Product Information as approved by the CHMP on 25 February 2016, pending endorsement by the European Commission

Amendments to relevant sections of the summary of product characteristics and package leaflet

Note:

These amendments to the relevant sections of the Summary of Product Characteristics and package leaflet are the outcome of the referral procedure.

[For Forxiga, Xigduo, Invokana, Vokanamet, Jardiance and Synjardy, the existing product information shall be amended (insertion, replacement or deletion of the text, as appropriate) to reflect the agreed wording as provided below]

Summary of product characteristics

4.4 Special warnings and precautions for use

[A warning should be added as follows]

Diabetic ketoacidosis

Rare cases of diabetic ketoacidosis (DKA), including life-threatening cases, have been reported in clinical trials and post-marketing in patients treated with SGLT2 inhibitors, including <INN>. In a number of cases, the presentation of the condition was atypical with only moderately increased blood glucose values, below 14 mmol/l (250 mg/dl). It is not known if DKA is more likely to occur with higher doses of <INN>.

The risk of diabetic ketoacidosis must be considered in the event of non-specific symptoms such as nausea, vomiting, anorexia, abdominal pain, excessive thirst, difficulty breathing, confusion, unusual fatigue or sleepiness. Patients should be assessed for ketoacidosis immediately if these symptoms occur, regardless of blood glucose level.

In patients where DKA is suspected or diagnosed, treatment with <INN> should be discontinued immediately.

Treatment should be interrupted in patients who are hospitalised for major surgical procedures or acute serious medical illnesses. In both cases, treatment with <INN> may be restarted once the patient's condition has stabilised.

Before initiating <INN>, factors in the patient history that may predispose to ketoacidosis should be considered.

Patients who may be at higher risk of DKA include patients with a low beta-cell function reserve (e.g. type 2 diabetes patients with low C-peptide or latent autoimmune diabetes in adults (LADA) or patients with a history of pancreatitis), patients with conditions that lead to restricted food intake or severe dehydration, patients for whom insulin doses are reduced and patients with increased insulin requirements due to acute medical illness, surgery or alcohol abuse. SGLT2 inhibitors should be used with caution in these patients.

Restarting SGLT2 inhibitor treatment in patients with previous DKA while on SGLT2 inhibitor treatment is not recommended, unless another clear precipitating factor is identified and resolved.

The safety and efficacy of <INN> in patients with type 1 diabetes have not been established and <INN> should not be used for treatment of patients with type 1 diabetes. Limited data from clinical trials suggest that DKA occurs with common frequency when patients with type 1 diabetes are treated with SGLT2 inhibitors.

4.8 Undesirable effects

[The following adverse reaction should be added to the table of adverse events under the SOC Metabolism and nutrition disorders with a frequency "rare" and a cross reference to section 4.4 as a footnote of the table]

Diabetic Ketoacidosis*

*(see section 4.4)

Package leaflet

2. What you need to know before you take <invented name>

[A warning should be amended as follows]

Talk to your doctor, pharmacist or nurse before taking this medicine, and during treatment:

[...]

- if you experience rapid weight loss, feeling sick or being sick, stomach pain, excessive thirst, fast and deep breathing, confusion, unusual sleepiness or tiredness, a sweet smell to your breath, a sweet or metallic taste in your mouth, or a different odour to your urine or sweat, contact a doctor or the nearest hospital straight away. These symptoms could be a sign of "diabetic ketoacidosis" – a problem you can get with diabetes because of increased levels of "ketone bodies" in your urine or blood, seen in tests. The risk of developing diabetic ketoacidosis may be increased with prolonged fasting, excessive alcohol consumption, dehydration, sudden reductions in insulin dose, or a higher need of insulin due to major surgery or serious illness.

4. Possible side effects

[An adverse event should be added as follows]

Contact a doctor or the nearest hospital straight away if you have any of the following side effects:

Rare (may affect up to 1 in 1,000 people)

- diabetic ketoacidosis

These are the signs of diabetic ketoacidosis (see also section 2 Warnings and precautions):

- increased levels of "ketone bodies" in your urine or blood

- rapid weight loss

- feeling sick or being sick

- stomach pain

- excessive thirst

- fast and deep breathing

- confusion

- unusual sleepiness or tiredness

- a sweet smell to your breath, a sweet or metallic taste in your mouth or a different odour to your urine or sweat.

This may occur regardless of blood glucose level. Your doctor may decide to temporarily or permanently stop your treatment with <invented name>.

[In addition, for Xigduo only, the sub-headers existing in section 4 of the package leaflet shall be corrected (insertion, or replacement of the text, as appropriate) to reflect the wording as provided below]

Package leaflet

4. Possible side effects

Stop taking Xigduo and contact a doctor straight away if you notice any of the following serious or potentially serious side effects:

[information related to the risk of lactic acidosis]

Stop taking Xigduo and see a doctor as soon as possible if you notice any of the following serious or potentially serious side effects:

[information related to the risks of dehydration and urinary tract infection]

Contact your doctor as soon as possible if you have any of the following side effects:

[information related to the risk of hypoglycaemia]