intraoperative cataract complication rates (posterior capsular rupture with vitreous loss) with undiagnosed intraoperative floppy iris syndrome as high as 12%,[2] falling to 0.6% when the surgeon is aware the patient has used tamsulosin.[1]

## Conclusion

As cataracts and the use of alpha$_1$ adrenergic antagonists increase with age, it is not surprising that the incidence of intraoperative floppy iris syndrome has been reported to occur in up to 3.7% of cataract surgeries.[2] It is important that patients due for cataract surgery are told to remind their ophthalmologist if they have ever taken tamsulosin. The ophthalmologist should also seek this history. Preoperative cessation of the drug is not currently recommended. With recognition of the potential problem and careful pre- and intraoperative planning, the ophthalmologist can minimise surgical complications associated with intraoperative floppy iris syndrome.

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*Conflict of interest: none declared*

## Drug information resources

As of 1 July 2010 the Therapeutic Advice and Information Service (TAIS) national drug information service for health professionals will no longer be operational. The National Prescribing Service acknowledges the dedication and expertise of the staff who contributed to the high quality of TAIS over its ten years of operation.

Closer to the cessation date, health professionals will be able to access an index of other sources of drug information on the NPS website at www.nps.org.au/health_professionals. Please note that while some of these linked resources are open access, others may require a subscription fee.

# New drugs

Some of the views expressed in the following notes on newly approved products should be regarded as tentative, as there may be limited published data and little experience in Australia of their safety or efficacy. However, the Editorial Executive Committee believes that comments made in good faith at an early stage may still be of value. As a result of fuller experience, initial comments may need to be modified. The Committee is prepared to do this. Before new drugs are prescribed, the Committee believes it is important that full information is obtained either from the manufacturer's approved product information, a drug information centre or some other appropriate source.

## Azacitidine

Vidaza (Celgene)

vials containing 100 mg as lyophilised powder for reconstitution

Approved indication: myelodysplasia, leukaemia

Australian Medicines Handbook section 14

The myelodysplastic syndromes are disorders in which the pluripotent stem cells function abnormally. As any cell lines can be affected the patient may have anaemia, neutropenia or thrombocytopenia. The syndromes include chronic myelomonocytic leukaemia and the myelodysplasia may progress to acute myeloid leukaemia.

In myelodysplasia, tumour suppressor genes may be inactivated by hypermethylation. Preventing hypermethylation may reduce the proliferation of abnormal cells.

Azacitidine is an analogue of cytidine, one of the nucleosides which make up nucleic acids. When azacitidine is incorporated into DNA it inhibits DNA methyltransferase, reducing hypermethylation, and has a direct cytotoxic effect on abnormally proliferating cells.

In the first treatment cycle azacitidine is given by daily subcutaneous injection for seven days. This cycle is repeated every four weeks for as long as the patient continues to benefit.

Most of the dose is excreted in the urine as azacitidine and its metabolites. Azacitidine is contraindicated in patients with malignant hepatic tumours and those with renal failure.

After phase II trials of intravenous and subcutaneous doses produced favourable results, a phase III trial was carried out in 191 patients with myelodysplasia. These patients were randomly assigned to azacitidine or supportive care. They were assessed after four treatment cycles, and those who had responded to azacitidine could continue. Responses were assessed by changes in the blood and bone marrow and the need for transfusion. In the azacitidine group, 16% of the patients had a partial response and 7% had a complete response. The median duration of all the improvements was 15 months. No-one in the supportive care group had a complete or a partial

response. With supportive care, the median time to death or the development of acute leukaemia was 12 months, compared with 21 months in the patients treated with azacitidine.[1]

Data from this trial and the phase II trials were reanalysed when an application was made to market the drug in the USA. The assessment criteria had changed and the reanalysis showed that few patients had partial remissions, but 10–17% had complete remissions and 23–36% had some haematological improvement. Under the new criteria some patients were found to have had acute myeloid leukaemia at the start of the studies. Those treated with azacitidine had a median survival of 19.3 months compared with 12.9 months for supportive care.[2]

