

## In Brief

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

#### **Nicotine patches for Aboriginal and Torres Strait Islander people**

Nicotine patches (Nicorette, 15 mg per 16 hours) were authority listed on 1 December 2008 for nicotine dependence in Aboriginal and Torres Strait Islander people. This is the only nicotine replacement therapy subsidised for people who identify as Aboriginal and Torres Strait Islanders. The listing is part of the 2004–05 Budget measure to improve access to medicines for Aboriginal and Torres Strait Islander people.\*

#### **Up to 2 courses per year — one strength only**

The authority-required listing allows for up to two courses per year.<sup>1</sup> The maximum duration of a course is 12 weeks, with the aim being to stop the patches within this period.<sup>2,3</sup> The listing is for the 15 mg per 16 hours strength of nicotine patches only. Although the manufacturer recommends gradual withdrawal after 8 weeks using lower-strength patches<sup>4</sup>, trials found no benefit of tapering over abrupt withdrawal.<sup>5</sup>

#### **Supporting readiness to quit**

Before starting nicotine patches, a person must be motivated to quit and must stop smoking.<sup>4</sup> There are specific barriers to quitting for Aboriginal and Torres Strait Islander people (for example, social pressures in communities<sup>6</sup> and stressful life events<sup>7</sup>). Resources for smokers who wish to quit are available from Quit (The National Tobacco Campaign) at [www.Quitnow.info.au](http://www.Quitnow.info.au). Further support materials and contact details for tobacco-control programs for Aboriginal and Torres Strait Islander people are available from the Centre for Excellence in Indigenous Tobacco Control at [www.ceitc.org.au](http://www.ceitc.org.au)

#### **Prescribing nicotine patches**

When a person starts nicotine patches, ensure that support services are provided to improve the outcome of treatment.<sup>2,8</sup> Advise them of the following before prescribing<sup>4</sup>:

- avoid smoking while using nicotine patches; smoking at the same time can cause nausea, vomiting, palpitations, chest pain and other symptoms

- local skin reactions, such as redness, itch or rash, are common with nicotine replacement therapy
- apply the nicotine patch to an area of clean, dry hairless skin on the upper part of the body and change the site each day to reduce the risk of skin irritation
- smoking cessation with or without nicotine patches can cause dizziness, headache and sleep disturbances and other symptoms; these usually resolve within a couple of weeks of quitting.

#### **High prevalence of smoking among Aboriginal and Torres Strait Islander people**

The prevalence of tobacco smoking among Aboriginal and Torres Strait Islander people is twice that of other Australians, and consequently the rates of tobacco-related disease are higher.<sup>9</sup> The effectiveness of nicotine replacement therapies in Aboriginal and Torres Strait Islander people has not been established; small studies indicate that nicotine patches in combination with counselling may benefit some individuals<sup>8,10,11</sup>, but quit rates are likely to be lower than those reported in major trials with other populations<sup>10</sup>).

\* For details of all listings on the PBS for Aboriginal and Torres Strait Islander people and how to prescribe these items, refer to the Schedule at [www.pbs.gov.au](http://www.pbs.gov.au), click on the Health Professional tab, then 'For PBS Prescribers' and follow the link.

#### **References**

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## Second human papillomavirus vaccine (Cervarix) included on the National Immunisation Program

A second human papillomavirus (HPV) vaccine (Cervarix) has been accepted for use through the National HPV Vaccination Program. This Program allows free vaccination for girls aged 12 and 13 years, with a catch-up program for all females aged 13–26 years\* through the National Immunisation Program (NIP) due to finish at the end of June 2009.<sup>1</sup> Individual State or Territory Health Departments will decide which of the 2 approved HPV vaccines (Gardasil or Cervarix) to supply in the future.

Cervarix is a bivalent HPV vaccine that protects against infection with HPV types 16 and 18. These 2 types are responsible for 70% to 80% of cervical cancers and around 45% of high-grade cervical lesions in Australia.<sup>2,3</sup>

The Pharmaceutical Benefits Advisory Committee (PBAC) recommended listing Cervarix on the NIP on the basis of acceptable cost-effectiveness compared with Gardasil.<sup>4</sup> The PBAC accepted that both vaccines provide similarly high levels of protection against persistent infection with HPV-16 and HPV-18 and related precancerous cervical lesions.

