

## In Brief

*A digest of news items about NPS RADAR, new drugs and changes to PBS listings.*

### Rizatriptan (Maxalt) 10 mg wafers for migraine, and revised listings for other 5HT<sub>1</sub> agonists ('triptans')

Rizatriptan 10 mg wafers were listed on the Pharmaceutical Benefits Scheme (PBS) as authority required (streamlined) on 1 March 2010 for people with past migraines that have usually failed to respond to analgesics.<sup>1</sup>

Rizatriptan has been available overseas for more than 10 years.<sup>2</sup> All triptans are effective for migraine<sup>3,4</sup> but individual response cannot be predicted.<sup>5</sup> If the first triptan fails, try another.

As of 1 April 2010, the PBS restriction for naratriptan, sumatriptan and zolmitriptan has changed: there is no longer a requirement for past migraines to have failed to respond to ergotamine\*.<sup>6</sup> This change brings the restriction into line with that of rizatriptan.

\* Injectable dihydroergotamine is the only ergot alkaloid indicated for migraine listed on the PBS.

### References

1. Pharmaceutical Benefits Advisory Committee. Positive recommendations made by the Pharmaceutical Benefits Advisory Committee (PBAC) in November 2009 relating to the listing of drugs on the Pharmaceutical Benefits Scheme (PBS). Canberra: Australian Government Department of Health and Ageing, 2009. <http://www.health.gov.au/internet/main/publishing.nsf/Content/pbacrec-nov09-positive> (accessed 6 January 2010).
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### Albendazole (Zentel) listing extended to treat hookworm and strongyloidiasis

The streamlined authority listing for albendazole tablets (200 mg) has been extended as of 1 March 2010 to include treatment of strongyloidiasis and hookworm.<sup>1</sup>

Strongyloidiasis and hookworm are endemic in tropical and subtropical regions, including Africa, Asia and the Americas. They are also common in Aboriginal and Torres Strait Islander communities in northern Australia.<sup>2–4</sup>

Albendazole is the treatment of choice for hookworm.<sup>3,5</sup> In strongyloidiasis, ivermectin (Stromectol) is the treatment of choice but albendazole is an alternative for those in whom ivermectin is unsuitable (see below).<sup>3,5</sup>

### Life cycle

Both hookworms and *Strongyloides stercoralis* infect humans via larvae that penetrate the skin, are carried by the blood to the lungs and then migrate to the small intestine via the trachea and oesophagus. There they become adults and attach themselves to the intestinal wall to feed and lay eggs.<sup>2,6,7</sup>

Adult hookworms can live in the human body for up to 5–7 years but they are unable to reproduce solely within a human host.<sup>6</sup> Instead eggs are excreted in faeces, hatch in contaminated soil and then develop into larvae that can infect another person.<sup>7</sup>

In contrast, without adequate treatment *S. stercoralis* infection may be lifelong due to auto-infection. *S. stercoralis* larvae hatch from eggs while still in the intestinal tract. Some of these newly hatched larvae re-infect the host and repeat the cycle while others are passed in the faeces. Excreted larvae can infect other people or develop into free-living adults that continue laying eggs.<sup>2</sup>

### Symptoms

Strongyloidiasis and light hookworm infections are often asymptomatic. However, local itching and rash may occur where larvae penetrate the skin and respiratory symptoms may occur when larvae migrate into the lungs.<sup>2,7</sup>

In heavy hookworm infections, blood loss where adult hookworms attach themselves to the intestinal wall can cause anaemia.<sup>6</sup> Other symptoms may include abdominal pain, diarrhoea, loss of appetite, weight loss, and stunted growth and mental development.<sup>7</sup>

Auto-infective *S. stercoralis* larvae can disseminate throughout the body and may carry intestinal bacteria to other parts of the body.<sup>2,8</sup> Disseminated disease is potentially fatal and poses the greatest risk to people who are immunocompromised or taking corticosteroids.<sup>8</sup> People with disseminated disease may present with abdominal pain, distension, shock, pulmonary and neurological complications and septicaemia.<sup>2</sup>

