

# Sitagliptin, vildagliptin and saxagliptin – dipeptidyl peptidase-4 inhibitors ('gliptins') for add-on therapy in type 2 diabetes mellitus

Effective for lowering blood glucose in type 2 diabetes in dual combination therapy with metformin or a sulfonylurea.

## KEY POINTS

### **Gliptins improve glycaemic control in type 2 diabetes**

Sitagliptin (Januvia), vildagliptin (Galvus) and saxagliptin (Onglyza) are dipeptidyl peptidase-4 (DPP-4) inhibitors. They improve glycaemic control in diabetes that has not been adequately controlled with metformin or sulfonylurea.

### **Gliptins are PBS listed for add-on combination therapy**

Gliptins are listed on the PBS as dual oral combination therapy with metformin or a sulfonylurea and where a combination of metformin and a sulfonylurea is contraindicated or not tolerated.

### **Efficacy is similar across the class**

All the PBS-listed gliptins provide similar improvements in glycaemic control when combined with metformin or a sulfonylurea.

### **The effect of gliptins on diabetes-related complications and mortality is unknown**

There are no long-term data on the effects of gliptins on diabetes-related complications and mortality.

### **Gliptins are weight neutral and not associated with increased risk of hypoglycaemia except with sulfonylurea**

Gliptins do not affect weight and there is no significant increase in the rate of hypoglycaemic events when combined with metformin. Weight gain may occur, and the risk of hypoglycaemic events can increase, when a gliptin is combined with a sulfonylurea.

### **Adverse effects may relate to impaired immunity**

Be vigilant for infection (especially upper respiratory tract) and hypersensitivity reactions. There have been postmarketing reports of pancreatitis with gliptins, although a causal association has not been confirmed.

### **Caution is required in people with renal and hepatic impairment**

Avoid vildagliptin and saxagliptin in people with creatinine clearance < 50 mL/min and reduce the dose of sitagliptin in these people. Vildagliptin is not recommended in people with hepatic impairment. Use sitagliptin cautiously in severe hepatic impairment, as there is limited clinical experience.



## EVIDENCE SNAPSHOT

### WHAT IS KNOWN ABOUT THESE DRUGS?

Sitagliptin, vildagliptin and saxagliptin provide similar improvements in HbA<sub>1c</sub> levels when combined with metformin, a sulfonylurea or a glitazone. Gliptins do not contribute to weight loss or gain. Trials have found no significant increase in the rate of hypoglycaemia when a gliptin was combined with metformin, however, the risk of hypoglycaemia is greater when a gliptin is combined with a sulfonylurea than for a sulfonylurea alone.

### AREAS OF UNCERTAINTY

The long-term safety profile of the gliptins is yet to be established and their effect on incidence of diabetes-related complications and mortality is uncertain.

Cases of acute pancreatitis have been reported in people taking sitagliptin and vildagliptin, but this has not been observed in clinical trials and a causal association has not been confirmed. There is limited postmarketing experience with saxagliptin.

The potential for adverse immune effects has been raised and may be reflected in higher infection rates.

The safety of vildagliptin in people with liver disease has not been established.

### WHAT DOES NPS SAY?

Gliptins are an alternative therapy to improve glycaemic control in type 2 diabetes mellitus when used with metformin (preferred combination) or a sulfonylurea as add-on therapy when a combination of metformin and sulfonylurea is contraindicated or not tolerated. Caution is required when choosing the gliptin in people with renal or hepatic impairment. The long-term safety profile of the gliptins is yet to be established.

## PBS listing

### Authority required (streamlined)

Sitagliptin (Januvia), vildagliptin (Galvus) and saxagliptin (Onglyza) are listed on the Pharmaceutical Benefits Scheme (PBS) for use in type 2 diabetes mellitus as dual oral therapy in combination with either metformin or a sulfonylurea, in patients whose glycosylated haemoglobin (HbA<sub>1c</sub>) is > 7% prior to initiation of a dipeptidyl peptidase 4 (DPP-4) inhibitor (gliptin), a thiazolidinedione (glitazone) or a glucagon-like peptide-1 despite treatment with either metformin or a sulfonylurea, and when a combination of metformin and a sulfonylurea is contraindicated or not tolerated.

