<table>
<thead>
<tr>
<th>Indication</th>
<th>Sitagliptin(1)</th>
<th>Vildagliptin(2)</th>
<th>Saxagliptin(3)</th>
<th>Linagliptin(4)</th>
<th>Alogliptin(5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mono</td>
<td>T2DM</td>
<td>T2DM</td>
<td>T2DM</td>
<td>T2DM</td>
<td>T2DM</td>
</tr>
<tr>
<td>Dual</td>
<td>With met or SU or TZD</td>
<td>With met or SU or TZD</td>
<td>With met or SU or TZD</td>
<td>With met</td>
<td>With met or SU</td>
</tr>
<tr>
<td>Triple</td>
<td>With met+SU or met+TZD</td>
<td>With met+SU</td>
<td>With met+SU</td>
<td>With met+SU</td>
<td>With met+SU (safety not assessed but have licence) or met+TZD</td>
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<tr>
<td>Insulin</td>
<td>Add on to insulin +/- met</td>
<td>Combination insulin +/- met</td>
<td>Combination with insulin +/- met</td>
<td>Combination with insulin +/- met</td>
<td>Combination with insulin +/- met</td>
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</tbody>
</table>

**Use in renal impairment:**

<table>
<thead>
<tr>
<th></th>
<th>Sitagliptin(1)</th>
<th>Vildagliptin(2)</th>
<th>Saxagliptin(3)</th>
<th>Linagliptin(4)</th>
<th>Alogliptin(5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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<tr>
<td>Moderate</td>
<td>Reduce dose to 50mg daily</td>
<td>Reduce dose to 50mg daily</td>
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<td>Reduce dose to 12.5mg daily</td>
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<tr>
<td>Severe</td>
<td>Reduce dose to 25mg daily</td>
<td>Reduce dose to 50mg daily</td>
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<td>Reduce dose to 6.25mg daily</td>
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<tr>
<td>ESRD</td>
<td>Reduce dose to 25mg daily</td>
<td>Reduce dose to 50mg daily</td>
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<td>Yes</td>
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**Use in hepatic impairment**

<table>
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<tr>
<th></th>
<th>Sitagliptin(1)</th>
<th>Vildagliptin(2)</th>
<th>Saxagliptin(3)</th>
<th>Linagliptin(4)</th>
<th>Alogliptin(5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>Yes</td>
<td>No</td>
<td>No dose adjustment</td>
<td>No dose adjustment but use with caution</td>
<td>Yes</td>
</tr>
<tr>
<td>Moderate</td>
<td>Yes</td>
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<td>No dose adjustment but use with caution</td>
<td>Yes</td>
<td>Yes</td>
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<tr>
<td>Severe</td>
<td>No data</td>
<td>No</td>
<td>No</td>
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**Use in cardiac failure**

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<th>Sitagliptin(1)</th>
<th>Vildagliptin(2)</th>
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<th>Linagliptin(4)</th>
<th>Alogliptin(5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No data</td>
<td>NYHA Class I II – yes, NYHA Class III – limited data</td>
<td>NYHA class I-II : limited experience</td>
<td>NYHA Class III-IV.: no experience</td>
<td>No data</td>
<td>NYHA class III-IV: no experience</td>
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**Cost / 28days(6) (6)**

<table>
<thead>
<tr>
<th></th>
<th>Sitagliptin(1)</th>
<th>Vildagliptin(2)</th>
<th>Saxagliptin(3)</th>
<th>Linagliptin(4)</th>
<th>Alogliptin(5)</th>
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<tr>
<td>£33.26</td>
<td>£31.76</td>
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<td>£33.26</td>
<td>£26.60</td>
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**Patent expiry**

<table>
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<th>Sitagliptin(1)</th>
<th>Vildagliptin(2)</th>
<th>Saxagliptin(3)</th>
<th>Linagliptin(4)</th>
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</thead>
<tbody>
<tr>
<td>2022</td>
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</tr>
<tr>
<td>2024</td>
<td>(awaiting confirmation of date from company but should be around this time)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2024</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Pros**

- Weight neutral, low incidence of hypos.
- Weight neutral, low incidence of hypos.
- Weight neutral, low incidence of hypos.
- Weight neutral, low incidence of hypos.
- Weight neutral, low incidence of hypos.