### Diagnosis and treatment

Use a single dose of albendazole to treat hookworm. Albendazole is less effective than ivermectin in treating strongyloidiasis and should be reserved for those in whom ivermectin is not recommended (Table 1).<sup>3,9</sup>

Ivermectin is not recommended in children < 5 years because of a lack of data.<sup>11</sup> Refer young children with strongyloidiasis to a paediatrician or infectious-disease specialist.<sup>3</sup> In remote areas where access to a specialist may be difficult, albendazole may be given.<sup>5</sup> Use 200 mg once daily for 3 days if the child is < 10 kg, and 400 mg once daily for 3 days if the child is > 10 kg. Take on an empty stomach to increase intestinal absorption and repeat after 1 week.<sup>4,9</sup>

	Hookworm	Strongyloidiasis
<b>Diagnosis</b>	Examine stool sample for eggs	Use serology: examining a stool sample is relatively insensitive
<b>Treatment</b>	Single dose of albendazole Adults and children > 10 kg: 400 mg dose (2 × 200 mg tablets) Children > 6 months and < 10 kg: 200 mg	Albendazole is second choice. Use ivermectin* except in: • children < 5 years • people with <i>Loa loa</i> ('eye worm')

\* 200 micrograms/kg orally with fatty food; repeat 7–14 days later<sup>3,10</sup>

Ivermectin should not be used in people who also have *Loa loa* (loiasis), as there is a risk of severe encephalopathy or death in these patients.<sup>3,11</sup> Use serology to rule out *L. loa* in people from West and Central Africa (where it is endemic) or in people who report episodic subcutaneous swellings or an 'eye-worm'.<sup>3</sup> Refer people with loiasis to an infectious-disease specialist.<sup>3</sup>

### Safety

Albendazole should not be used in pregnancy or in children aged < 6 months.<sup>9,12</sup> The manufacturer recommends discontinuing breastfeeding during, and for 5 days after, treatment.<sup>12</sup>

The most common adverse effect is abdominal pain, reported by 1% of trial participants. Other less common side effects include diarrhoea, nausea, headache, dizziness and skin rashes.<sup>9,12</sup>

### Federal government assistance for refugee health assessments

Medicare Benefits Schedule (MBS) item numbers 714 and 716 reimburse general practitioners who perform refugee and humanitarian entrant health assessments within 12 months of the patient's arrival in Australia.

Refugee health assessments should always be undertaken with an appropriate interpreter, preferably someone who is not known to the patient personally.<sup>3</sup> The Telephone Interpreting Service (TIS) is available free of charge to general practitioners who provide a Medicare service to non-English speaking permanent residents or Australian citizens. Call the TIS Doctors' Priority Line (1300 131 450) to access this service.<sup>13</sup>

### References

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## Postmarketing reports of pancreatitis with sitagliptin products (Janumet, Januvia)

Cases of acute pancreatitis have been reported with sitagliptin (Januvia) and sitagliptin with metformin (Janumet).<sup>1</sup> Health professionals should be vigilant for signs and symptoms of pancreatitis during treatment and should use sitagliptin products cautiously in people with a history of pancreatitis.

Report suspected adverse reactions to the Therapeutic Goods Administration (TGA) online ([www.ebs.tga.gov.au](http://www.ebs.tga.gov.au) [click 'Adverse reaction to a medicine' at left]) or by using the 'Blue Card' distributed 3 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)).

Sitagliptin was first listed on the PBS in 2008, followed by sitagliptin with metformin in 2009. For more information about sitagliptin, see the *NPS RADAR* review 'Sitagliptin (Januvia) for type 2 diabetes' and In Brief item 'Sitagliptin with metformin (Janumet) fixed dose combination tablets PBS listed for type 2 diabetes mellitus'.

