Bedfordshire, Luton and Milton Keynes Health and Care Partnership

NHS

BEDFORDSHIRE, LUTON AND MILTON KEYNES (BLMK) AREA PRESCRIBING COMMITTEE (APC)

Guidance for General Practitioners to support prescribing of Empagliflozin (Jardiance®) for children and young people under 18 years with Type 2 Diabetes (T2DM)

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(Version 2)
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The following organisations contribute to and participate in the BLMK APC – Bedfordshire, Luton and Milton Keynes Integrated Care Board; Bedfordshire Hospitals NHS Foundation Trust; Cambridgeshire Community Services NHS Trust; Central and North West London NHS Foundation Trust; East London NHS Foundation Trust; Milton Keynes University Hospital NHS Foundation Trust

Introduction

There has been a global upsurge in childhood overweight and obesity leading to increased occurrence of type 2 diabetes (T2DM) in children and young people (CYP). T2DM in young people is an aggressive disease with increased risk of complications leading to increased morbidity and mortality during most productive years of life. The pharmacological treatment options for CYP have been limited to metformin and insulin. However, the availability of the other glycaemic agents such as the off -label use of the SGLT2 inhibitor, **empagliflozin (Jardiance®)** adds an additional option before consideration for increasing insulin therapy.

Empagliflozin (Jardiance®)

SGLT2 inhibitors improve glycaemic control in patients with type 2 diabetes(T2DM) by reversibly inhibiting sodium-glucose co-transporter 2 (SGLT2) in the renal proximal convoluted tubule to reduce glucose reabsorption and increase urinary glucose excretion.

NICE guideline NG18 recommends empagliflozin(off-label) as an add-on in CYP with T2DM of 10 years of age or above if no improvement in glycaemic control (HbA1c >48mmol/mol or 6.5%) with metformin therapy +/- basal insulin therapy and +/- diet and exercise. (Empagliflozin as an add-on is an option if there is a clear preference or patient is unable to tolerate subcutaneous injection of liraglutide or dulaglutide)

Initiation and Dose

The lowest dose of empagliflozin that enables achievement of target glycaemic control (HbA1c ≤48mmol/mol or 6.5%) should be used. In CYP a dose of 10mg once daily is recommended. For additional glycaemic control in patients with CrCl >60ml/min, 25mg once daily dose may be considered in **exceptional circumstances** and only on the advice of the paediatric consultant.

For the indication of type 2 diabetes(T2DM), empagliflozin should not be initiated if CrCl <30ml/min.

The dose and HbA1c levels will be stabilised before the GP is asked to take over prescribing. Three monthly follow-ups, monitoring and any dose adjustment (*if applicable*) etc. will be done by the paediatric specialist hospital team.

Prescribing Guidance

To minimise risk of serious cases of diabetic ketoacidosis (DKA) in CYP with T2DM taking an SGLT2 inhibitor, patients +/- parents/carers need to be given the following advice before initiation of therapy:

- Signs and symptoms of diabetic ketoacidosis (DKA) – (including rapid weight loss, abdominal pain, fast and deep breathing, sleepiness, a sweet smell to the breath, a sweet or metallic taste in the mouth, or a different odour to urine or sweat) Advise them to seek immediate medical advice if they develop any of these.

- Risk factors for DKA - e.g., conditions leading to restricted food intake or severe hydration, sudden insulin reduction, increase insulin requirements due to acute illness, surgery, or alcohol abuse. Provide patient information on 'sick day' rules.
- When to discontinue treatment with the SGLT2 inhibitor immediately DKA is suspected or diagnosed.
- When to interrupt treatment with the SGLT2 inhibitor in patients who are hospitalised for major surgery or acute serious illnesses; treatment may be restarted once the patient's condition has stabilised.
- Advise also to seek urgent medical attention if experiencing severe pain, tenderness, erythema, or swelling in the genital or perineal area accompanied by fever or malaise.
- Fournier's gangrene (necrotising fasciitis of the genitalia or perineum) – rare but potentially life-threatening infection which has been associated with the use of SGLT2 inhibitors. If suspected SGLT2 inhibitor should be stopped and treatment should be started urgently.
- An increase in cases of lower limb amputation (primarily of the toe) has been observed in long-term clinical studies in adults with another SGLT2 inhibitor. It is unknown whether this constitutes a class effect. Like for all diabetic patients it is important to counsel patients on routine preventative foot-care.

