

## Medicine Update - Vildagliptin

Vildagliptin (Galvus®) is an oral anti-diabetic drug that selectively inhibits the dipeptidyl peptidase-4 (DPP-4) enzyme. This increases levels of metabolic hormones such as glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP) which results in increased insulin synthesis and secretion from the pancreatic beta cells. Other effects are possibly reduced appetite as GLP-1 also reduces glucagon secretion from pancreatic alpha cells.<sup>1,2</sup>

### Place in therapy

- Vildagliptin is indicated as mono- or combination therapy, as an adjunct to diet and exercise to improve glycaemic control in type 2 diabetes. NICE guidelines<sup>3</sup> recommend adding vildagliptin as second-line therapy to first-line metformin when control of blood glucose remains or becomes inadequate (HbA1c  $\geq$ 48 mmol/mol) and if a sulfonylurea is not tolerated or is contraindicated. Similarly, it can be added to a first-line sulfonylurea if metformin is not tolerated.
- Vildagliptin can be considered as third-line therapy to first-line metformin and a second-line sulfonylurea when control of blood glucose remains or becomes inadequate (HbA1c  $\geq$ 58 mmol/mol) and insulin is unacceptable or inappropriate.<sup>3</sup>
- A DPP-4 inhibitor (vildagliptin, sitagliptin) should only be continued if the person has had a beneficial metabolic response (a reduction of at least 5.5 mmol/mol in HbA1c in 6 months).<sup>3</sup>

### How effective is vildagliptin?

- Monotherapy with vildagliptin 100 mg daily reduced baseline HbA1c by 1% compared to 1.4% for metformin (titrated to 2 g/day)<sup>2</sup>
- Combination therapy with vildagliptin 50mg twice daily plus metformin demonstrated non-inferiority to gliclazide plus metformin in terms of change from baseline in HbA1c<sup>2,4</sup>
- Mean HbA1c reductions were significantly greater with vildagliptin plus metformin fixed-dose combination therapy compared to either monotherapy<sup>2</sup>
- In triple therapy, vildagliptin 50 mg twice daily added to a stable combination of metformin and a sulfonylurea provided a clinically relevant reduction in HbA1c<sup>5</sup>

### Key Messages:

- Funded from 1 October without restriction
- Available as 50 mg tablet
- Maximum daily dose is 100 mg
- As monotherapy, it is weight-neutral and does not contribute to hypoglycaemia
- Is well tolerated with the majority of adverse effects being mild and transient
- Avoid in hepatic impairment
- Has low potential for drug interactions
- Sulfonylurea and insulin doses may need to be reduced if used in combination with vildagliptin
- Also available in fixed dose combination as vildagliptin/metformin 50 mg/850 mg or 50 mg/1000 mg (Galvus Met®)

### Cautions

**Hepatic impairment:** vildagliptin is not recommended in patients with hepatic impairment, including patients with a pre-treatment ALT or AST  $>2.5x$  the upper limit of normal. Rare cases of hepatic dysfunction (including hepatitis) have been reported. LFTs should be performed prior to treatment initiation, monitored at three-monthly intervals during the 1<sup>st</sup> year, and periodically after that.<sup>2</sup>

**Heart failure:** no information available but manufacturer recommends to avoid<sup>1</sup>

**Acute pancreatitis:** discontinue if symptoms (persistent, severe abdominal pain) occur<sup>1,2</sup>

**Pregnancy and breastfeeding:** recommended to avoid – insufficient data<sup>1,2</sup>

**Renal impairment:** eGFR  $< 50$  mL/min/1.73m<sup>2</sup> dose reduction to 50mg daily. Galvus Met® (combination product vildagliptin/metformin) is contraindicated in patients with creatinine clearance  $<60$  mL/min. Dosage adjustment may be required in patients with creatinine clearance between 60 and 90 mL/min<sup>6</sup>

## Dosing regimen

	Adult dose*
<b>Vildagliptin monotherapy</b>	50 mg once daily (in the morning) or twice daily
<b>Combination with metformin, pioglitazone or insulin</b>	50 mg once daily (in the morning) or twice daily ( <i>dose of insulin may need to be reduced</i> )
<b>Combination with a sulfonylurea</b>	50 mg once daily in the morning ( <i>dose of sulphonylurea may need to be reduced</i> )
<b>Combination with metformin AND a sulfonylurea</b>	50 mg twice daily
<b>Renal impairment** – eGFR &lt; 50 mL/min/1.73m<sup>2</sup></b>	50 mg once daily
<b>Fixed dose combination (vildagliptin/metformin)<sup>4</sup></b>	should be based on the patient's current regimen of vildagliptin and/or metformin

\*No dose reduction is required for vildagliptin monotherapy in elderly patients.

\*\*No dose reduction is required for vildagliptin in mild renal impairment.

## Adverse effects

Vildagliptin is well tolerated with the majority of adverse effects being mild and transient. It is weight-neutral when given as monotherapy or in combination with metformin, and hypoglycaemia is uncommon. GI adverse effects for the fixed-dose combination are more attributable to metformin.<sup>2,6</sup>

For a full list of adverse effects refer to product data sheets or monographs in NZ Formulary ([www.nzf.org.nz](http://www.nzf.org.nz))

## Interactions

Vildagliptin has a low potential for drug interactions. Since it is not a cytochrome P (CYP) 450 enzyme substrate nor does it inhibit nor induce CYP 450 enzymes, it is not likely to interact with medications that are substrates, inhibitors or inducers of these enzymes.

Efficacy may be reduced by drugs that can increase blood glucose concentrations e.g. oral corticosteroids, thiazide and related diuretics at higher doses.<sup>1</sup>

A full list of interactions can be found on the NZF interaction checker ([www.nzf.org.nz](http://www.nzf.org.nz))

## References:

1. Vildagliptin monograph. New Zealand Formulary. [https://nzf.org.nz/nzf\\_3746](https://nzf.org.nz/nzf_3746)
2. Vildagliptin datasheet. Medsafe. <http://www.medsafe.govt.nz/profs/Datasheet/g/galvustab.pdf>
3. NICE Guidance. Type 2 diabetes in adults: management. May 2017.
4. Keating GM. Vildagliptin: a review of its use in Type 2 Diabetes Mellitus. *Drugs*. 2010; 70 (16): 2089-2112.
5. Lukashevich V, Del Prato S, Araga M & Kothny W. Efficacy and safety of vildagliptin in patients with type 2 diabetes mellitus inadequately controlled with dual combination of metformin and sulphonylurea. *Diabetes, Obesity and Metabolism*. 2014; 16:403-409.
6. Vildagliptin/metformin hydrochloride datasheet. Medsafe. <http://www.medsafe.govt.nz/profs/Datasheet/g/galvusmettab.pdf>