Sitagliptin-with-metformin fixed-dose combination tablets (Janumet) and vildagliptin-with-metformin fixed-dose combination tablets (Galvumet) are listed on the PBS for use in a patient whose

HbA<sub>1c</sub> is > 7% prior to initiation of a gliptin, a thiazolidinedione (glitazone) or a glucagon-like peptide-1 despite treatment with metformin and where a combination of metformin and a sulfonylurea is contraindicated or not tolerated. Treatment is also subsidised for patients who have previously received and been stabilised on a PBS-subsidised regimen that included sitagliptin or vildagliptin and metformin.

Blood glucose monitoring may be used as an alternative to HbA<sub>1c</sub> levels in certain circumstances. See the PBS website at [www.pbs.gov.au](http://www.pbs.gov.au) for more information.

### May be prescribed by nurse practitioners

Authorised nurse practitioners may prescribe sitagliptin, vildagliptin or saxagliptin. See the PBS website ([www.pbs.gov.au/browse/nurse](http://www.pbs.gov.au/browse/nurse)) for more information on nurse practitioner PBS prescribing.

## What is it?

Sitagliptin, vildagliptin and saxagliptin are dipeptidyl peptidase-4 (DPP-4) inhibitors. DPP-4 inhibitors ('gliptins') are a recently introduced class of oral drugs for type 2 diabetes.

Gliptins block the metabolism by the DPP-4 enzyme of incretin hormones, including GLP-1 and glucose-dependent insulinotropic polypeptide (GIP), which are secreted by the intestine in response to food.<sup>1</sup> This increases the levels of active incretins, prolonging their effect in stimulating insulin release and decreasing glucagon secretion.<sup>1</sup>

## Who is it for?


Sitagliptin, vildagliptin and saxagliptin are TGA-approved for glycaemic control as dual combination therapy with metformin or a sulfonylurea (PBS-subsidised) or a glitazone\* (non PBS-subsidised) in patients with type 2 diabetes mellitus:

- ▶ whose HbA<sub>1c</sub> is > 7% despite treatment with either metformin or a sulfonylurea and when a combination of metformin and a sulfonylurea is contraindicated or not tolerated.
- ▶ as an add-on therapy, with metformin, a sulfonylurea, or a glitazone, when the single agent alone does not provide adequate glycaemic control.

Only the combination with metformin or a sulfonylurea is subsidised on the PBS (see PBS listing).

## Where does it fit?

### Dual therapy for glycaemic control

PBS-subsidised sitagliptin, vildagliptin or saxagliptin are treatment options for dual therapy with either metformin or a sulfonylurea when diet, exercise and the single drug alone inadequately controls blood glucose.<sup>2-5</sup> 


Insulin, a glitazone (rosiglitazone or pioglitazone) or a GLP-1 analogue (eg. exenatide) are alternatives to a gliptin when initial drug monotherapy becomes inadequate for glycaemic control.<sup>6-8</sup> The choice of drug should take into account the effect on diabetes-related clinical outcomes, safety profile and the patient's preference. Other treatment options include a glitinide (eg. repaglinide) and acarbose (alpha glucosidase inhibitor).

Sitagliptin, vildagliptin and saxagliptin are **not** PBS subsidised as monotherapy, for use in combination with metformin and a sulfonylurea (triple therapy), in combination with a glitazone or a GLP-1 analogue, or in combination with other drugs for diabetes (including acarbose, insulin and repaglinide).

### **Gliptins may be preferred for some patients but their long-term harm-benefit profile is yet to be established**

As add-on therapy, sitagliptin, vildagliptin and saxagliptin may be useful alternatives to a sulfonylurea, a glitazone, a glitinide or insulin for people who are overweight or at high risk of hypoglycaemia (see Safety issues). They are also an option for people in whom a glitazone may be unsuitable (see the *NPS RADAR* reviews 'Rosiglitazone (Avandia) and rosiglitazone with metformin (Avandamet) for type 2 diabetes mellitus' [December 2008] and 'Pioglitazone (Actos) for type 2 diabetes mellitus' [April 2008] for safety issues with the glitazones).

However, when choosing between treatments consider that the long-term harm-benefit profile of the gliptins has not been established. Gliptins have not been proven to reduce the risk of diabetes-related complications. They also have specific safety concerns that might make them an unsuitable choice for certain patients (see Safety issues).

 Refer to this review at [www.nps.org.au](http://www.nps.org.au) for additional information on intolerance and contraindications to metformin.