### Pancreatitis is a possible adverse effect, but a causal association has not been confirmed

Between October 2006 and February 2009 the US Food and Drug Administration (FDA) received 88 reports of acute pancreatitis in people taking sitagliptin or sitagliptin with metformin.<sup>1</sup> Symptoms most commonly reported in these cases were nausea, vomiting and abdominal pain.<sup>1</sup> Many cases were severe: 58 required hospitalisation (4 in intensive care) and 2 involved haemorrhagic or necrotising pancreatitis.<sup>1</sup>

In some reports the onset of pancreatitis was soon after starting sitagliptin or sitagliptin with metformin. Nineteen cases were within a month of starting treatment, and more than half of all cases resolved when treatment was stopped.<sup>1</sup>

A causative relationship between sitagliptin and pancreatitis has not been established. Diabetes itself is a risk factor for pancreatitis. Other risk factors such as hypercholesterolaemia, hypertriglyceridaemia and obesity were also present in 51% of the US cases.<sup>1</sup> In clinical trials, the incidence of pancreatitis did not differ significantly between the sitagliptin (0.1%) and non-exposed groups (0%)<sup>2</sup>, although the data do not rule out a rare adverse effect.

In September 2009 the FDA issued a warning to health professionals about the reports of pancreatitis, and accordingly updated the US prescribing information in December 2009.<sup>3,4</sup> The Australian product information for products containing sitagliptin was updated earlier that year to include pancreatitis as a postmarketing adverse event.<sup>5,6</sup>

### Monitor and warn about signs and symptoms, particularly in people with risk factors

Be vigilant for the onset of persistent severe abdominal pain (sometimes radiating to the back), nausea, vomiting and/or anorexia in patients taking sitagliptin or sitagliptin with metformin.<sup>1</sup> Advise them to promptly report any signs and symptoms, especially if they have any additional risk factors for pancreatitis.<sup>1</sup>

Use cautiously and closely monitor treatment in people with a history of pancreatitis.<sup>1</sup> Sitagliptin has not been studied in these people.<sup>1</sup> It is unknown whether patients with a history of pancreatitis are at increased risk of developing pancreatitis with sitagliptin or sitagliptin with metformin.<sup>1</sup>

If pancreatitis is suspected, stop treatment and investigate (e.g. with a serum amylase test).<sup>1</sup>

## References

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## Authority listing for terbinafine extended to children and adolescents

The authority listing for terbinafine 250 mg tablets was extended on 1 March 2010. Any child or adolescent (< 18 years) may now receive treatment for a dermatophyte infection that has not responded to topical treatment and oral griseofulvin. Similarly, the streamlined authority listing for terbinafine 1% cream now includes the treatment of fungal or yeast infections in this age group.<sup>1</sup> These authority listings were previously restricted to Aboriginal and Torres Strait Islander people only.<sup>2</sup>

The Pharmaceutical Benefits Advisory Committee (PBAC) recommended the extended listings on the basis of clinical need for children and adolescents.<sup>1</sup> The TGA-approved product information does not recommend terbinafine tablets for children or adolescents, and the cream is not recommended for children < 12 years.<sup>3,4</sup> However, there are some small trials to support use in children and adolescents<sup>5–7</sup> and paediatric oral dose recommendations are available (see Box 1).<sup>5,8</sup> Terbinafine oral granules\* are indicated for people > 4 years in the US (with slightly higher mg/kg dose recommendations).<sup>9</sup>

Prescribe terbinafine tablets only if terbinafine cream and oral griseofulvin have not treated the fungal infection: if > 6 weeks of terbinafine tablets are required, monitor blood count and liver enzymes.<sup>10</sup> Oral terbinafine is associated with rare but serious adverse effects (e.g. blood dyscrasias, liver failure).<sup>3,11–13</sup> The US FDA found that skin reactions were the most often reported postmarketing adverse event for terbinafine for children.<sup>14</sup>

### Box 1: Paediatric dose recommendations for terbinafine tablets†

Weight (kilogram)	Daily dose (mg)
< 20	62.5
20–40	125
> 40	250

† 250 mg scored tablets are the only strength available in Australia, so doses for children < 40 kg require tablets to be broken.

\* Not available in Australia.

