Hertfordshire and West Essex Integrated Care System

NHS Hertfordshire and West Essex Integrated Care Board

# Sodium-glucose cotransporter-2 (SGLT2) inhibitors (Gliflozins) in Adults with Type 2 Diabetes (T2DM)

- There are currently four SGLT2 inhibitors (dapagliflozin, canagliflozin, empagliflozin and ertugliflozin) licensed in the UK for the management of adults with T2DM.
- Dapagliflozin (generic) is preferred 1st line choice of SGLT2 inhibitor (least expensive SGLT2 inhibitor).
- No head-to-head trials between the SGLT2 inhibitors have been conducted.
- Prescribing of SGLT-2 inhibitors to be in line with NICE NG28 and relevant NICE TAs. See table below for further details. Cardiovascular outcome data should be considered when making a decision on choice of SGLT-2 inhibitor. If patients and their clinicians consider ertugliflozin to be 1 of a range of equally suitable treatments, including canagliflozin, dapagliflozin and empagliflozin, the least expensive should be chosen.
- Dapagliflozin, canagliflozin and empagliflozin in combination with insulin with or without other antidiabetic drugs should only be initiated by community or secondary care specialists or by GPs with expertise in the treatment of patients with T2DM with insulin-AMBER INITIATION
- Saxagliptin/Dapagliflozin (QTERN®) for the treatment of T2DM in adults is NOT RECOMMENDED for prescribing in primary or secondary care (DOUBLE RED)

**Comparative data for SGLT-2 inhibitors**

| | 28 day cost for standard daily doses[1,2] | 28 day cost for increased daily doses | Monotherapy | With Insulin (+/- MET) | | Dual therapy | Triple therapy | Hepatic Impairment | Renal impairment (eGFR ml/min/1.73m$^2$) | | |
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| | | | License and NICE TA | License | NICE | License and NICE | License and NICE | | **≥60 MILD** | **≥45 <60 MODERATE** | **<45 SEVERE** |
| **Dapagliflozin (preferred choice of SGLT2 inhibitor)** | 10mg daily £13.92<br>5mg daily £15.05 | - | ✓[1] NICE TA390 | ✓[2] | ✓ NICE TA288 | ✓ (with MET)[3] NICE TA288 | ✓ (with MET & SU) NICE TA418 | Mild/moderate – 10mg daily<br>Severe – start at 5mg daily, titrate to 10mg if tolerated | No dose adjustment needed | **New patients** – No dose adjustment needed<br>**Existing Patients** can continue without dose adjustment | **New patients** –If <15 then not recommended.<br>**New and Existing Patients** consider additional antidiabetic drugs as reduced efficacy. |
| **Canagliflozin** | 100mg daily £36.59 (£39.20 for 30 tablet pack) | 300mg daily[4,5] £36.59 (£39.20 for 30 tablet pack) | ✓[1] NICE TA390 | ✓[2] | ✓ NICE TA315 | ✓ (with MET)[3] NICE TA315 | ✓ (with MET & SU or MET & PIO) NICE TA315 | Mild/moderate - No dose adjustment<br>Severe – not recommended | [6]No dose adjustment needed | **New patients** – Initiate with 100mg<br>**Existing patients** – Continue 100 mg. | **New patients** – Initiate with 100mg. If <30 then it should not be initiated.<br>**Existing Patients** - Continue 100 mg daily. |
| **Empagliflozin** | 10mg daily[7] £36.59 | 25mg daily[4] £36.59 | ✓[1] NICE TA390 | ✓[2] | ✓ NICE TA336 | ✓ (with MET)[3] NICE TA336 | ✓ (with MET & SU or MET & PIO) NICE TA336 | Mild/moderate - No dose adjustment<br>Severe – not recommended | [6]No dose adjustment needed | **New patients** – Not recommended.<br>**Existing patients** – Adjust/maintain dose at 10mg OD | **New patients** – Not recommended.<br>**Existing Patients** - discontinue. |

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| **Ertugliflozin ▼** | 5mg daily £29.40 | 15mg daily £29.40[8,9] | ✓[1] NICE TA572 | ✓[2] | Not stated | ✓ (with MET)[3] NICE TA572 | ✓ (with MET & DPP-4)[10] NICE TA583 | Mild/moderate - No dose adjustment Severe – not recommended | [11]No dose adjustment needed | **New patients** - Not recommended. **Existing Patients** can continue without dose adjustment | **New patients** - Not recommended. **Existing Patients** - discontinue. |

MET= metformin; SU= sulphonylurea; PIO=pioglitazone DPP-4 = dipeptidyl peptidase inhibitor

1= Where MET is inappropriate and only if a DPP-4 inhibitor (gliptin) would otherwise be prescribed and a SU or PIO is not appropriate.