Adverse effects & cautions

- Genital Infection – e.g., vaginal moniliasis, vulvovaginitis, balanitis
- Constipation
- Hypoglycaemia (in combination with insulin) increased risk of infection
- Skin reactions., pruritus
- Thirst and increased urination
- Urinary disorders

For further details please see Jardiance 10 mg film-coated tablets - Summary of Product Characteristics (SmPC) - (emc) (medicines.org.uk)

Monitoring

Undertaken by secondary care:

- Full blood count, liver profile, bone profile, ferritin, folate, vitamin B12, selenium, magnesium, phosphate.
- Serum amylase / lipase
- Renal function

Undertaken by secondary care at review clinics:

- Annual U&Es.
- HbA1c
- Weight
- Foot check
- Renal function
  In patients with T2DM, the glucose lowering efficacy of empagliflozin is reduced if CrCl <45 ml/min and likely absent when CrCl <30 ml/min. Therefore, if CrCl < 45 ml/min, additional glucose lowering treatment should be considered.

Follow up (in secondary care) and criteria for continuation.

After initiation patient should be monitored/followed up at the following intervals:

- At 1 month – review compliance and discuss any possible side-effects.
- At 3 monthly intervals – check HbA1c, renal function, weight, review compliance and discuss any possible side effects.
- At 12 month – review compliance and treatment target and discuss any possible side effects. Consultant to discuss continuation of treatment if the HbA1c target is not maintained, taking into consideration the progressive nature of type 2 diabetes.

Missed Doses

If a dose is missed, it should be taken as soon as the patient remembers; however, a double dose should not be taken on the same day.

Advice and Guidance

Healthcare professionals in General Practice may seek advice and guidance (as appropriate) from the paediatric diabetes consultant and paediatric diabetes specialist nurse if:

- Problems arise with tolerating empagliflozin.
- Patient develops any acute/serious diabetes complications or serious adverse effects.
- The patient is a young woman with diabetes who is planning a pregnancy or becomes pregnant. If the patient becomes pregnant, treatment should be stopped immediately, and the patient urgently referred to the Paediatric Consultant.

Key references

Diabetes (type 1 and type 2) in children and young people: diagnosis and management. NICE guideline [NG18] 01 August 2015. Last updated: 11 May 2023. https://www.nice.org.uk/guidance/ng18

Laffel, Lori M., Thomas Danne, Georgeanna J. Klingensmith, William V. Tamborlane, Steven Willi, Philip Zeitler, Dietmar Neubacher et al. (2023) Efficacy and safety of the SGLT2 inhibitor empagliflozin versus placebo and the DPP-4 inhibitor linagliptin versus placebo in young people with type 2 diabetes (DINAMO): a multicentre, randomised, double-blind, parallel group, phase 3 trial. The Lancet Diabetes & Endocrinology 11(3): 169-181.

Jardiance 10 mg film-coated tablets - Summary of Product Characteristics (SmPC) - (emc) (medicines.org.uk).

MHRA Drug Safety Update**:** SGLT2 inhibitors: reports of Fournier's gangrene (necrotising fasciitis of the genitalia or perineum) https://www.gov.uk/drug-safety-update/sglt2-inhibitors-reports-of-fournier-s-gangrene-necrotising-fasciitis-of-the-genitalia-or-perineum.

MHRA Drug Safety Update: SGLT2 inhibitors: updated advice on the risk of diabetic ketoacidosis- https://www.gov.uk/drug-safety-update/sglt2-inhibitors-updated-advice-on-the-risk-of-diabetic-ketoacidosis.