\* *Vildagliptin is TGA approved for use in combination with pioglitazone but not rosiglitazone.*<sup>4</sup>

## How does it compare?

Gliptins improve glycaemic control in patients inadequately controlled with metformin, a sulfonylurea or a glitazone. They are well tolerated, have a neutral effect on weight and have a low hypoglycaemia event rate.<sup>3-5,9,10</sup> Gliptins may be associated with increased rates of infection, especially respiratory and urinary tract infections, and pancreatitis needs to be considered as a potential adverse effect, although a causal link has yet to be established.<sup>9</sup>

### **Gliptins with metformin or a sulfonylurea improve glycaemic control**

In people inadequately controlled with metformin alone, adding sitagliptin (100 mg once daily), vildagliptin (50 mg twice daily) or saxagliptin (5 mg once daily) to metformin reduced mean HbA<sub>1c</sub> by 0.5-1.1% compared with adding placebo.<sup>11-17</sup> Combining metformin with a gliptin provides comparable improvements in glycaemic control to those achieved by a combination of metformin with either a sulfonylurea<sup>18-21</sup> or a glitazone.<sup>16,22,23</sup>

In people inadequately controlled on a sulfonylurea alone, adding sitagliptin (100 mg once daily), vildagliptin (50 mg once or twice daily) or saxagliptin (5 mg once daily) to a sulfonylurea reduced mean HbA<sub>1c</sub> by 0.5-0.6% compared with adding placebo.<sup>24-27</sup> Trials found similar improvements in glycaemic control when a gliptin was combined with pioglitazone in people inadequately controlled on glitazone monotherapy (note that this is a TGA-approved but not PBS-listed indication).<sup>28-31</sup>

### **Gliptins have similar efficacy in improving glycaemic control**

Only one head-to-head trial has been reported comparing relative efficacy and safety of gliptins, in which saxagliptin plus metformin was non-inferior to sitagliptin plus metformin.<sup>32</sup> However, other indirect comparisons suggest that sitagliptin, vildagliptin and saxagliptin provide similar

improvements in HbA<sub>1c</sub> when combined with metformin, a sulfonylurea or a glitazone.<sup>11-18,26,27,30,31,33,34</sup>

Although saxagliptin is 10-fold more potent in DPP-4 inhibition than either sitagliptin or vildagliptin<sup>35</sup> this has no clinical relevance and saxagliptin shows no greater improvement in metabolic control than the other gliptins in type 2 diabetes in combination with metformin,<sup>11,17</sup> a sulfonylurea<sup>27</sup> or a glitazone.<sup>10,31</sup> In the head-to-head trial, in 801 patients with HbA<sub>1c</sub> 6.5-10% on stable metformin doses, adjusted mean changes in HbA<sub>1c</sub> after the addition of saxagliptin or sitagliptin to metformin therapy were similar, demonstrating non-inferiority for saxagliptin 5 mg compared with sitagliptin 100 mg.<sup>32</sup>

### **The effect of gliptins on morbidity and mortality is unknown**

There are no long-term data on the effects of gliptins on diabetes-related complications and mortality. The gliptins have little to no effect on fasting lipids.<sup>12-16,19,22,24,28,2</sup> Their long-term impact on cardiovascular events is uncertain at present. A systematic assessment of cardiovascular adverse events reported in 19 clinical trials of sitagliptin<sup>36</sup>, 25 clinical trials of vildagliptin<sup>37</sup> and 8 clinical trials of saxagliptin<sup>38</sup> found no increased rate of cardiovascular events, although these were post-hoc analyses of adverse effects in trials with different comparators, and patients were only followed for up to 102 weeks; trials designed to assess clinical outcomes are needed to confirm the impact of gliptins on cardiovascular events.

In contrast, there is evidence that metformin reduces the incidence of diabetes-related complications and mortality.<sup>39</sup> Sulfonylureas and insulin also reduce the incidence of microvascular complications.<sup>40</sup>

## Safety issues

The long-term safety profile of the gliptins is yet to be established. The adverse-effect profile of gliptins includes<sup>3,4,41-46 47-49</sup>:

- ▶ infections (especially respiratory tract and urinary tract infections)
- ▶ gastrointestinal disorders
- ▶ musculoskeletal disorders
- ▶ fatigue.