2=when used in combination with insulin or an insulin secretagogue, a lower dose of insulin or the insulin secretagogue may be required to reduce the risk of hypoglycaemia.

3= In combination with metformin only if SU contraindicated or not tolerated or if there is significant risk of hypoglycaemia

4=Where standard daily dose is tolerated and 'tighter glycaemic control is needed' and eGFR ≥ 60 ml/min.

5=Care should be taken when increasing the dose in patients ≥ 75 years of age, patients with known cardiovascular disease, or other patients for whom the initial canagliflozin-induced diuresis poses a risk. In patients with evidence of volume depletion, correcting this condition prior to initiation of canagliflozin is recommended.

6= Monitor renal function before initiating and at least annually. Thereafter, prior to concomitant medical products that may reduce renal function.

7= in patients 75 years old and older, an increased risk for volume depletion should be considered. In patients aged 85 years and older, initiation is not recommended due to limited therapeutic experience.

8= In patients who tolerate 5mg and additional glycaemic control is required the dose can be increased to 15mg

9= In patients with volume depletion, correcting this condition prior to initiation is recommended. Limited experience in patients older than 75 years.

10= In triple therapy with MET and a DPP-4 only if the disease is not controlled and a SU or PIO is not appropriate.

11= Monitor renal function before initiating and periodically during treatment. More frequently in patients with an eGFR < 60 ml/min.

12= Prices as per drug tariff November 2025.

## Common side effects

**Canagliflozin**

- Balanoposthitis; constipation; dyslipidaemia; hypoglycaemia (in combination with insulin or sulfonylurea); increased risk of infection; nausea; thirst; urinary disorders; urosepsis

**Dapagliflozin**

- Back pain; balanoposthitis; cystitis; dizziness; dyslipidaemia; hypoglycaemia (in combination with insulin or sulfonylurea); increased risk of infection; prostatitis; skin reactions; urinary disorders' vulvovaginal disorders

**Empagliflozin**

- Balanoposthitis; constipation; hypoglycaemia (in combination with insulin or sulfonylurea); hypovolaemia (more common in elderly); increased risk of infection; skin reactions; thirst; urinary disorders; urosepsis

**Ertugliflozin ▼**

- Hypoglycaemia; hypovolaemia; increased risk of infection; polydipsia; thirst; urinary disorders; vulvovaginal pruritus;

**Drug Interactions- see full SPC for further details under each drug (www.medicines.org.uk )**

**All SGLT-2 inhibitors (Canagliflozin, Dapagliflozin, Empagliflozin and Ertugliflozin)**

- Effect of diuretics may be increased, increased risk of dehydration and hypotension.
- Hypoglycaemic effects of insulin and insulin secretagogues, such as sulphonylureas may be enhanced

**Dapagliflozin**

- Lithium- may increase renal lithium excretion and the blood lithium levels may be decreased. Serum concentration of lithium should be monitored more frequently after dapagliflozin initiation and dose changes

**Canagliflozin**

- Lithium- may decrease serum lithium concentrations. Monitor serum lithium concentration more closely during treatment with canagliflozin
- Digoxin- No dose adjustment of digoxin is recommended but patients should be monitored.
- Dabigatrin- concentrations of dabagatrin may be increased in the presence of canagliflozin, monitoring should be exercised when combined.
- Enzyme inducers such as St. John's wort [*Hypericum perforatum*], rifampicin, barbiturates, phenytoin, carbamazepine, ritonavir and efavirenz may decrease canagliflozin concentrations and may lead to decreased efficacy.
- Cholestyramine may decrease canagliflozin absorption. Administer canagliflozin 1 hour before or 4 hours after cholestyramine.