In clinical trials, Cervarix was highly effective (> 90%) in preventing infection with HPV-16 or HPV-18 in previously uninfected females, and in preventing cervical dysplasia caused by these subtypes.<sup>5–7</sup> High levels of protection against infection were maintained in fully vaccinated females, for up to 4.5 years after the first vaccine dose was administered.<sup>6</sup>

There is some evidence that Cervarix provides cross-protection against infection with other oncogenic HPV types not included in the vaccine.<sup>7</sup>

Unlike the quadrivalent HPV vaccine Gardasil (see [www.npsradar.org.au](http://www.npsradar.org.au)), Cervarix does not protect against HPV-6 and HPV-11, which cause most cases of genital warts<sup>8</sup>, and it is not approved for use in males.<sup>9</sup>

A full course of vaccination consists of 3 doses (0, 1 and 6 months) administered intramuscularly into the deltoid region.<sup>9</sup> Local injection-site symptoms (pain, redness, or swelling) are very common. These and other systemic symptoms (fatigue, headache, or myalgia) were more commonly reported with Cervarix in the 7-day post-vaccination period than with placebo.<sup>9</sup>

HPV vaccines do not protect against all oncogenic HPV types. Advise all females who have ever been sexually active, whether vaccinated or unvaccinated, to have regular Pap smears from the age of 18 years, or within two years of first intercourse, whichever is later.<sup>1</sup>

\* Cervarix is TGA approved in females aged 10–45 years for the prevention of cervical cancer.<sup>9</sup>

## References

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## Quetiapine extended-release tablets (Seroquel XR) PBS listed for schizophrenia

Quetiapine extended-release<sup>†</sup> tablets (Seroquel XR) were added to *the Schedule of Pharmaceutical Benefits* on 1 November 2008 as a streamlined authority-required listing for schizophrenia.

The extended-release tablets come in different strengths to those of the existing immediate-release tablets, and dosing and administration is slightly different. Prescribers will need to instruct patients carefully to prevent confusion between the two formulations. There is no compelling reason to switch people who are currently stable on quetiapine immediate-release tablets to extended-release tablets.

Quetiapine extended-release tablets are not currently indicated or PBS listed for mania. The existing streamlined authority listings of immediate-release quetiapine for schizophrenia and acute mania remain unchanged. See the December 2007 *NPS RADAR* brief item 'Quetiapine (Seroquel) PBS listed for acute mania' for details of this listing.

<sup>†</sup> This formulation is referred to as 'modified release' in the TGA-approved product information and the *Schedule of Pharmaceutical Benefits*.

### There is no evidence that extended-release tablets improve efficacy, tolerability or adherence

Once-daily dosing with quetiapine extended-release tablets is equivalent to twice-daily dosing with quetiapine immediate-release tablets, e.g. quetiapine extended release 600 mg once daily is equivalent to quetiapine immediate release 300 mg twice daily. Comparative trials have found no difference in efficacy or tolerability between the 2 formulations, and have not assessed the relationship between dosing frequency and adherence.<sup>1,2</sup>

Some people may prefer once-daily dosing with the extended-release tablets, but immediate-release tablets give greater flexibility in dosing and in timing with respect to meals.

When switching is appropriate, patients can switch directly from twice-daily immediate-release tablets to an equivalent total daily dose of the extended-release tablets, taken once daily.<sup>3</sup> Some people may need dose adjustment.<sup>3</sup>

The PBAC found that the extended-release tablets were as effective as quetiapine immediate-release tablets (Seroquel) for no greater cost.<sup>4</sup>

### Quetiapine extended-release tablets are taken once daily

People may prefer evening dosing to minimise any daytime sleepiness. Extended-release tablets should not be chewed, crushed or split.<sup>3</sup>

Extended-release quetiapine should *not* be taken with food. In one study using this formulation, a high-fat meal increased the peak blood levels of quetiapine and overall absorption.<sup>3</sup> Raised blood levels of quetiapine may increase the risk of adverse effects.

### Provide clear information to patients to help avoid confusion

Most of the extended-release tablets have different shapes and markings to the immediate-release tablets (see Table 1). **Note however that the quetiapine extended-release 400 mg tablet has a similar appearance to the quetiapine immediate-release 300 mg tablet.**

**Table 1: Appearance of immediate-release and extended-release quetiapine tablets**

Immediate release		Extended release	
25 mg	Peach Round 'SEROQUEL 25'	50 mg	Peach Capsule-shaped 'XR 50'
100 mg	Yellow Round 'SEROQUEL 100'	200 mg	Yellow Capsule-shaped 'XR 200'
		300 mg	Pale yellow Capsule-shaped 'XR 300'
200 mg	White Round 'SEROQUEL 200'	400 mg	White Capsule-shaped 'XR 400'
300 mg	White Capsule-shaped 'SEROQUEL' (on reverse) '300'		

If switching from another antipsychotic or from quetiapine immediate-release tablets, provide written instructions about how many tablets to take each day and at what time, and remind the patient to dispose of any old medicines that are no longer needed.