However, in a meta-analysis of 19 sitagliptin trials<sup>36</sup> and 38 vildagliptin trials<sup>50</sup> the increased risk for respiratory infections was non-significant. For saxagliptin, depression has been reported,<sup>2,5</sup> and an increased risk of bone fractures has been reported in clinical trials with saxagliptin.<sup>51</sup> Saxagliptin, and to a lesser extent sitagliptin, are metabolised by the cytochrome P450 isoenzyme CYP 3A4, and so may carry a risk of drug interactions.<sup>3,5</sup>

Combining a gliptin with metformin resulted in a similar incidence of adverse effects to that for metformin alone.<sup>11-17,33,34</sup>

Report suspected adverse reactions to the Therapeutic Goods Administration (TGA) online ([www.ebs.tga.gov.au](http://www.ebs.tga.gov.au)) or by using the 'Blue Card' distributed three times a year with *Australian Prescriber*. For information about reporting adverse reactions, see the TGA website ([www.tga.gov.au](http://www.tga.gov.au)).

### Weight gain may occur in combination with a sulfonylurea

There are no significant changes in body weight when sitagliptin, vildagliptin or saxagliptin is added to metformin.<sup>11-17,20-22,33,34,52</sup> In contrast, adding a sulfonylurea or a glitazone to metformin leads to weight gain (mean increase of 1.3–2.5 kg compared with a combination of metformin with a gliptin).<sup>16,19-22,52</sup>

Weight gain can occur when a gliptin is added to a sulfonylurea. For example sitagliptin 100 mg once daily in combination with sulfonylurea (glimepiride) resulted in mean weight increase of 1.1 kg.<sup>24</sup> A similar but dose-dependent effect was found in a trial with

vildagliptin: weight gain occurred when glimepiride was combined with vildagliptin 50 mg twice daily (+1.3 kg) but this effect was not seen with vildagliptin 50 mg once daily, the recommended combination dose with sulfonylurea.<sup>25</sup>

In a study of saxagliptin added to submaximal sulfonylurea, weight gain was recorded in all groups but was more pronounced in the saxagliptin treatment groups at 24 weeks (+0.8 kg) and at 76 weeks (+1.0 kg).<sup>26,27</sup>

### Low risk of hypoglycaemia unless combined with a sulfonylurea

Trials have found no significant increase in the rate of hypoglycaemia when a gliptin was combined with metformin.<sup>12-16,19-21</sup> However, the risk of hypoglycaemia is greater when a gliptin is combined with a sulfonylurea than for a sulfonylurea alone.

More patients reported hypoglycaemia when glimepiride 4–8 mg daily was combined with sitagliptin (12%) than with placebo (2%).<sup>24</sup> The incidence of hypoglycaemia was also higher when glimepiride 4 mg daily was combined with vildagliptin 50 mg twice daily (3.6%) rather than placebo (0.6%), although the risk was not as great when the recommended dose with sulfonylurea of 50 mg once daily was used (1.2%).<sup>25</sup>

If starting a gliptin with a sulfonylurea, lower doses of either drug may be required to minimise the risk of hypoglycaemia (see Dosing issues).

### Be vigilant for infection and hypersensitivity reactions

Inhibiting the DPP-4 enzyme prolongs the action of neuropeptides, including substance P, which may increase the risk of inflammatory and allergic reactions.<sup>9</sup> DPP-4 is also found on T cells, raising theoretical concerns that this drug class may affect the immune system,<sup>9</sup> although infections characteristic of impaired T-cell function, such as herpes simplex virus infection, were not reported more frequently with gliptins than with placebo.<sup>9,43,45</sup>

Meta-analyses of randomised controlled trials have found a slightly increased risk of infection in patients treated with gliptins:

- ▶ upper respiratory tract infections ranged from 2.9% to 8.8% for sitagliptin,<sup>15,16,28</sup> 4.1% to 5.5% for vildagliptin<sup>42</sup> and 4.4% to 8.3% for saxagliptin<sup>11,26</sup>; however, in a recent meta-analysis of sitagliptin trials, the elevation in risk for bronchitis and nasopharyngitis was non-significant<sup>46</sup>
- ▶ urinary tract infections ranged from 2.0% to 5.4% for sitagliptin,<sup>14,15,19,53</sup> 2.8% to 3.4% for vildagliptin<sup>42</sup> and 5.2% to 10.7% for saxagliptin<sup>26</sup>
- ▶ risk of all-cause infection was significantly elevated in patients treated with sitagliptin (RR 1.15, 95% CI 1.02 to 1.31,  $p = 0.03$ ), but not in those treated with vildagliptin<sup>41</sup>

With sitagliptin there have been postmarketing reports of<sup>3</sup>:

- ▶ anaphylaxis
- ▶ angioedema
- ▶ rash
- ▶ urticaria
- ▶ cutaneous vasculitis
- ▶ exfoliative skin conditions, including Stevens–Johnson syndrome.