Another study compared azacitidine with conventional care which could include chemotherapy. This study randomised 358 patients with myelodysplastic syndromes including chronic myelomonocytic leukaemia. Acute myeloid leukaemia developed after a median of 17.8 months with azacitidine and 11.5 months with conventional care. The patients had a median survival of 24.5 months with azacitidine and 15 months with conventional care. However, only 25 patients in the conventional care group received intensive chemotherapy and their survival rate was not statistically different from that of the azacitidine group. Patients given azacitidine had higher haemoglobin concentrations so there was a reduced need for red blood cell transfusions. The approved indications for azacitidine are based on this trial. These are specified forms of myelodysplastic syndromes, chronic myelomonocytic leukaemia, and acute myeloid leukaemia, when allogenic stem cell transplant is not indicated.[3]

Although azacitidine may reduce transfusion requirements it is a cytotoxic drug so patients still need to be monitored for anaemia, neutropenia and thrombocytopenia, particularly at the start of treatment. Infections are common and some patients will develop febrile neutropenia. In addition to full blood counts the patient's liver and renal function should be regularly checked because of the risk of toxicity. As gastrointestinal problems are frequent, antiemetic drugs should be given before each treatment. Other frequent adverse reactions include injection site reactions, dyspnoea, anorexia, arthralgia, dizziness and bruising. Despite the wide range of potentially severe adverse effects, there is evidence that azacitidine leads to a better quality of life by improving the patient's physical functioning, fatigue and dyspnoea.[1]

Most of the patients with myelodysplastic syndromes are elderly. They are not usually suitable for stem cell transplantation, so management has involved supportive care. Azacitidine seems to offer improved survival to specific groups of these patients.

T T manufacturer provided additional useful information

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## Caffeine citrate

Cafnea (Phebra)

2 mL vials containing 40 mg/2 mL for injection and 7 mL vials containing 25 mg/5 mL oral solution

Approved indication: apnoea of prematurity

Australian Medicines Handbook section 19

Premature babies are at risk of apnoea. This can occur in the absence of other problems, such as infection. Primary apnoea appears between two and seven days after birth and is most common in premature babies with a low birth weight. If the apnoea of prematurity is recurrent and prolonged, ventilation may be needed. Methylxanthines such as theophylline have been used as respiratory stimulants. Caffeine is also a methylxanthine and it has been used overseas to treat the apnoea of prematurity.

The mechanism of action is uncertain, but caffeine is thought to increase the response to hypercapnia and increase the respiratory rate. A loading dose is given intravenously over 30 minutes. The subsequent daily maintenance doses can be given intravenously or by mouth. Some of the dose is converted to theophylline, but this occurs slowly in premature babies. The half-life of caffeine in these babies is 80–120 hours. Most of the dose is excreted unchanged in the urine.

A study compared caffeine citrate with placebo in 82 babies, born between 25 and 32 weeks of gestation, who were having at least six episodes of apnoea in 24 hours. Over 7–10 days 69% of the caffeine group, but only 43% of the placebo group, achieved at least a 50% reduction in episodes of apnoea.[1]

A larger placebo-controlled study included babies with birth weights of 500–1250 g. The 2006 babies had an average gestational age of 27 weeks. Many were being treated for apnoea, but some babies were given treatment to prevent apnoea or to assist the removal of an endotracheal tube. The

first doses were given at a median age of 28 weeks and were stopped before 35 weeks. Supplemental oxygen was needed by 36% of the babies given caffeine citrate and 47% of those given a placebo. Compared to the placebo group, babies given caffeine citrate were significantly less likely to require surgical closure of a patent ductus arteriosus.[2]

Babies given caffeine may initially gain less weight than other premature babies. Most adverse effects are probably related to the stimulant action of caffeine. They include tachycardia, tachypnoea and jitteriness. Maternal consumption of caffeine should be considered when prescribing caffeine citrate.

Premature babies are very vulnerable patients. In long-term follow-up, 40% of the babies given caffeine died or survived with a neurodevelopmental disability. This was a statistically better outcome than the 46% rate seen in the placebo group. To prevent one adverse outcome 16 babies need to be treated for 37 days. Much of the benefit of caffeine is from earlier discontinuation of positive airways pressure.[3]

The results of the larger study are difficult to interpret because of the different indications for giving caffeine. In Australia the use of caffeine citrate will be restricted to the short-term treatment of the apnoea of prematurity in babies between 28 and 33 weeks of gestational age.

T T T manufacturer provided clinical evaluation

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## Human C1 esterase inhibitor

Berinert (CSL)

vials containing 500 units as freeze-dried powder for reconstitution

Approved indication: hereditary angioedema

Australian Medicines Handbook Appendix A

C1 esterase inhibitor is a protein derived from human plasma. It is indicated for the treatment of acute attacks of hereditary angioedema. This condition is characterised by episodes of swelling in the skin or mucosa and can occur anywhere in the body (face, larynx, gut, limbs). It can be painful, particularly with gastrointestinal attacks, and if the larynx is affected asphyxiation and death can occur.