**Cons**

- Safety concerns include skin disorders, pancreatitis, and hypersensitivity reactions.
- Safety concerns include skin disorders, pancreatitis, and hypersensitivity reactions.
- Safety concerns include skin disorders, pancreatitis, and hypersensitivity reactions.
- Safety concerns include skin disorders, pancreatitis, and hypersensitivity reactions.
- Safety concerns include skin disorders, pancreatitis, and hypersensitivity reactions.

Only CVD POO data.
Sitagliptin (7):

Sitagliptin was more effective than placebo when it was taken alone or in combination with other antidiabetes medicines.

- In patients taking sitagliptin on its own, HbA1c levels fell from around 8.0% at the start of the studies by 0.48% after 18 weeks and 0.61% after 24 weeks. In contrast, they rose by 0.12% and 0.18%, respectively, in the patients taking placebo.
- Adding sitagliptin to metformin reduced HbA1c levels by 0.67% after 24 weeks, compared with a fall of 0.02% in the patients adding placebo.
- When added to pioglitazone, sitagliptin reduced HbA1c levels by 0.85% after 24 weeks, compared with a fall of 0.15% in the patients adding placebo.

In the studies comparing sitagliptin with other medicines, the effectiveness of adding sitagliptin to metformin was similar to that of adding glipizide. When taken on their own, sitagliptin and metformin produced similar reductions in HbA1c levels, but the effectiveness of sitagliptin seemed to be slightly lower than that of metformin.

In the additional studies,
- adding sitagliptin to glimepiride (with or without metformin) led to a reduction in HbA1c levels of 0.45% after 24 weeks, compared with an increase of 0.28% in the patients adding placebo.
- HbA1c levels were reduced by 1.03% after 18 weeks in patients adding sitagliptin to metformin and rosiglitazone, compared with a fall of 0.31% in those adding placebo.
- Finally, they were reduced by 0.59% in patients adding sitagliptin to insulin (with or without metformin), compared with a fall of 0.03% in those adding placebo.

Vildagliptin (8):

Vildagliptin used on its own, was effective at reducing levels of HbA1c, but was less effective than the comparator medicines.

- In the study comparing vildagliptin with metformin, significantly better results were seen with metformin: a reduction in HbA1c of 1.5 percentage points after 52 weeks compared with a reduction of around 1 percentage point in patients treated with vildagliptin.

When used as an add-on to existing treatment for type 2 diabetes, vildagliptin was more effective than placebo in reducing HbA1c levels.
- With metformin and with pioglitazone, the 100 mg daily dose was more effective than the 50 mg daily dose, with a reduction in HbA1c levels of between 0.8 and 1.0 percentage points.
- In combination with glimepiride, both 50 mg and 100 mg daily doses caused a reduction of around 0.6 percentage points.
- In contrast, patients adding placebo to their existing treatment showed smaller changes in HbA1c levels, ranging from a fall of 0.3 to a rise of 0.2 percentage points.
- In combination with metformin and glimepiride, 50 mg vildagliptin taken twice a day reduced HbA1c levels by 1 percentage point, compared with a reduction of 0.3 percentage points in patients taking placebo.
- In the study involving 296 patients taking insulin, adding vildagliptin caused a greater reduction in HbA1c levels than adding placebo, but the size of this effect was small possibly due to the fact that the study included long-term patients who were less likely to show improvement. However, in another study involving 449 patients taking insulin, the size of this effect was significant.
- Patients taking vildagliptin in addition to insulin, with or without metformin, had a reduction in HbA1c levels of 0.77 percentage points, compared with 0.05 percentage points in patients taking placebo in addition to insulin.
**Saxagliptin (9):**

Saxagliptin was more effective than placebo at controlling blood glucose, when used as an ‘add-on’ in patients in whom previous treatment had failed.