Discuss the Seroquel XR consumer medicine information (CMI) leaflet with the patient.

### Dose escalation over 2–3 days is recommended for some people

The manufacturer has introduced a faster dose-escalation protocol with the extended-release formulation, although some people may require slower titration. For people not currently taking an antipsychotic, the manufacturer recommends dose escalation over 2–3 days, with a dose of quetiapine extended release 300 mg on the first day, 600 mg on the second day and up to 800 mg on subsequent days.<sup>3</sup> The usual maintenance dose consists of 2 × 300 mg tablets, taken once daily.

Start people with hepatic impairment and elderly people on a lower dose of extended-release quetiapine 50 mg daily. Increase in increments of 50 mg to an effective dose, monitoring carefully for adverse effects, at a rate appropriate to the patient.<sup>3</sup>

Faster dose escalation was not associated with a significant increase in adverse effects in people with schizophrenia (mean age 34) and no serious comorbidities.<sup>1</sup> Dizziness and somnolence were the most commonly reported treatment-related adverse effects in the first week of treatment (see Table 2), but there were few adverse events that led to discontinuation.

Switching patients from other antipsychotics to quetiapine extended-release tablets requires tailoring of doses to the individual's response — there is insufficient evidence to support any particular protocol. Gradual discontinuation of the old drug may be appropriate, but in all cases minimise the period of overlapping antipsychotic administration.<sup>5</sup>

### The approved dose range differs from that for immediate-release tablets

Adjust the dose within the usual effective range of 400–800 mg daily, depending on the clinical response

and adverse effects.<sup>3</sup> Elderly or frail patients, people with hepatic impairment or a predisposition to hypotensive reactions may require a lower target dose.<sup>3,5</sup> Daily doses higher than 600 mg have not shown greater efficacy in trials, although some individuals may benefit from a higher dose.<sup>6</sup> Note that the dose range of 400–800 mg daily for quetiapine extended release differs from the approved dose range for quetiapine immediate release of 150–750 mg daily for schizophrenia.<sup>7</sup>

### References

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**Table 2: Incidence of selected adverse events during week 1 of treatment.<sup>1</sup>**

Adverse event	Placebo — (n = 118)	Quetiapine target total daily dose			
		Extended release (fast dose escalation)			Immediate release (conventional dose escalation)
		400 mg (n = 113)	600 mg (n = 113)	800 mg (n = 121)	
Somnolence	0.8%	5.3%	6.2%	9.9%	7.3%
Dizziness	0.8%	1.8%	6.2%	5.8%	4.1%
Discontinuation	0	0.9%	0.9%	0	1.6%

## Rosiglitazone: listings for triple oral therapy and combination with insulin removed

Rosiglitazone (Avandia) is no longer PBS listed for use in combination with metformin and a sulfonylurea (i.e. triple oral therapy) or for use in combination with insulin. Rosiglitazone with metformin combination tablets (Avandamet) are no longer PBS listed for use in combination with a sulfonylurea as part of triple oral therapy. The combination tablets have never been listed for use in combination with insulin.

An updated *NPS RADAR* review of rosiglitazone is available at [www.npsradar.org.au](http://www.npsradar.org.au) and in the December software updates of Medical Director (MD2) and Genie.

The PBS-listing changes follow safety-related changes to the product information for products containing rosiglitazone. People taking rosiglitazone as part of triple oral therapy or in combination with insulin have an increased risk of heart failure.<sup>1,2</sup> Rosiglitazone should no longer be used in any person with heart failure, a history of heart failure, ischaemic heart disease or peripheral vascular disease.

If dual therapy with metformin and a sulfonylurea fails, consider adding insulin, as it reduces the risk of diabetic complications.<sup>3</sup> Other third-line oral antidiabetic drugs include pioglitazone, repaglinide (not currently PBS listed), sitagliptin or acarbose; however, the long-term benefit–harm profiles of these drugs are yet to be established. Insulin should not be delayed when oral drug therapy no longer controls blood glucose.

The PBAC reviewed the listing for pioglitazone at its November 2008 meeting in light of the changes to the TGA-approved indications for rosiglitazone.<sup>4</sup> The outcome of this review was not publicly known at the time of writing.

### References

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## Alendronate with cholecalciferol (Fosamax Plus): new formulation contains more vitamin D

A new formulation of alendronate with cholecalciferol (Fosamax Plus) containing a higher cholecalciferol dose was PBS listed in August 2008.