Type I and type II hereditary angioedema are caused by mutations in the gene encoding the C1 esterase inhibitor. Although not well defined, the absence or dysfunction of this protein is thought to lead to increased vascular permeability due to unregulated bradykinin activation. Replacing C1 esterase inhibitor intravenously during an acute attack reduces ongoing inflammatory processes. Treatments for histamine-induced angioedema, such as corticosteroids, antihistamines or adrenaline, have no effect in patients with hereditary angioedema.

The efficacy of C1 esterase inhibitor has been investigated in a randomised controlled trial in 125 adults and children with confirmed acute moderate to severe hereditary angioedema. Overall, 79% of patients presented with a gastrointestinal attack and 20.2% with a facial attack. Patients were randomised to receive C1 esterase inhibitor 10 U/kg or 20 U/kg (39 and 43 patients) or placebo (42 patients). Within four hours of treatment, 70% of patients had responded in the C1 esterase inhibitor 20 U/kg group compared to 43% in the placebo group. The median time to onset of symptom relief was significantly shorter for C1 esterase inhibitor 20 U/kg (0.5 hours) than for placebo (1.5 hours). The median response time for the lower-dose C1 esterase inhibitor (10 U/kg) was only slightly shorter than for placebo (1.2 vs 1.5 hours). Median time to complete resolution of symptoms was much shorter for C1 esterase inhibitor 20 U/kg than for placebo (4.9 vs 7.8 hours) but not for C1 esterase inhibitor 10 U/kg (20 hours).[1] The 20 U/kg dose is currently recommended for hereditary angiodema.

In the trial, the most frequent adverse events were nausea, diarrhoea, abdominal pain and muscle spasms. Most of the adverse events were more common with placebo than with C1 esterase inhibitor 20 U/kg (43.9% vs 19.6%) and may have been related to the patients' angioedema attacks.[1] Taste disturbance was reported with C1 esterase inhibitor 20 U/kg (2/46 patients) but not with placebo (0/41 patients). An increase in severity of pain associated with hereditary angioedema was the most severe adverse effect reported by patients who received the active treatment. Antibodies to C1 esterase inhibitor and their effect on efficacy or adverse reactions were not measured in the trial.

In an observational study of three women, the commencement of frequent treatments with C1 esterase inhibitor was associated with an increase in angioedema attacks (4-fold, 5-fold and 12-fold). A control group of 24 age-matched men and women did not show the same increase in attacks over a nine-year period. It was not clear what caused this increase, but investigators speculated that frequent treatments may have lowered the threshold for activation of an attack.[2]

This C1 esterase inhibitor is made from human plasma sourced from overseas. Like all plasma products, it has

the potential to transmit infections caused by viruses and prions (e.g. variant Creutzfeldt-Jakob disease). During the randomised controlled trial, none of the patients seroconverted to produce antibodies to HIV, hepatitis or human parvovirus 19 virus.[1] The infectious disease risk of C1 esterase inhibitor has been reduced by screening blood donors and their plasma for evidence of viral infections such as HIV and hepatitis C. Also during fractionation, plasma undergoes processes to inactivate or remove certain viruses. Nevertheless, patients should be warned that there is still an infectious disease risk with this product. Vaccination against viruses that could potentially be present in plasma, such as hepatitis B, should be considered.

Severe hypersensitivity reactions can occur with C1 esterase inhibitor and adrenaline should be available when injections are given. For patients who are known to have a tendency to allergies, antihistamines and corticosteroids should be given prophylactically. Prescribers should be aware that thrombosis has been reported with C1 esterase inhibitor when used at doses higher than 20 U/kg and for unapproved indications.

C1 esterase inhibitor seems to be an effective treatment for hereditary angioedema and has been used overseas for more than 30 years. However, there have been reports in a minority of patients that it may increase the frequency of angioedema attacks.

☒ manufacturer declined to supply data

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## Miglustat

Zavesca (Actelion)

100 mg capsules

Approved indication: type I Gaucher disease and Niemann-Pick disease type C

Australian Medicines Handbook Appendix A

Miglustat is indicated for people with mild to moderate type I Gaucher disease, and for progressive neurological manifestations in adults and children with Niemann-Pick type C disease. These are both rare inherited disorders which result in the build-up of glycosphingolipids in the body.

