EMEA/H/C/004910

Qtrilmet (*metformin / saxagliptin / dapagliflozin*)

An overview of Qtrilmet and why it is authorised in the EU

What is Qtrilmet and what is it used for?

Qtrilmet is a diabetes medicine that contains the active substances metformin, saxagliptin and dapagliflozin. It is used to treat type 2 diabetes in:

- adults whose blood sugar is not controlled well enough with metformin combined with either saxagliptin or dapagliflozin (including those also taking a sulphonylurea, another type of diabetes medicine);
- adults who are already taking metformin, saxagliptin and dapagliflozin.

How is Qtrilmet used?

Qtrilmet can only be obtained with a prescription. It is available in two strengths of tablets containing: metformin 850 mg, saxagliptin 2.5 mg and dapagliflozin 5 mg; and metformin 1,000 mg, saxagliptin 2.5 mg and dapagliflozin 5 mg.

The dose of Qtrilmet is calculated to match the dose of metformin the patient has been taking. It is given as 2 tablets of the appropriate strength once a day with food.

How does Qtrilmet work?

Type 2 diabetes is a disease in which the pancreas does not make enough insulin or when the body cannot use insulin effectively. Insulin is important for controlling how the body converts glucose (a type of sugar) to energy and how the glucose is stored in the body. Diabetes leads to high levels of glucose in the blood.

Qtrilmet contains three active substances which all work in different ways.

- Metformin works mainly by reducing glucose production and reducing its absorption from the gut. It has been available in the EU since the 1950s.
- Saxagliptin blocks the breakdown of incretin hormones, which are released after a meal and cause the pancreas to produce insulin. By blocking their breakdown, saxagliptin causes the pancreas to produce more insulin when blood glucose levels are high. Saxagliptin also reduces the amount of glucose made by the liver, by increasing insulin levels and decreasing the levels of the hormone

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000 An agency of the European Union

glucagon. Saxagliptin, a dipeptidyl-peptidase-4 (DPP-4) inhibitor, has been authorised in the EU as Onglyza since 2009.

- Dapagliflozin blocks the action of a protein in the kidneys called sodium-glucose co-transporter 2 (SGLT2). As blood is filtered by the kidneys, SGLT2 stops glucose in the bloodstream from being passed out into the urine. By blocking the action of SGLT2, dapagliflozin causes the kidneys to pass out more glucose in the urine, thereby reducing the levels of glucose in the blood. Dapagliflozin has been authorised in the EU as Forxiga since 2012

What benefits of Qtrilmet have been shown in studies?

Three main studies have shown that the combination of metformin, saxagliptin and dapagliflozin was effective at lowering blood glucose in adults with type 2 diabetes. These studies measured the change in HbA1c levels after 24 weeks of treatment. HbA1c (glycosylated haemoglobin) is an indicator of glucose levels in the blood over the previous 2 to 3 months. The HbA1c levels of patients in the studies were at least 8% and treatment was aimed at reducing HbA1c levels to 7% or less.

In the first main study in 534 patients, the combination of metformin, saxagliptin and dapagliflozin reduced average HbA1c by 1.47 percentage points compared with metformin combined with either saxagliptin (0.88 percentage point reduction) or dapagliflozin (1.20 percentage point reduction).

In the second study in 315 patients, the combination of metformin, saxagliptin and dapagliflozin reduced average HbA1c by 0.51 percentage points compared with a reduction of 0.16 percentage points in patients receiving metformin, dapagliflozin and placebo (dummy treatment).

In the third study in 320 patients, the combination of metformin, saxagliptin and dapagliflozin reduced average HbA1c by 0.82 percentage points compared with a reduction of 0.10 percentage points in patients receiving metformin, saxagliptin and placebo.

What are the risks associated with Qtrilmet?

The most common side effects with Qtrilmet (which may affect more than 1 in 10 people) are infections of the nose and throat, hypoglycaemia (low blood sugar) when used with a sulphonylurea and effects on the gut such as nausea (feeling sick), vomiting, diarrhoea, abdominal (tummy) pain and loss of appetite.

Qtrilmet must not be used in people who are hypersensitive (allergic) to metformin, saxagliptin or dapagliflozin or to any of the other ingredients or in people who have had serious allergic reactions to a DPP-4 inhibitor (medicines similar to saxagliptin) or to a SGLT2 inhibitor (medicines similar to dapagliflozin). Qtrilmet must also not be used in patients with certain kidney, liver or heart problems or metabolic acidosis (build-up of acid in the blood), or in patients with certain conditions that can lead to metabolic acidosis.

For the full list of side effects and restrictions of Qtrilmet, see the package leaflet.

Why is Qtrilmet authorised in the EU?

The European Medicines Agency considered that the combined use of the active ingredients in Qtrilmet produces worthwhile reduction in HbA1c and that all the active ingredients contribute to this effect. Having all three active ingredients in one tablet reduces the number of tablets the patient needs to take and may improve adherence to treatment, which can improve overall management of the disease.

The pattern of Qtrilmet's side effects is manageable and similar to that in patients treated with saxagliptin and dapagliflozin added to metformin. However, reducing doses or interrupting treatment with Qtrilmet is more complicated than using the active ingredients separately.

The Agency decided that Qtrilmet's benefits are greater than its risks and it can be authorised for use in the EU.

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

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

As for all medicines, data on the use of Qtrilmet are continuously monitored. Side effects reported with Qtrilmet are carefully evaluated and any necessary action taken to protect patients.

Other information about Qtrilmet

Further information on Qtrilmet can be found on the Agency's website: ema.europa.eu/medicines/human/EPAR/qtrilmet.