The new formulation contains 5600 units in a once-weekly dose, equivalent to 800 units per day. The previous formulation contained cholecalciferol 2800 units, equivalent to 400 units per day. The lower-dose formulation will be gradually phased out by the manufacturer, but stock in pharmacies may vary.

### The dose of vitamin D in Fosamax Plus is not intended to treat vitamin D deficiency

When prescribing Fosamax Plus, consider the risk of vitamin D deficiency. If deficiency is suspected, test the serum 25-hydroxyvitamin D (25-OHD) concentration. The correct dose of cholecalciferol depends on the extent of vitamin D deficiency (or insufficiency). Treat moderate to severe deficiency (25-OHD  $\leq$  25 nmol/L) with high-dose supplements of 3000–5000 units daily for 6–12 weeks, until normal levels are achieved.<sup>1</sup> A maintenance dose of around 1000 units daily is then required — possibly indefinitely.<sup>1,2</sup> Current recommendations are to maintain serum 25-OHD concentration above 50 nmol/L.<sup>1,2</sup>

The cholecalciferol content of Fosamax Plus is not intended to correct moderate to severe vitamin D deficiency.<sup>3</sup> It may help improve vitamin D levels in patients with mild deficiency (serum 25-OHD concentration of 37.5–50 nmol/L<sup>3,4</sup>), and/or inadequate sunlight exposure.<sup>5</sup>

Ensure adequate vitamin D and calcium for people with osteoporosis. For people with inadequate sun exposure at least 800–1000 units per day is recommended. Higher-dose supplements may be indicated in some cases (up to 2000 units per day).<sup>2,5</sup> However, vitamin D supplementation does not clearly benefit people with osteoporosis who have normal vitamin D status — there is no reason to switch such patients from alendronate to the combination product.

A similar dose of vitamin D is PBS subsidised in a combination formulation of risedronate (Actonel Combi D) which includes sachets of calcium and vitamin D<sub>3</sub> 880 units for use on 6 days of the week. Fosamax Plus contains cholecalciferol formulated in the same tablet as alendronate.

The *NPS RADAR* review for this medicine was updated online in December 2008. Visit [www.npsradar.org.au](http://www.npsradar.org.au) to read the full review.

### References

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## Prescribing for up to 12 months allowed for some medicines for some people with chronic conditions

The period for which a PBS prescription (with repeats) can be written has increased from 6 to 12 months — for **some** medicines prescribed for **some** people with chronic conditions.

People with a stable chronic condition whose care is being managed by a general practitioner management plan or team care arrangement are eligible to receive up to 12 months' supply of some medicines in accordance with their GP's clinical judgement. The prescribing GP must be satisfied that there will be adequate follow-up.

No increased maximum quantities and/or repeats are allowed with these new PBS listings.

The first medicines were listed under the new arrangement on 1 November 2008, followed by a second group of medicines on 1 December 2008. Some diagnostic agents will be added on 1 January 2009 (see Box 1).

### Box 1: Medicines that may be prescribed for up to 12 months under the new arrangement\*

From 1 November 2008	Some eye preparations (e.g. for dry eye) Sulfasalazine
From 1 December 2008	Some digestive enzyme capsules (e.g. for cystic fibrosis) Statins (excluding rosuvastatin) Fibrates Bile-acid sequestrants
From 1 January 2009	Some diagnostic agents (e.g. glucose test strips)

\* Refer to the *Schedule of Pharmaceutical Benefits* at [www.pbs.gov.au](http://www.pbs.gov.au)

### Erratum: Memantine (Ebixa) for dementia in moderately severe Alzheimer's disease

Information on the dose titration of memantine contained in Table 1 of the August 2008 *NPS RADAR* review of memantine was incorrect. The dose for the tablet formulation was correct but the dose for the oral solution was mistakenly halved.

The error has been rectified on the NPS website and all electronic copies of the review now show the correct dose (Table 1). We apologise for any confusion.

**Table 1: Initial dose titration**

Week	Dose
Week 1	<b>Morning:</b> half a tablet or 10 drops of solution
Week 2	<b>Morning:</b> half a tablet or 10 drops of solution <b>Evening:</b> half a tablet or 10 drops of solution
Week 3	<b>Morning:</b> 1 tablet or 20 drops of solution <b>Evening:</b> half a tablet or 10 drops of solution
Week 4	<b>Morning:</b> 1 tablet or 20 drops of solution <b>Evening:</b> 1 tablet or 20 drops of solution