Key points

- Ertugliflozin is indicated in adults (≥18 years of age) with type 2 diabetes mellitus, as an adjunct to diet and exercise to improve glycaemic control\(^1\).
- Ertugliflozin significantly reduced HbA1c, body weight*, and systolic blood pressure* compared with placebo and reductions were sustained over the course of the VERTIS clinical trial programme\(^2\).
- Switching patients on other SGLT-2 inhibitors to Steglatro® could generate estimated potential annual savings of £17,485 per 100,000 people, and of £51,243 for an average CCG (see assumptions).\(^3,4\)

\(^*\) Ertugliflozin is not indicated for body weight or systolic blood pressure reduction.

**Drug name**

Steglatro® (Ertugliflozin)

**Indication**

- Ertugliflozin is indicated in adults (≥18 years of age) with type 2 diabetes mellitus, as an adjunct to diet and exercise to improve glycaemic control;\(^1\)
  - as monotherapy in patients for whom the use of metformin is considered inappropriate due to intolerance or contraindications
  - in addition to other medicinal products for the treatment of diabetes.

**Dosage**

- The recommended starting dose of ertugliflozin is 5 mg once daily—the dose can be increased to 15 mg once daily if additional glycaemic control is needed\(^1\).
- Renal impairment;\(^1\)
  - do not initiate in patients with an eGFR < 60 ml/min/1.73m\(^2\) or creatinine clearance (CrCl) < 60 ml/min
  - discontinue when eGFR is persistently < 45 ml/min/1.73m\(^2\) or CrCl is persistently < 45 ml/min
- When ertugliflozin is used in combination with insulin or an insulin secretagogue, a lower dose of insulin or of the insulin secretagogue may be required to reduce the risk of hypoglycaemia\(^1\).
- In patients with volume depletion, correcting this condition prior to initiation of ertugliflozin is recommended.\(^1\)

**Cardiovascular safety**

- The VERTIS-CV trial achieved its primary endpoint of non-inferiority for major adverse cardiovascular events compared with placebo in patients with type 2 diabetes mellitus and established atherosclerotic cardiovascular (CV) disease (Hazard ratio [HR]: 0.97 [95% CI: 0.85–1.11], p < 0.001)\(^5\).
- The key secondary endpoints were not met. Statistical significance was not reached for the secondary composite endpoint of CV death or hospitalisation for heart failure (HHF); no further testing could be performed due to the hierarchical statistical testing method employed\(^2\).
- HHF was a pre-specified secondary endpoint but did not have an associated hypothesis and was not part of the hierarchical statistical plan; a relative risk reduction of 30% was observed (absolute risk reduction = 1.1%, 2.5% pooled ertugliflozin group vs 3.6% placebo) (HR: 0.70 [95% CI: 0.54–0.90])\(^3\).
- Ertugliflozin was generally well tolerated, with a safety profile consistent with the SGLT-2 inhibitor class\(^2\).
- The incidence of adverse events, serious adverse events, and discontinuation due to adverse events was similar between ertugliflozin and placebo treatment arms, consistent with that observed across the VERTIS programme\(^2\).
- The incidences of symptomatic hypoglycaemia, hypovolemia, pancreatitis and bone fracture were low and similar in the ertugliflozin and placebo treatment arms\(^2\).
- No adverse events of Fournier’s gangrene were reported\(^2\).
- The frequencies of urinary tract infections and genital mycotic infections were higher with ertugliflozin vs. placebo\(^2\).
- The incidence of amputations, was numerically higher with ertugliflozin vs. placebo.\(^2\)

**Budgetary implications**

- Ertugliflozin offers an opportunity to realise cost savings when prescribing an SGLT-2 inhibitor.
- Ertugliflozin list price is approximately 20% lower than all other SGLT-2 inhibitors\(^3\).

<table>
<thead>
<tr>
<th>SGLT-2 inhibitor</th>
<th>28 days supply(^4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ertugliflozin</td>
<td>£29.40</td>
</tr>
<tr>
<td>Dapagliflozin</td>
<td>£36.59</td>
</tr>
<tr>
<td>Canagliflozin</td>
<td>£36.59</td>
</tr>
<tr>
<td>Empagliflozin</td>
<td>£36.59</td>
</tr>
</tbody>
</table>

- In 2017, 3799 packs of SGLT-2 inhibitors were used per 100,000 people at the cost of £36.59 per pack;\(^3,4\) this represents a cost of £88,979 in patients without established cardiovascular disease (eCVD). Switching patients without eCVD to ertugliflozin could generate estimated potential savings of £17,485 per 100,000 people and £51,243 for an average clinical commissioning group (CCG)\(^1\).
- **Estimate the potential savings for your CCG using this budget impact model** (this link will take you to an MSD promotional website).

\(^1\) The costs were calculated using the following data:
\(a\). annual sales of SGLT-2 inhibitors (2017) = 2,523,000 in the UK
\(b\). current costs at £36.59 per pack\(^3\)
\(c\). Steglatro® costs at £29.40 per pack\(^3\)
\(d\). type 2 diabetes mellitus population without established cardiovascular disease = 64%\(^6\)
\(e\). average CCG population = 293,074\(^6\)

**Evidence for use**

- Ertugliflozin provides significant HbA1c reductions as well as body weight and systolic blood pressure reductions, consistent across the VERTIS clinical trial program\(^7\)–\(^9\).
- Steglatro® is not licensed for body weight or blood pressure reduction.

**Guidelines in Practice**

Steglatro® (Ertugliflozin)

This formulary decision guide was developed from content provided by MSD Ltd in a format developed by Guidelines in Practice. MSD Ltd carried out full medical approval to ensure compliance with regulations. Prescribing information and adverse event reporting can be found overleaf.