**Empagliflozin**

- Co-medication with known inducers of UGT enzymes (such as St. John's wort [*Hypericum perforatum*], barbiturates, phenytoin, carbamazepine, ritonavir, efavirenz) should be avoided due to a potential risk of decreased efficacy.
- Lithium- may increase renal lithium excretion and the blood lithium levels may be decreased. Serum concentration of lithium should be monitored more frequently after dapagliflozin initiation and dose changes

**MHRA Drug Safety Update**

- MHRA Drug Safety update April 2016: SGLT-2 inhibitors: updated advice on the management of the risk of diabetic ketoacidosis
- MHRA Drug Safety update March 2017: Canagliflozin (Invokana, Vokanamet): increased risk of lower-limb amputation (mainly toes) in patients with type 2 diabetes.
- MHRA Drug Safety update February 2019: SGLT2 inhibitors: reports of Fournier's gangrene (necrotising fasciitis of the genitalia or perineum).
- MHRA Drug safety update March 2020: SGLT2 inhibitors: monitor ketones in blood during treatment interruption for surgical procedures or acute serious medical illness.

**Cardiovascular Outcome Trial (CVOT) Data from RCTs**

- Empagliflozin: **EMPA-REG Outcomes study**. Secondary prevention population. Primary endpoint: 3 point MACE (major adverse cardiovascular events) showed a relative risk reduction of 14% compared to placebo. Mean observation time in the study was 3.1 years.
- Canagliflozin: **CANVAS program**. 1/3 primary prevention and 2/3 secondary prevention population. Primary endpoint: 3 point MACE relative risk reduction of 14% compared to placebo. Mean duration of follow up in the study was 188.2 weeks.
- Dapagliflozin: **DECLARE-TIMI58.** 60% primary prevention and 40 % secondary prevention population. Primary endpoints: (1) 3 point MACE not significantly reduced compared to placebo, (2) Hospitalization for heart failure or cardiovascular death relative risk reduction of 17% compared to placebo. Median follow up in the study was 4.2 years.
- Ertugliflozin: **VERTIS-CV.** Primary endpoint: Showed non-inferiority for 3 point MACE compared with placebo. Secondary key endpoints were not met (outcome of CV death/hospitalisation for heart failure, CV death and renal composite. Patients were followed for a mean of 3.5 years. Major adverse cardiac event reductions were not statistically significant for Ertugliflozin.

**References**


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- NICE TA679**:** Dapagliflozin for treating chronic heart failure with reduced ejection fraction, February 2021. Available at http://www.nice.org.uk/guidance/TA679
- EMPA-REG OUTCOME- Zinman, B., Inzucchi, S., Lachin, J., Wanner, C., Ferrari, R., Fitchett, D., Bluhmki, E., Hantel, S., Kempthorne-Rawson, J., Newman, J., Johansen, O., Woerle, H. and Broedl, U. (2014). Empagliflozin cardiovascular outcome event trial in type 2 diabetes mellitus patients (EMPA-REG OUTCOME™). New England Journal of Medicine (2015) https://www.nejm.org/doi/full/10.1056/NEJMoa1504720
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| Version | 1.3 Update making dapagliflozin first choice of treatment. |
| Developed by | Pharmacy and Medicines Optimisation Team, Hertfordshire and West Essex (HWE) ICB with relevant HWE ICS stakeholders. |
| Approved by | Hertfordshire & West Essex Area Prescribing Committee |
| Date approved/updated | Updated September 2024<br>Updated October 2025 |
| Review date: | The recommendation is based upon the evidence available at the time of publication. This recommendation will be reviewed upon request in the light of new evidence becoming available. |
| Superseded version | 1.1 Harmonisation of Hertfordshire Medicines Management Committee (HMMC) guidance and West Essex Medicines Optimisation Programme Board (WEMOPB) guidance updates include:<br>• Rebadging with HWE ICB and removal of ENHCCG and HVCCG headers<br>• Review date removed and replaced with standard statement.<br>1.2 Update following June 2024 HWE APC decision to adopt NICE NG28 treatment algorithm for type 2 diabetes in adults |