Pan Mersey
Area Prescribing Committee

ERTUGLIFLOZIN film-coated tablets (Steglatro® ▼) in a triple therapy regimen for treating type 2 diabetes

The Pan Mersey Area Prescribing Committee recommends the prescribing of ERTUGLIFLOZIN film-coated tablets (Steglatro® ▼) in a triple therapy regimen for treating type 2 diabetes in accordance with NICE TA583.

GREEN

NICE technology appraisal (TA) 583 (5 June 2019)[1] states:

- Ertugliflozin **with metformin and a dipeptidyl peptidase-4 (DPP-4) inhibitor** is recommended as an option for treating type 2 diabetes in adults when diet and exercise alone do not provide adequate glycaemic control, only if:
  - the disease is uncontrolled with metformin and a DPP-4 inhibitor, **and**
  - a sulfonylurea or pioglitazone is not appropriate
- If patients and their clinicians consider ertugliflozin to be one of a range of suitable treatments including canagliflozin, dapagliflozin and empagliflozin, the least expensive should be chosen.

See NICE Guideline 28 (last updated May 2017), Type 2 diabetes in adults: management Algorithm for blood glucose lowering therapy in adults with type 2 diabetes for further information on prescribing of blood glucose lowering therapy agents.

NB: the effectiveness of SGLT-2 inhibitors is dependent on adequate renal function; see the "Implementation Notes" for further details.

For the current advice on ertugliflozin used as monotherapy or in combination with metformin to treat type 2 diabetes, see the separate Pan Mersey policy statement and NICE TA572.

Note: Patients who are not eligible for treatment under this statement may be considered on an individual basis where their GP or consultant believes exceptional circumstances exist that warrant deviation from the rule of this policy. In this situation, follow locally defined processes.

ERTUGLIFLOZIN film-coated tablets (Steglatro® ▼) in a triple therapy regimen for treating type 2 diabetes

Effectiveness	**Safety**[2]
Ertugliflozin is the fourth sodium-glucose cotransporter-2 (SGLT-2) inhibitor available in the UK. It lowers blood glucose by reducing renal reabsorption of filtered glucose and lowers the renal threshold for glucose, thereby increasing urinary glucose excretion.[2] Other SGLT-2 inhibitors are already used with metformin and a DPP-4 inhibitor for treating type 2 diabetes.[1] NICE TA583 concluded that ertugliflozin appears to have similar health benefits to other SGLT-2 inhibitors when taken with metformin and a DPP-4 inhibitor, and it has a lower acquisition cost. But it has only been compared with other SGLT-2 inhibitors, not with other third-line treatments for type 2 diabetes (sulfonylureas or pioglitazone). Ertugliflozin is therefore recommended as an option for treating type 2 diabetes that is uncontrolled with metformin and a DPP-4 inhibitor, only if a sulfonylurea or pioglitazone is not appropriate.[1]	Contraindications: hypersensitivity to the active ingredient or any excipients, type 1 diabetes, treatment of diabetic ketoacidosis. Ertugliflozin causes an osmotic diuresis, which may lead to intravascular volume contraction causing symptomatic hypotension, particularly in impaired renal function, elderly, patients on diuretics or on anti-hypertensive therapy with a history of hypotension. Before initiation, volume status should be assessed and corrected if indicated. In case of conditions that may lead to fluid loss (e.g. GI illness), careful monitoring of volume status and electrolytes is recommended. Temporary interruption of ertugliflozin treatment should be considered until the fluid loss is corrected. Urinary glucose excretion may be associated with an increased risk of urinary tract infections. Increased risk of genital mycotic infections. Limited experience in heart failure NYHA class I - II, none in NYHA class III – IV. The MHRA issued an updated alert on increased risk of lower extremity amputations with another SGLT-2 inhibitor. Patients should be counselled about the importance of routine preventative foot care and maintaining adequate hydration Drug Safety Update (Feb 19) advised of post-marketing reports of Fournier's gangrene associated with SGLT-2 inhibitors. Consult the SPC for full information.
Cost[3] annual cost per patient Canagliflozin: £477 Dapagliflozin: £477 Empagliflozin: £477 Ertugliflozin: £383	**Patient factors**[2] Should not be initiated in patients with an eGFR <60 ml/min/1.73 m^2. Discontinue when eGFR is persistently <45 ml/min/1.73 m^2. Should not be used in patients with severe renal impairment, with end-stage renal disease (ESRD), or receiving dialysis, as it is not expected to be effective in these patients Hepatic impairment: Mild/moderate, no dosage adjustment. Severe, not recommended. There is limited experience with ertugliflozin in patients ≥ 75 years of age.

Prescribing information[2]

The recommended starting dose of ertugliflozin is 5 mg once daily. In patients tolerating ertugliflozin 5 mg once daily, the dose can be increased to 15 mg once daily if additional glycaemic control is needed. Ertugliflozin should be taken orally once daily in the morning, with or without food. In case of swallowing difficulties, the tablet could be broken or crushed as it is an immediate-release dosage form.

When ertugliflozin is used in combination with an insulin secretagogue, a lower dose of the insulin secretagogue may be required to reduce the risk of hypoglycaemia.

Implementation notes

Renal function should be monitored prior to initiation of ertugliflozin and at least yearly thereafter. Additional monitoring is recommended prior to initiation of concomitant medicines that may reduce renal function and periodically thereafter.

Ertugliflozin should not be initiated in patients with an eGFR <60 ml/min/1.73m^2 and should be discontinued if eGFR persistently < 45 ml/min/1.73m^2.[2]

Consideration should be given to stopping treatment with ertugliflozin in patients who develop events which may precede amputation such as lower-extremity skin ulcer, infection, osteomyelitis or gangrene.[2]

References

1. National Institute for Health and Care Excellence. NICE TA583: Ertugliflozin with metformin and a dipeptidyl peptidase-4 inhibitor for treating type 2 diabetes, 05 June 2019. Accessed online 05 June 2019.
2. Merck, Sharp and Dohme Limited. Summary of Product Characteristics: Steglatro 5 mg and 15 mg film-coated tablets, 02 April 2019. Accessed online 03 May 2019.
3. NHSBA Dictionary of Medicine and Devices (dm+d Browser). Accessed 03 May 2019.