These reactions occurred within 3 months of starting treatment, with some reports after the first dose.<sup>3</sup> Angioedema and urticaria have also been reported with vildagliptin<sup>4,43</sup> and saxagliptin.<sup>2</sup>

### Postmarketing cases of pancreatitis have been reported with gliptins

There have been no postmarketing reports of pancreatitis with saxagliptin to date; however, cases of acute pancreatitis have been reported in people taking sitagliptin<sup>3,54</sup> and vildagliptin<sup>4</sup> but a causal association has not been confirmed. In clinical trials there was no increased incidence of pancreatitis-related adverse events with saxagliptin, sitagliptin or vildagliptin compared with non-exposed groups<sup>31,46,50,55</sup> and their use did not raise risk for pancreatitis beyond that incurred from diabetes itself.<sup>56</sup> This does not rule out pancreatitis as a rare adverse effect of gliptin therapy.

For more information, see the *NPS RADAR* in-brief item 'Postmarketing reports of acute pancreatitis with sitagliptin products (Janumet, Januvia)'.

### Precautions in people with renal dysfunction

Gliptins are primarily cleared by the kidney. Vildagliptin and saxagliptin should not be used in patients with moderate or severe renal impairment (creatinine clearance [CrCl] < 50 mL/min) or in patients with end-stage renal disease on haemodialysis.<sup>2,42</sup> Sitagliptin was associated with small increases in serum creatinine concentrations in trials that, although not clinically significant, were greater in people with moderate to severe renal impairment.<sup>45</sup> Use a reduced dose for sitagliptin in people with moderate or severe renal impairment (see Dosing issues).<sup>3</sup>

### Limited data in people with hepatic impairment

Sitagliptin should be used with caution in people with severe hepatic impairment, as there is no clinical experience in this context.<sup>3</sup> Vildagliptin is not recommended in people with hepatic impairment, including those with an alanine aminotransferase (ALT) or aspartate aminotransferase (AST) level greater than 2.5 times the upper limit of normal.<sup>4</sup> No dosage adjustment for saxagliptin is recommended for patients with hepatic impairment.<sup>2</sup>

### Monitor liver function with vildagliptin

Liver function tests are required before starting vildagliptin, and liver enzyme levels should be monitored every 3 months during the first year of treatment and periodically thereafter.<sup>4</sup> Stop vildagliptin if an ALT or AST elevation persists above three times the upper limit of normal or if jaundice or other signs of hepatic dysfunction develop.<sup>4</sup>

### Gliptins may be a preferred add-on to metformin in older people

Older people with diabetes have an increased risk of hypoglycaemia.<sup>57</sup> If an oral therapy is required, adding a gliptin may be preferred to adding a sulfonylurea, with its increased risk for hypoglycemia, or a glitazone, with its increased cardiovascular risk, which should be avoided in the elderly.<sup>25,57</sup>

## Reason for PBS listing

Sitagliptin was listed on the PBS in August 2008 on a cost-minimisation basis — that is, similar efficacy and cost — compared with rosiglitazone.<sup>58</sup>

Vildagliptin was listed on the PBS in August 2010 on a cost-minimisation basis compared with sitagliptin.<sup>59</sup> Equi-effective doses compared with sitagliptin 100 mg daily were vildagliptin 50 mg twice daily (with metformin) and vildagliptin 50 mg once daily (with a sulfonylurea).<sup>59</sup>

Saxagliptin was listed on the PBS in June 2011 on a cost-minimisation basis compared with sitagliptin, with the equi-effective doses of saxagliptin 5 mg/day and sitagliptin 100 mg/day.<sup>59</sup>

Sitagliptin-with-metformin combination tablets were listed on the PBS in August 2009 on a cost-minimisation basis compared with the individual components sitagliptin and metformin.<sup>60</sup> Vildagliptin-with-metformin combination tablets were listed on the PBS in April 2011 on a cost-minimisation basis compared with the individual components vildagliptin and metformin.<sup>61</sup>

The PBAC has recommended that the restriction wording for all currently PBS subsidised gliptins, glitazones and GLP-1 analogues be modified to allow patients to switch between agents in these three classes without having to requalify with respect to HbA<sub>1c</sub> levels. Although the evidence to support switches from a gliptin to a glitazone, and vice versa, is limited, the PBAC considered it unreasonable to require a loss of diabetic control prior to switching.