Miglustat is a synthetic analogue of D-glucose and is a competitive inhibitor of glucosylceramide synthase, an enzyme involved in the synthesis of most glycosphingolipids. Treatment with miglustat aims to reduce the production of glycosphingolipids.

Type I Gaucher disease is caused by a deficiency in beta-glucocerebrosidase – an enzyme which breaks down the glycosphingolipid glucocerebroside. This lipid builds up in macrophages found primarily in the liver, spleen and bone marrow. Clinical features of this disease include hepatomegaly, splenomegaly, anaemia, thrombocytopenia and bone lesions.

Regular intravenous infusion of recombinant glucocerebroside (see Aust Prescr 1999;22:95–8) is the mainstay of treatment and benefits most patients with type I Gaucher disease. Miglustat is an oral option for people who cannot have enzyme therapy.

The safety and efficacy of miglustat has been assessed in several open-label studies.[1–4] In the main trial of 28 patients, treatment with oral miglustat 100 mg three times a day reduced mean liver size by 12% (CI‡ 7.8–16.4) and mean spleen size by 19% (CI 14.3–23.7) after 12 months. (Seven patients had had a previous splenectomy.) Nine of the 22 patients who completed treatment had anaemia (<115 g/L) at baseline. After 12 months, haemoglobin had increased by more than 5 g/L in five of these people. Of the 21 patients who could be assessed for platelet count, four had an increase of at least 15 x $10^9$/L platelets. Glycolipid biosynthesis – assessed by measuring surface expression of $G_{m1}$ on leucocytes – was found to have decreased by an average of 38.5% over 12 months in a sample of five patients. Plasma chitotriosidase activity – a measure of stored lipids – had also decreased by the end of the trial.[1] The benefits of miglustat were maintained for up to three years in an extension of the trial.[2] Similar effects on the liver and spleen were observed in the other open-label trials.[2–4]

The most frequent adverse event during the trial was diarrhoea (79% of patients). Six patients dropped out – two of these were because of gastrointestinal problems. Two patients were withdrawn because of paraesthesiae which were confirmed to be peripheral neuropathy.[1] Other common adverse events reported in the open-label trials included weight loss, tremor, flatulence and abdominal pain.[2–4]

Dose reduction or discontinuation may be required for tremor. Peripheral neuropathy may be related to vitamin $B_{12}$ deficiency, which is common in type I Gaucher disease, so regular monitoring of vitamin $B_{12}$ as well as neurological evaluation is recommended.

Niemann-Pick type C disease is an incurable progressive disease that leads to premature death. Impaired transport of lipids within cells causes some fatty acids including glycosphingolipids to accumulate in tissues and organs,

‡ confidence interval

particularly the brain. This can lead to supranuclear gaze palsy, ataxia, problems with speech and swallowing, dystonia, seizures, dementia, psychiatric problems and gelastic cataplexy[§].

Until now, treatment for this disease has mainly been supportive. As miglustat can cross the blood–brain barrier, its efficacy has been assessed in Niemann-Pick type C disease. In a randomised controlled 12-month trial, oral miglustat 200 mg given three times a day was compared to standard care (drug treatment and physical, speech and occupational therapy) in a 2:1 ratio in 28 patients aged 12 years or older. In addition, 12 children aged under 12 years enrolled in the trial were all given miglustat (dose was adjusted according to body surface area). Most of the participants had severe clinical manifestations at baseline and were allowed to continue their medications which included analgesics, antibiotics, antidiarrhoea drugs, sedatives and hypnotics, antiepileptics and drugs to treat dystonia.[5]

The main measure of efficacy in the trial was the speed of horizontal eye movements between fixed points. After a year of treatment, improvements were observed in patients given miglustat, but this was not significantly different to results seen in patients given standard care alone. Improvements in the ability to swallow and in intellectual performance (mini-mental status examination) were also seen in older patients (>12 years old) given miglustat compared to those who received standard care.[5] Open-label extensions of this study (up to three years) reported that patients' neurological symptoms did not progress while taking miglustat.[6,7]

A retrospective observational study analysed physician questionnaires about ambulation, manipulation, language and swallowing in patients who had been taking miglustat for an average of 1.5 years. Overall, 74.5% (49/65) of patients had reduced disease progression or stabilisation of neurological symptoms.[8]