- Saxagliptin in addition to metformin, HbA1c levels had fallen by around 0.7% after 24 weeks (from around 8.1% to around 7.4%) compared with an increase of around 0.1% in patients taking placebo.
- For patients who took saxagliptin with a sulphonylurea and a thiazolidinedione, HbA1c levels fell by around 0.6% and 0.9%, respectively, compared with an increase of around 0.1% and a decrease of around 0.3%, respectively, in patients who took placebo.
- For patients who took saxagliptin in addition to insulin (with or without metformin), HbA1c levels fell by around 0.7%, compared with a decrease of around 0.3% in patients who took placebo.
- For patients who took saxagliptin with metformin and a sulphonylurea, a reduction in HbA1c levels of 0.7% was seen, compared with a reduction of 0.1% in patients who were given placebo in place of saxagliptin.
- The studies with saxagliptin on its own showed that, on average, in patients given saxagliptin HbA1c levels fell by around 0.5% more than in patients given placebo.

The results of study with saxagliptin plus metformin in patients who had not previously received substantial treatment with antidiabetes medicines were not considered to be clinically relevant and the company withdrew its application for the use of saxagliptin as an initial combination medicine in previously untreated patients.

**Linagliptin (10):**

Linagliptin was shown to be more effective than placebo at reducing HbA1c levels in all combinations studied:

- when used in combination with metformin, a reduction of 0.56 percentage points was seen with linagliptin compared with a rise of 0.10 percentage points with placebo;
- when used in combination with a metformin plus a sulphonylurea, a reduction of 0.72 percentage points was seen with linagliptin compared with a reduction of 0.10 percentage points with placebo;
- in combination with pioglitazone, a reduction of 1.25 percentage points was seen with linagliptin compared with a reduction of 0.75 percentage points with placebo;
- in combination with insulin with or without metformin and/or pioglitazone, a reduction of 0.55 percentage points was seen with linagliptin compared with a rise of 0.10 percentage points with placebo.
- Linagliptin was also more effective than placebo when used on its own, reducing HbA1c levels by 0.46 percentage points compared with a rise of 0.22 percentage points seen with placebo.

**Alogliptin (11):**

Alogliptin has been studied in seven main studies involving 5,675 adults with type 2 diabetes. Five of the studies compared alogliptin with placebo, when used alone or added to other diabetes medicines, in patients in whom previous treatment had failed. In two other studies, alogliptin was compared with glipizide and pioglitazone in patients who were already taking metformin.

In all of the studies, the main measure of effectiveness was the change in the level of glycosylated haemoglobin (HbA1c).
HbA1c levels were measured after 26 weeks when alogliptin was used alone or added to other diabetes medicines, and after 52 weeks when alogliptin was compared with glipizide or pioglitazone.

In all studies alogliptin led to a decrease in HbA1c. When used alone or in combination with other anti-diabetes medicines, alogliptin reduced HbA1c levels by 0.48–0.61% more than placebo. alogliptin was as least as effective as pioglitazone in lowering HbA1c when added to metformin, but the study comparing alogliptin with glipizide was not conclusive.

- For the combination with TZD (with or without metformin), alogliptin 25 mg was associated with a reduction in HbA1c of -0.61% (95% CI -0.80 to -0.41) after 26 weeks in comparison to placebo.
- Compared to placebo, alogliptin 25 mg was associated with a reduction in HbA1c of -0.57% (-0.80 to -0.35).

References:

1. Summary of product characteristics: Sitagliptin (accessed April 14): [https://www.medicines.org.uk/emc/medicine/19609/SPC/JANUVIA+25mg,+50mg,+100mg+film-coated+tablets/](https://www.medicines.org.uk/emc/medicine/19609/SPC/JANUVIA+25mg,+50mg,+100mg+film-coated+tablets/)