## Dosing issues

### Sitagliptin

The recommended dose of sitagliptin as add-on combination therapy with metformin or a sulfonylurea is 100 mg once daily with or without food.<sup>3</sup> When combining sitagliptin with a sulfonylurea, the dose of the sulfonylurea may need to be decreased to reduce the risk of hypoglycaemia.<sup>3</sup>

### Vildagliptin

The recommended dose of vildagliptin as add-on combination therapy with metformin or a sulfonylurea is 50 mg once daily (in the morning) or twice daily, with or without food.<sup>4</sup> Use a dose of 50 mg once daily with a sulfonylurea to reduce the risk of hypoglycaemia.<sup>4</sup>

### Saxagliptin

The recommended dose of saxagliptin as add-on combination therapy with metformin or a sulfonylurea is 5 mg once daily taken with or without food.<sup>2</sup> A lower dose of sulfonylurea may be required to reduce the risk of hypoglycaemia when used in combination with saxagliptin.<sup>5</sup>

### Sitagliptin-with-metformin and vildagliptin-with-metformin fixed-dose combinations

Sitagliptin-with-metformin or vildagliptin-with-metformin fixed-dose combination tablets should be taken twice daily with meals.<sup>62,63</sup> Individualise the starting or switching dose according to the patient's current regimen of metformin, level of glycaemic control and tolerability, while maintaining a dose of 100 mg/day for sitagliptin<sup>62</sup> and 50 mg twice daily for vildagliptin.<sup>63</sup>

### Reduce the dose of sitagliptin in people with renal dysfunction

For patients with CrCl of 30 mL/min to < 50 mL/min, the recommended dose of sitagliptin is 50 mg once daily.<sup>3</sup> For patients with CrCl < 30 mL/min or end-stage renal failure requiring haemodialysis or peritoneal dialysis, the recommended dose is 25 mg once daily.<sup>3</sup>

### **Avoid vildagliptin and saxagliptin in people with creatinine clearance < 50 mL/min**

Vildagliptin and saxagliptin should not be used in patients with moderate or severe renal impairment (CrCl < 50 mL/min). In patients with mild renal impairment (CrCl >50 mL/min) no dosage adjustment is recommended.<sup>2,4</sup>

### **Avoid vildagliptin in people with liver impairment**

Vildagliptin is not recommended in people with any degree of hepatic impairment.<sup>4</sup> Use sitagliptin cautiously in severe hepatic impairment, as there is no clinical experience in this context.<sup>3</sup> No dosage adjustment for saxagliptin is necessary for patients with mild, moderate, or severe hepatic impairment.

### **Age-related dosing issues**

No dosage adjustment for a gliptin is required based solely on age. Because elderly patients are more likely to have decreased renal function, in this population care should be taken in dose selection based on renal function.



### **MEDICINE UPDATE**

NPS *Medicine Update* articles on sitagliptin, vildagliptin and saxagliptin are available for consumers. *Medicine Update* helps consumers to ask the right questions about new medicines, and helps them compare the potential benefits and risks of a new medicine with those of other medicines.

## **Information for patients**

Provide patients and carers with the following information about gliptins:

- ▶ gliptins improve glycaemic control when added to existing therapy. The long-term benefits and adverse effects of these medicines are not fully known
- ▶ a gliptin may cause headache and nausea, and may increase the chance of catching a cold
- ▶ seek urgent medical attention if rash, hives or swelling of the face, lips, mouth, tongue or throat occur during treatment
- ▶ low blood sugar and weight gain may occur when a gliptin is used with a sulfonylurea
- ▶ lifestyle changes including a healthy diet and exercise remain important for controlling blood sugar in conjunction with prescribed medicines
- ▶ treatment is long term and should be continued subject to regular monitoring of blood sugar
- ▶ tell your health care professional about any other medicines you are currently using before taking this medicine
- ▶ seek medical advice if you do not feel well at any time while taking this medicine.

Discuss the Januvia, Galvus, Onglyza, Janumet or Galvumet consumer medicine information (CMI) leaflet with the patient.

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