# SMC advice for SGLT2 inhibitors

<table>
<thead>
<tr>
<th></th>
<th>JARDIANCE empagliflozin&lt;sup&gt;14&lt;/sup&gt; (10mg, 25mg)</th>
<th>canagliflozin&lt;sup&gt;15&lt;/sup&gt; (100mg, 300mg)</th>
<th>dapagliflozin&lt;sup&gt;16&lt;/sup&gt; (5mg, 10mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SMC</strong></td>
<td>October 2014</td>
<td>June 2014</td>
<td>Jan 2013</td>
</tr>
<tr>
<td>Dual therapy</td>
<td>✔️*</td>
<td>✔</td>
<td>✔️**</td>
</tr>
<tr>
<td>Triple (Met + SU) therapy</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>Triple (Met + TZD) therapy</td>
<td>✔</td>
<td>✔</td>
<td>No guidance provided†</td>
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<tr>
<td>With insulin</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
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SU - sulphonylurea, TZD - thiazolidinediones

* when a sulphonylurea is inappropriate

** when metformin alone with diet and exercise does not provide adequate glycaemic control and a sulphonylurea is inappropriate.

† Dapagliflozin is not recommended for use in combination with pioglitazone.
empagliflozin (Jardiance®) is accepted for restricted use within NHS Scotland.

**Indication under review:** Treatment of type 2 diabetes to improve glycaemic control in adults as add-on combination therapy: in combination with other glucose-lowering medicinal products including insulin, when these, together with diet and exercise, do not provide adequate glycaemic control.

**SMC restriction:** to use in the following situations:
- dual therapy in combination with metformin, when a sulphonylurea is inappropriate
- triple therapy in combination with metformin plus standard of care
- add-on to insulin therapy in combination with insulin plus standard of care

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**Prescribing Information (UK)**

**JARDIANCE® 10mg and 25mg film-coated tablets**

Film-coated tablets containing 10mg or 25mg empagliflozin. **Indication:** Treatment of type 2 diabetes mellitus to improve glycaemic control in adults: As monotherapy when diet and exercise alone do not provide adequate glycaemic control in patients for whom use of metformin is considered inappropriate due to intolerance; as add-on combination therapy with other glucose-lowering medicinal products including insulin when these together with diet and exercise do not provide adequate glycaemic control. **Dose and Administration:**

- **Monotherapy or add-on combination:** The recommended starting dose is 10mg once daily. In patients tolerating empagliflozin 10mg once daily who have eGFR ≥ 60ml/min/1.73m² and need tighter glycaemic control, the dose can be increased to 25mg once daily. The maximum daily dose is 25mg. When used with sulphonylurea or insulin a lower dose of these may be considered to reduce the risk of hypoglycaemia. **Renal impairment:** Efficacy is dependent on renal function. No dose adjustment is required for patients with an eGFR > 60ml/min/1.73m² or CrCl > 60ml/min. Do not initiate in patients with an eGFR < 60ml/min/1.73m² or CrCl < 60ml/min. In patients tolerating empagliflozin whose eGFR falls persistently below 60ml/min/1.73m² or CrCl below 60ml/min, the dose of empagliflozin should be reduced to or maintained at 10mg once daily. Discontinue when eGFR is persistently below 45ml/min/1.73m² or CrCl persistently below 45ml/min. Not for use in patients with end stage renal disease (ESRD) or on dialysis. **Hepatic impairment:** No dose adjustment is required when eGFR is persistently below 45ml/min/1.73m² or CrCl persistently below 45ml/min. Not for use in patients with hepatic impairment. Elderly patients: No dose adjustment is recommended based on age. In patients 75 years and older, an increased risk for volume depletion should be taken into account. Not recommended in patients ≥ 80 years or older. Paediatric population: No data are available. The tablets can be taken with or without food, swallowed whole with water. If a dose is missed, it should be taken as soon as the patient remembers. A double dose should not be taken on the same day. **Contraindications:**

- Hypersensitivity to the active substance or to any of the excipients.

**Warnings and Precautions:**

Jardiance should not be used in patients with type 1 diabetes or for the treatment of diabetic ketoacidosis. Renal impairment and elderly patients: See under Dose and Administration. Monitor renal function prior to initiation and at least annually. Cases of hepatic injury have been reported with empagliflozin in clinical trials. A causal relationship between empagliflozin and hepatic injury has not been established. Osmotic diuresis accompanying therapeutic glucosuria may lead to a modest decrease in blood pressure. Therefore, caution should be exercised in patients with known cardiovascular disease, patients on anti-hypertensive therapy with a history of hypotension or patients aged 75 years and older. In case of conditions that may lead to fluid loss (e.g. gastrointestinal illness), careful monitoring of volume status and electrolytes is recommended. Temporary interruption of treatment with empagliflozin should be considered until the fluid loss is corrected. Temporary interruption of empagliflozin should be considered in patients with complicated urinary tract infections. Experience in New York Heart Association (NYHA) class I-ll is limited, and there is no experience in clinical studies with empagliflozin in NYHA class III-IV. Due to its mechanism of action, patients taking Jardiance will test positive for glucose in their urine. The tablets contain lactose and should not be used in patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency, or glucose-galactose malabsorption. **Interactions:** Use with diuretics may increase the risk of dehydration and hypotension. Insulin and insulin secretagogues may increase the risk of hypoglycaemia therefore, a lower dose of insulin or an insulin secretagogue may be required. The effect of UGT induction on empagliflozin has not been studied. Co-medication with known inducers of UGT enzymes should be avoided due to a potential risk of decreased efficacy. Interaction studies conducted in healthy volunteers suggest that the pharmacokinetics of empagliflozin were not influenced by coadministration with metformin, glimepiride, pioglitazone, sitagliptin, linagliptin, warfarin, verapamil, ramipril, simvastatin, torasemide and hydrochlorothiazide. Interaction studies conducted in healthy volunteers suggest that empagliflozin had no clinically relevant effect on the pharmacokinetics of metformin, glimepiride, pioglitazone, sitagliptin, linagliptin, simvastatin, warfarin, ramipril, digoxin, diuretics and oral contraceptives. **Fertility, pregnancy and lactation:** There are no data from the use of empagliflozin in pregnant women. Use should be avoided avoid during early pregnancy and is not recommended during the second and third trimester of pregnancy. No data in humans are available on excretion of empagliflozin into milk. Jardiance should not be used during breast-feeding. No studies on the effect on human fertility have been conducted for Jardiance. **Undesirable effects:**

- Frequencies are defined as very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1,000 to <1/100). Very common: Hypoglycaemia (when used with sulphonylurea or insulin). Common: Vaginal moniliasis, vulvovaginitis, balanitis and other genital infections, urinary tract infection, pruritus (generalised), increased urination. Uncommon: Volume depletion, dysuria. Prescribers should consult the Summary of Product Characteristics for further information on side effects. **Pack sizes and NHS price:**

10mg: 28 tablets £36.59, 25mg: 28 tablets £36.59. **Legal category:** POM MA numbers: 10mg: 28 tablets EU/1/14/930/013; 25mg: 28 tablets EU/1/14/930/004. **Marketing Authorisation Holder:** Boehringer Ingelheim International GmbH, D-55216 Ingelheim am Rhein, Germany. Prescribers should consult the Summary of Product Characteristics for full prescribing information. **Prepared in February 2015.**

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**SMC UK/EMP/00196 Date of preparation: July 2015**

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**Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/ yellowcard Adverse events should also be reported to Boehringer Ingelheim Drug Safety on 0800 328 1627 (freephone). (UK only)**