Adverse events in Niemann-Pick disease were similar to those seen in type I Gaucher disease, with diarrhoea being the most common (85% of patients). Weight loss (63%), tremor (46%) and flatulence (44%) were also frequently reported. Severe adverse events included severe confusional state and salivary hypersecretion, severe dehydration and respiratory syncytical virus infection. These were thought to be unrelated to miglustat. Three people were withdrawn from the trial because of an adverse event – one because of insomnia and confusional state, one due to diarrhoea related to Crohn's disease and one from lethargy, impaired memory and depression (in a child).[5]

As weight loss was commonly reported with miglustat, growth rate should be monitored in children and adolescents taking miglustat. Reductions in platelet counts have occurred with miglustat in Niemann-Pick disease so blood counts should be monitored. Dizziness was a common adverse effect and patients should not drive if they experience this. The benefit of miglustat in Niemann-Pick disease should be reviewed at six-month intervals.

To reduce gastrointestinal effects such as diarrhoea, miglustat should not be taken with food. After a 100 mg dose, maximum plasma concentrations are reached after approximately two hours. Its half-life is about 6–7 hours so steady-state concentrations are predicted to be reached after 1.5–2 days. Miglustat is excreted mainly by the kidneys so dose adjustment may be necessary with milder renal impairment. It is not recommended in severe renal impairment.

Miglustat showed modest efficacy in mild to moderate type I Gaucher disease and Niemann-Pick disease, although numbers of patients in the trials were small. It has been approved as an orphan drug in Australia and is only available through the Life Saving Drugs Program.

T manufacturer provided only the product information

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§ sudden weakness or collapse associated with strong emotion, particularly laughter

## Vildagliptin

Galvus (Novartis)

50 mg tablets

Approved indication: type 2 diabetes

Australian Medicines Handbook section 10.1.3

Patients with type 2 diabetes often need more than one drug to control their blood glucose. When first-line treatment fails, the incretin mimetics and enhancers are a class of drugs which can be added to treatment (see Aust Prescr 2008;31:102–8). Within this class are the inhibitors of dipeptidyl peptidase 4 (DPP4) such as sitagliptin. These drugs block incretin metabolism and this leads to reductions in blood glucose concentrations.

Vildagliptin is a DPP4 inhibitor which is taken twice daily with metformin or a thiazolidinedione and once daily with a sulfonylurea. A 50 mg dose will inhibit most DPP4 activity for at least 12 hours. Most of the dose is converted to inactive metabolites. This metabolism does not involve the cytochrome P450 system so the potential for metabolic drug interactions is reduced. The elimination half-life is three hours with most of the metabolites being excreted in the urine. Vildagliptin is not recommended for patients with hepatic or moderate or severe renal impairment.

A systematic review which included 14 trials of vildagliptin involving 6121 patients concluded that treatment reduces glycated haemoglobin (HbA1c) by 0.6%.[1] Several studies have investigated if this makes a significant difference when vildagliptin is added to other drugs.

Vildagliptin 50 mg daily was added to the treatment of 56 people whose diabetes was not completely controlled by metformin. After 12 weeks their mean HbA1c had reduced by 0.6% from a baseline of 7.7%. There was no change in control in 51 other patients who were given a placebo to take with their metformin. Some of the patients continued in an extension of the trial with 32 of the vildagliptin group and 26 of the placebo group completing one year of treatment. There was no significant change in the vildagliptin group, but HbA1c increased in the placebo group so that there was a difference of 1.1% between the groups after a year. An HbA1c below 7% was achieved by 41.7% of those who added vildagliptin, but only 10.7% of those who added a placebo.[2]

Another trial studied vildagliptin 100 mg, as well as 50 mg, as an addition to treatment with metformin. After 24 weeks the HbA1c concentration had fallen by 0.9% in the 185 people randomised to add 50 mg twice daily, by 0.5% in the 177 randomised to add 50 mg once daily, and increased by 0.2% in the 182 randomised to add a placebo. The proportion of patients achieving an HbA1c under 7% depended on their baseline concentrations. If the baseline HbA1c was greater than 8.5%, it was only reduced below 7% in 16.3% of patients given vildagliptin 100 mg, 7.5% of those given 50 mg and 2.1% of those given placebo.[3]

