East and North Hertfordshire Clinical Commissioning Group

Herts Valleys Clinical Commissioning Group

HERTFORDSHIRE MEDICINES MANAGEMENT COMMITTEE (HMMC)
NICE TECHNOLOGY APPRAISALS – RECOMMENDED

NICE TAs 336, 390: EMPAGLIFLOZIN THERAPY FOR TREATING TYPE 2 DIABETES (T2DM)
RECOMMENDED FOR RESTRICTED USE

Name: generic (trade)	What it is	Indication	Date decision last revised	Decision status	NICE / SMC Guidance
Empagliflozin (Jardiance®)	Sodium-glucose co-transporter 2 inhibitor	Treatment of type 2 diabetes (T2DM)	September 2016 (Update of April 2015)	Final	NICE TAs 336, 390– recommended SMC – restricted recommendation

HMMC Recommendation, in line with NICE technology appraisal guidance 336 and 390:

RECOMMENDED FOR RESTRICTED USE AS AN OPTION FOR TREATING T2DM:

In monotherapy:

- Empagliflozin as monotherapy is recommended as an option for treating type 2 diabetes in adults for whom metformin is contraindicated or not tolerated and when diet and exercise alone do not provide adequate glycaemic control, only if:
  - A dipeptidyl peptidase-4 (DPP-4) inhibitor would otherwise be prescribed and
  - A sulfonylurea or pioglitazone is not appropriate.

Only continue if the person has had a reduction of at least 5.5mmol/mol (0.5%) in HbAlc in 6 months.
Initiation can be undertaken by primary, community or secondary care.

- **In a dual therapy regimen** in combination with metformin [as an alternative to pioglitazone and DPP4 inhibitors (gliptins)]:
  - Instead of a sulfonylurea as second line therapy to first line metformin when control of blood glucose remains or becomes inadequate (HbA1c ≥48mmol/mol [6.5%]), or higher level agreed with patient if:
    - The person is at significant risk of hypoglycaemia or its consequences (for example, older people and people in certain jobs [e.g. those working at heights or with heavy machinery] or people in certain social circumstances [for example, those living alone]) OR
    - The person does not tolerate a sulfonylurea or a sulfonylurea is contraindicated.
  - Only continue if the person has had a reduction of at least 5.5mmol/mol (0.5%) in HbAlc in last 6 months.
  - Initiation can be undertaken by primary, community or secondary care.

- **In combination with insulin** with or without other antidiabetic drugs (metformin +/- sulfonylurea):
  - only continue if the person has had a reduction of at least 5.5 mmol/mol (0.5%) in HbA1c in 6 months.
  - initiation should be undertaken by community or secondary care specialists or by GPs with expertise in the treatment of patients with T2DM with insulin.

- **In a triple therapy regimen** in combination with metformin and a sulfonylurea **or** metformin and a thiazolidinedione.
  - only continue if the person has had a reduction of at least 5.5 mmol/mol (0.5%) in HbA1c in 6 months.
  - initiation should be undertaken by community or secondary care specialists or by GPs where appropriate

Produced by Hertfordshire Pharmacy and Medicines Optimisation Teams East and North Herts CCG and NHS Herts Valleys CCG. This HMMC recommendation is based upon the evidence available at the time of publication. The recommendation will be reviewed upon request in the light of new evidence becoming available.

Background information, costs, monitoring, contra-indications and adverse events

- **Costs – The SGLT2 inhibitors, (empagliflozin, canagliflozin and dapagliflozin) are currently the highest cost oral antidiabetic drugs (excluding tolbutamide which is rarely used).**
- Empagliflozin is licensed and recommended by NICE for monotherapy, dual and triple therapy.
- The efficacy of empagliflozin is dependent on renal function. Refer to table for dosage information:

Usual dose	10mg od
Where 10mg daily is tolerated and 'tighter glycaemic control is needed' and eGFR ≥ 60 mL/min/1.73 m^2	25mg od
New patients with eGFR < 60 mL/min/1.73 m^2 or CrCl < 60 mL/min	contraindicated
Existing patients whose eGFR falls persistently below 60 mL/min/1.73 m^2 or CrCl 60 mL/min	Adjust or maintain dose at 10mg od
Existing patients when eGFR is persistently below 45 mL/min/1.73 m^2 or CrCl persistently below 45 mL/min	discontinue

- Empagliflozin has a flat dose-price structure: the 25mg dose costs the same as the 10mg dose.
- Monitoring of renal function is recommended as follows:
  - Prior to initiation of empagliflozin and at least annually thereafter
  - Prior to initiation of concomitant medicinal products that may reduce renal function and periodically thereafter.
- In patients 75 years and older, an increased risk for volume depletion should be taken into account.
- In patients aged 85 years and older, initiation of empagliflozin therapy is not recommended due to the limited therapeutic experience.
- **Common adverse reactions**: include urinary tract and genital infections, pruritus and increased urination.
- There is an increased risk of hypoglycaemia when combined with insulin or sulfonylureas.
- **Empagliflozin has not been studied in combination with glucagon-like peptide 1 (GLP-1) analogues**.
- **MHRA Drug Safety update June 2015** reports that serious and life-threatening cases of diabetic ketoacidosis have been reported in patients taking sodium-glucose co-transporter 2 (SGLT2) inhibitors (canagliflozin, dapagliflozin or empagliflozin). It advises to test for raised ketones in patients with acidosis symptoms, even if plasma glucose levels are near-normal,
- **MHRA Drug Safety Update April 2016** on DKA recommends:
  - not to restart treatment with any SGLT2 inhibitor in patients who experienced DKA during use, unless another cause for DKA was identified and resolved
  - 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

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

Reference:

Refer to Summary of Product Characteristics for further information on empagliflozin SPC Empagliflozin
MHRA Drug Safety Update MHRA Drug Safety Update June 2015
NICE TA 390–Empagliflozin in monotherapy for treating type 2 diabetes (T2DM), May 2016 NICE TA390
NICE TA 336–Empagliflozin in combination therapy for treating type 2 diabetes (T2DM), March 2015 NICE TA336

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