Coventry & Warwickshire

Area Prescribing Committee

Drug Positioning Statement	DPS005
Vildagliptin (Galvus®)	October 2013

VERDICT

The Coventry & Warwickshire APC **does not recommend** the use of vildagliptin as all clinical scenarios are covered by the first and second-line options currently recommended and this DPP-4 inhibitor (Gliptin) offers no significant clinical advantage over them, [**FIRST LINE:** sitagliptin (DPS004) and **SECOND LINE:** linagliptin (DPS021)]. For details of the respective properties of the currently available DPP-4 inhibitors please consult the APC approved comparisons chart.

Specialist Drugs List Status: **Vildagliptin is not considered as a specialist drug and can be initiated in primary care although prescribers should note the verdict above**

Summary notes[1]

INDICATION: Vildagliptin is licensed for the treatment of type 2 diabetes mellitus

as **monotherapy**:

- in patients inadequately controlled by diet and exercise alone and for whom metformin is inappropriate due to contraindications or intolerance

as **dual therapy** with:

- metformin, in patients with insufficient glycaemic control despite maximal tolerated doses of metformin
- a sulfonylurea, in patients with insufficient glycaemic control, despite maximal tolerated doses of a sulfonylurea or for whom metformin is inappropriate due to contra-indications and intolerances
- a thiazolidinedione, in patients with insufficient glycaemic control and for whom the use of a thiazolidinedione (glitazone) is appropriate

as **triple oral therapy** in combination with

- a sulphonylurea and metformin when diet and exercise plus dual therapy with these medicinal products do not provide adequate glycaemic control.
- Vildagliptin is also indicated for use in combination with insulin (with or without metformin) when diet and exercise plus a stable dose of insulin do not provide adequate glycaemic control

PHARMACOLOGICAL ACTION: Vildagliptin is a potent and selective DDP-4 inhibitor, resulting in increased fasting and postprandial endogenous levels of the incretin hormones GLP-1 (glucagon-like peptide 1) and GIP (glucose-dependent insulinotropic polypeptide). By increasing the endogenous levels of these incretin hormones, vildagliptin enhances the sensitivity of beta cells to glucose, resulting in improved glucose-dependent insulin secretion.

PRESENTATION: 50mg tablets

DOSE: 50mg twice daily in combination with metformin or a thiazolidinedione or 50mg once daily in combination with a sulfonylurea.

COST COMPARISON[2] for 28 days supply:

Vildagliptin 50mg twice daily	£31.76
Linagliptin 5mg daily	£33.26
Sitagliptin 100mg daily	£33.26
Saxagliptin 5mg daily	£31.60

Drug profile[3,4]

Clinical Effectiveness

Efficacy data from three 24 week double-blind, randomized controlled trials (RCTs) showed that addition of vildagliptin, 50mg once or twice daily, to ongoing treatment with metformin or glimepiride or pioglitazone reduced $HbA1_c$ significantly more than the addition of placebo. Placebo subtracted reductions in $HbA1_c$ were 0.7%-1.1%, 0.6%- 0.7% 0.5-0.7% respectively.

In a 24 week RCT of patients receiving ongoing metformin, vildagliptin 50mg twice daily (bd) was found to be non inferior to pioglitazone 30mg once daily. Further detail is provided in the New drugs evaluation.

To date studies only include disease orientated outcomes (HbA1c) rather than the incidence of patient orientated outcomes.

Drug Interactions: hypoglycaemic effect of vildagliptin may be reduced by certain active substances, including thiazides, corticosteroids, thyroid products and sympathomimetics.

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The information in this review is believed to be true and accurate. It is issued on the understanding that it is the best available from the resources at our disposal at the time of issue

Drug profile[3,4] (Continued)

Safety[1,3]

Adverse effects: The majority of adverse effects were transient and mild. Addition of vildagliptin twice daily to metformin, pioglitazone or glimepiride increased mean body weight compared to placebo, but 50mg once daily did not when added to metformin, pioglitazone or glimepiride. Rare cases of liver dysfunction (including hepatitis) have been reported. Liver function tests (LFTs) should be performed before initiating treatment to know patients baseline levels and at three month intervals during the first year of treatment. The Medicines and Healthcare Regulatory Agency (MHRA) state that an increased risk of pancreatitis has been identified for all DDP-4 inhibitors. Reporting rates have ranged between 1/1000 to 1/100. **Patients should be informed of the characteristic symptoms of acute pancreatitis – persistent, severe abdominal pain (sometimes radiating to the back) – and encouraged to tell their healthcare provider if they have symptoms[5].**

Contra-indications: There is no experience of vildagliptin use in clinical trials in patients with cardiac failure NYHA functional class III-IV and therefore use is not recommended in these patients

Renal Impairment: No dose adjustment is needed in mild renal impairment. In moderate or severe impairment or end stage renal disease (ESRD) the dose is 50mg daily. Vildagliptin should be used with caution in patients with ESRD on haemodialysis as experience is limited in these patients.

Hepatic Impairment Vildagliptin should not be prescribed in patients with liver impairment.
Elderly: No dose adjustment necessary
Drug Interactions: hypoglycaemic effect of vildagliptin may be reduced by certain active substances, including thiazides, corticosteroids, thyroid products and sympathomimetics.

Current place in therapy

- NICE (National Institute for Health and Clinical Excellence) [6] recommends that DPP-4 inhibitors may be considered for dual therapy with metformin or a sulfonylurea for patients with inadequate glycaemic control (HbA1c >=6.5% or as agreed with the individual) , where the combination of a sulfonylurea and metformin is unsuitable, i.e. when either drug is contra-indicated or not tolerated, or in the case of sulfonylureas, there is a significant risk of hypoglycaemia.
- As with all DPP-4 inhibitors, vildagliptin **should only be continued if there is at least a 0.5% reduction in $HbA1_{c\ in}$ 6 months.**
- Vildagliptin should not be prescribed in patients with liver impairment. LFTs should be performed before initiating treatment and at three month intervals for the first year of treatment
- Patients should be informed of the characteristic symptoms of acute pancreatitis – persistent, severe abdominal pain (sometimes radiating to the back) – and encouraged to tell their healthcare provider if they have symptoms[5].

References

1. Summary of Product Characteristics. Novartis Pharmaceuticals UK Ltd. Galvus 50mg tablets 9.1.13. Available from www.medicines.org.uk/EMC/medicine/20734/SPC/Galvus+50+mg+Tablets/ <accessed 16.10.12>
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4. NDE. Regional Drugs and therapeutics centre. Vildagliptin . March 2008. http://rdtc.nhs.uk/sites/default/files/publications/nde_89_vildagliptin_final.pdf
5. Drug Safety Update September 2012, Vol. 6, issue 2: A3 . Available from www.mhra.gov.uk/home/groups/dsu/documents/publication/con185631.pdf <accessed 2.10.12>
6. National Institute for Health and Clinical Excellence. Clinical guideline 87. Type 2 diabetes: Newer agents. May 2009. Available from www.nice.org.uk/nicemedia/live/12165/44322/44322.pdf <accessed 17.10.12>

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