When type 2 diabetes is not controlled by metformin alone a sulfonylurea can be added. This approach has been compared with adding vildagliptin in a study of 2789 patients. There were 1396 who were randomised to add vildagliptin 50 mg twice daily and 1393 who were randomised to add glimepiride. After 52 weeks the mean reduction in HbA1c was 0.44% with vildagliptin and 0.53% with glimepiride. From a mean baseline of 7.3%, a target HbA1c of under 7% was reached by 54% of the vildagliptin group and 56% of the glimepiride group.[4]

Vildagliptin has also been added to the treatment of patients with diabetes which was inadequately controlled by a sulfonylurea. Their mean HbA1c was 8.5%. While 170 patients were randomised to add vildagliptin 50 mg once daily and 169 to add vildagliptin 50 mg twice daily, another 176 patients were given a placebo. All the patients also took glimepiride. After 24 weeks the mean HbA1c declined 0.58% with vildagliptin 50 mg and 0.63% with vildagliptin 100 mg while it increased by 0.07% in the placebo group. Only 12% of the patients in the placebo group achieved an HbA1c below 7% compared to 21% of the vildagliptin 50 mg group and 25% of the 100 mg group. As there was no significant advantage with the higher dose, the recommended daily dose of vildagliptin, in combination with a sulfonylurea, is 50 mg.[5]

Although monotherapy with a thiazolidinedione is not the usual first-line therapy, a trial, in 463 people with type 2 diabetes, has studied the effect of adding vildagliptin to treatment with pioglitazone. After 24 weeks, adding vildagliptin 50 mg once daily reduced the mean HbA1c by 0.8%, twice daily reduced it by 1%, while placebo reduced it by 0.3%. The HbA1c fell below 7% in 29% of those given 50 mg, 36% of those given 100 mg and 15% of those given a placebo.[6]

In trials of monotherapy the incidence of adverse events has been similar for vildagliptin and placebo. However, the frequency of infections (1.4% vs 0.3%) and neurological symptoms (0.9% vs 0.6%) was greater with vildagliptin than with placebo. Tremor, dizziness and headache are common when vildagliptin is given with metformin or a sulfonylurea. Peripheral oedema is more frequent with vildagliptin, than with placebo, when added to treatment with a thiazolidinedione.[6] Adding vildagliptin to other oral hypoglycaemic drugs can increase the risk of hypoglycaemia. The frequency with glimepiride is 1.2% and 1% with metformin. Hypoglycaemia is more likely to occur if glimepiride, rather than vildagliptin, is combined with metformin.[4] There have been rare cases of angioedema and hepatitis during treatment with vildagliptin. Liver function should be checked before and during treatment. The patient's renal function should also be checked before treatment with vildagliptin.

In animal studies vildagliptin has caused problems with skin ulceration and cardiac conduction, while the significance in humans is unknown. Animal studies also show increased mammary tumours at high doses.

Sulfonylureas can cause patients to gain weight and there was a significant difference between the weight of patients who added glimepiride compared to those who added vildagliptin to treatment with metformin. However, over a year the weight of the patients taking vildagliptin only fell an average of 0.23 kg.[4] This was similar to the 0.2 kg reduction seen in both groups in the 52-week placebo-controlled trial of metformin and vildagliptin.[2]

A role for the DPP4 inhibitors as add-on treatments is yet to be established, particularly in patients who are already using more than one drug. Their long-term safety is also unknown. The systematic review concluded that DPP4 inhibitors currently have no advantage over other drugs which lower blood glucose.[1]

☒ manufacturer declined to supply data

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The T-score (T) is explained in 'New drugs: transparency', Aust Prescr 2009;32:80–1.

* At the time the comment was prepared, information about this drug was available on the website of the Food and Drug Administration in the USA (www.fda.gov).

† At the time the comment was prepared, a scientific discussion about this drug was available on the website of the European Medicines Agency (www.emea.eu).

A At the time the comment was prepared, information about this drug was available on the website of the Therapeutic Goods Administration (www.tga.gov.au/pmeds/auspar.htm)

## Corrections

**Nebivolol** (Aust Prescr 2010;33:52–9)

In the SENIORS trial, the reduction of 4.2% in the composite end point of all-cause mortality or hospitalisation, is the absolute risk reduction, not the relative risk reduction.

**Ustekinumab T-score** (Aust Prescr 2010;33:52–9)

☒ manufacturer declined to supply data

Janssen-Cilag did respond to the request for data, but their response was not received in the *Australian Prescriber* office. The company declined to provide the clinical evaluation.

## Answers to self-test questions

1. False
2. True
3. True
4. False

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