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Date of preparation: June 2020
**Placebo-adjusted LS mean reduction from baseline at week 26:**

<table>
<thead>
<tr>
<th>Therapy and study</th>
<th>Dose (mg)</th>
<th>HbA1c (%)</th>
<th>Body weight (Kg)</th>
<th>Systolic blood pressure (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monotherapy</td>
<td>5</td>
<td>-0.99</td>
<td>-1.76</td>
<td>-3.31*</td>
</tr>
<tr>
<td>VERTIS-mono(^2)</td>
<td>15</td>
<td>-1.16</td>
<td>-2.16</td>
<td>-1.71*</td>
</tr>
<tr>
<td>Dual therapy</td>
<td>5</td>
<td>-0.7</td>
<td>-1.7</td>
<td>-3.7</td>
</tr>
<tr>
<td>(+ metformin)</td>
<td>15</td>
<td>-0.9</td>
<td>-1.6</td>
<td>-4.5</td>
</tr>
<tr>
<td>Triple therapy</td>
<td>5</td>
<td>-0.7</td>
<td>-2.0</td>
<td>-2.9</td>
</tr>
<tr>
<td>VERTIS-met(^6)</td>
<td>15</td>
<td>-0.8</td>
<td>-1.7</td>
<td>-3.9</td>
</tr>
<tr>
<td>VERTIS-sita(^2)</td>
<td>n=464</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\*superiority over placebo not statistically significant

**Safety profile**

- Ertugliflozin should not be used in patients with type 1 diabetes mellitus\(^1\)
- Very common reported adverse reactions are vulvovaginal mycotic infections and other female genital mycotic infections\(^1\)
- Common adverse events include: balanitis candida and other male genital mycotic infections, hypoglycaemia, volume depletion, increased urination, vulvovaginal pruritus, thirst, serum lipids changed, haemoglobin and blood urea nitrogen increase\(^1\)
- Serious diabetic ketoacidosis occurs rarely\(^1\)
- Ertugliflozin may add to the diuretic effect of diuretics and may increase the risk of dehydration and hypotension\(^1\)
- Ertugliflozin may increase the risk of hypoglycaemia when used in combination with insulin and/or an insulin secretagogue; therefore, a lower dose of insulin or an insulin secretagogue may be required to reduce the risk of hypoglycaemia when used in combination with ertugliflozin\(^1\)
- Please refer to the summary of product characteristics for a full list of safety information.\(^1\)

**References**

4. IQVIA. Retail dispensing audit—units MAT. December 2017.

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**STEGLATRO® (ertugliflozin)**

**PRESCRIBING INFORMATION**

Refer to Summary of Product Characteristics (SmPC) before prescribing.

**PRESENTATION**

Film-coated tablets containing 5 mg or 15 mg of ertugliflozin (as ertugliflozin L-pyroglutamic acid)

**USES**

Type 2 diabetes mellitus as an adjunct to diet and exercise to improve glycaemic control:

- as monotherapy in patients for whom the use of metformin is considered inappropriate due to intolerance or contraindications.
- with other anti-diabetic medicinal products.

**DOSE AND ADMINISTRATION**

Recommended starting dose is 5 mg once daily. Increase to 15 mg once daily if necessary. Assess renal function and correct volume depletion prior to initiation.

**Renal impairment:** Do not initiate in patients with eGFR <60mL/min/1.73m\(^2\). Discontinue when eGFR persistently <45 mL/min/1.73 m\(^2\). Haptic impairment: mild or moderate impairment: no dose adjustment required; severe impairment: not recommended. Elderly >65 years: no dose adjustment required; >75 years: limited data. Children <18 years: no data.

**CONTRA-INDICATIONS**

Hypersensitivity to active substance or excipients.

**PRECAUTIONS**

Do not use in patients with type 1 diabetes. Symptomatic hypotension may occur upon initiation of therapy, particularly in patients with impaired renal function. Assess volume status prior to initiation. Consider temporary interruption of therapy if volume depletion occurs. Use with caution in patients at risk of DKA. If DKA is suspected or diagnosed, discontinue ertugliflozin and treat promptly. No experience in NYHA class III-IV. Contains lactose monohydrate. Do not use in patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption. Do not use urine glucose or 1,5-AG assay to monitor glycaemic control.

**Drug interactions:** Diuretics, insulin, sulphonylureas.

**Pregnancy and Lactation:** Not recommended.

**SIDE EFFECTS**

Refer to SmPC for complete information on side effects. Very common (≥ 1/10): vulvovaginal mycotic infection and other female genital mycotic infections. Common (≥ 1/100 to < 1/10): balanitis candida and other male genital mycotic infections, hypoglycaemia, volume depletion, increased urination, vulvovaginal pruritus, thirst, serum lipid changes, increased haemoglobin and BUN. Uncommon (≥ 1/1,000 to <1/100): Dysuria, blood creatinine increased, glemorlar filtration decreased.

**Warning**

Common (≥ 1/100 to < 1/10): Hypoglycaemia. Not known: FOURIER’s gangrene.

**PACKAGING QUANTITIES AND BASIC NHS COST**

5 mg x 28: £29.40
15 mg x 28: £29.40

**Marketing Authorisation numbers**

5 mg x 28: EU/1/18/1267/002
15 mg x 28: EU/1/18/1267/008

**Marketing Authorisation Holder**

Merk Sharp & Dohme B.V.
Waarderweg 39
2031 BN Haarlem
The Netherlands

Legal category: POM

Date of review of prescribing information: December 2019

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