## References

1. Pharmaceutical Benefits Advisory Committee. Positive recommendations made by the Pharmaceutical Benefits Advisory Committee (PBAC) in November 2009 relating to the listing of drugs on the Pharmaceutical Benefits Scheme (PBS). Canberra: Australian Government Department of Health and Ageing, 2009. <http://www.health.gov.au/internet/main/publishing.nsf/Content/pbacrec-nov09-positive> (accessed 6 January 2010).
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## Extended PBS listings for zoledronic acid 5mg (Aclasta)

From 1 April 2010, zoledronic acid 5 mg (Aclasta) can be prescribed on the PBS as the sole anti-resorptive agent for:

- osteoporosis in men without hip fracture
- people with corticosteroid-induced osteoporosis
- people with symptomatic Paget's disease.<sup>1,2</sup>

The authority-required listing for zoledronic acid was previously restricted to:

- women with osteoporosis and any fracture due to minimal trauma
- women aged > 70 years with a bone mineral density (BMD) T-score of  $\leq -3.0$
- men with a hip fracture due to minimal trauma.

(See the NPS RADAR review: 'Zoledronic acid (Aclasta) for osteoporosis' for more information.<sup>3</sup>)

### No longer restricted to men with hip fracture only

The extended PBS listing for osteoporosis allows zoledronic acid to be prescribed for men with any type of minimal trauma fracture and for men aged > 70 years with a BMD T-score of  $\leq -3.0$ . This is similar to the listings for alendronate and risedronate — other PBS-listed bisphosphonates for osteoporosis (see Box 1).<sup>4</sup>

### Corticosteroid-induced osteoporosis

Zoledronic acid may now be prescribed for people on long-term high-dose ( $\geq 3$  months at  $\geq 7.5$  mg daily prednisolone or equivalent) corticosteroid therapy and with a BMD T-score  $\leq -1.5$ . Until now, risedronate was the only other PBS-listed medicine for corticosteroid-induced osteoporosis (see the *NPS RADAR* In Brief news item: 'Risedronate [Actonel and Actonel Once-a-Week] for corticosteroid-induced osteoporosis'<sup>5</sup> and Box 1 for more information).<sup>4</sup> The PBAC recommended extending the listing of zoledronic acid on a cost-minimisation basis — that is, similar efficacy and cost — compared with risedronate. The equi-effective doses for this comparison were zoledronic acid 5 mg once yearly and risedronate 5 mg once daily.<sup>1</sup>

### Symptomatic Paget's disease

This extended PBS listing is similar to those of alendronate, pamidronate, risedronate and tiludronate — the other PBS-listed bisphosphonates for symptomatic Paget's disease (see Box 1).<sup>4</sup> The PBAC recommended this listing on a cost-minimisation basis compared with pamidronate. The equi-effective doses for this comparison were 1 infusion of zoledronic acid 5 mg once yearly and 2 infusions of pamidronate 60 mg per year.<sup>1</sup>

### References

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### Box 1: PBS-listed bisphosphonates for osteoporosis, corticosteroid-induced osteoporosis and symptomatic Paget's disease\*<sup>4</sup>

Generic names	Brand names	PBS listing		
		Osteoporosis	Corticosteroid-induced osteoporosis	Symptomatic Paget's disease
Alendronate sodium	Adronat, Alendrobell, Alendro Once Weekly, Fosamax Once Weekly, Fosamax Plus, Ossmax	✓		✓
Disodium etidronate <sup>†</sup>	Didrocal, Didronel	✓		✓
Disodium pamidronate	Aredia, Pamisol			✓
Risedronate sodium	Actonel, Actonel Once-a-month, Actonel Once-a-week, Actonel Combi, Actonel Combi D	✓	✓	✓
Tiludronate disodium	Skelid			✓
Zoledronic acid	Aclasta	✓	✓	✓

\* Streamlined authority listings except for zoledronic acid (which is authority required)

<sup>†</sup> Restricted to osteoporosis in patients with fracture due to minimal trauma or for symptomatic Paget's disease when calcitonin has been found to be unsatisfactory due to either lack of efficacy or unacceptable side effects