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NPS RADAR provides timely, independent, evidence-based information on new drugs, research and PBS listings for general practitioners, specialists, pharmacists and other health professionals.

Where is the line between education and promotion? The debate about educational events sponsored by pharmaceutical companies is not a new one by any means. You may have seen the recent SBS *Insight* program on the relationship between doctors and pharmaceutical companies. The program covered too much ground for us to discuss the various viewpoints in detail here, but it set us thinking (again) about what the bottom line is for prescribers, especially because we've been developing an online learning program at NPS that touches on some related issues.

Educational events clearly are promotional opportunities — as one participant in the SBS show put it when asked about the value to companies of sponsoring educational events, 'We are able to promote our products at the same time as educating doctors, fundamentally.' It seems likely that mixing promotional and educational content increases the risk of an emphasis being placed on the benefits of the product being promoted.

Granted, events vary in the extent of promotion and sponsor involvement. A question for participants in company-sponsored education is how can you tell how you've been influenced by attending an event? And how can you ensure that you have balanced, objective and complete information to help you make decisions about using new drugs?

Two doctors writing in *Canadian Family Physician* have suggested a checklist to assess the extent that a sponsored event is aiming to influence attendees to prescribe the sponsoring company's product.*

The checklist includes items on who determined the educational content of the event, whether the event is used for overt promotion or relationship building, and what incentives are offered for attendance. While not all the items will be applicable to the Australian setting because of the standards set out by the Medicines Australia *Code of Conduct*, you might find it interesting to use a similar checklist and discuss the results with colleagues if you attend industry-sponsored events.

You might also be interested in an online learning program we're developing at NPS. The program is designed for prescribers and covers the key issues involved in finding and applying evidence about new drugs — without the need to comb through endless clinical trials yourself. It will demonstrate how you can set your own information agenda by asking focussed questions about new drugs, and how you can answer your questions quickly using high-quality information sources designed for health professionals. The program can also help you to expand your library of ready reference sources and to find decision aids to use with patients.

The program, *Finding Evidence — Recognising Hype*, will be available later in 2009. Details will be available on the NPS website soon, or if you are a subscriber to NPS RADAR email alerts (see www.npsradar.org.au) you'll be notified in one of our regular email updates.

* Dyck C, Kvern B. The PRESCRIBE acronym: a tool for appraising pharmaceutical industry-sponsored presentations. *Can Fam Physician* 2008;54:1701.

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Timely, independent information about new drugs

National Prescribing Service Limited

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Rivaroxaban (Xarelto) for preventing venous thromboembolism after hip or knee replacement surgery

(riv-ah-ROCKS-ah-ban)

Summary

- Rivaroxaban is an oral anticoagulant and the first direct factor Xa inhibitor.
- Rivaroxaban has only been evaluated for use in preventing deep vein thrombosis and pulmonary embolism after elective total hip or total knee replacement surgery.
- Duration of therapy is 14 days after knee replacement or 35 days after hip replacement, and no longer.
- Dose adjustment, dose titration and monitoring of prothrombin time are not required.
- There are only small differences in efficacy and safety between rivaroxaban, low molecular weight heparins, fondaparinux (Arixtra) and dabigatran (Pradaxa).
- Advise patients about the risk of bleeding.
- Rivaroxaban is contraindicated in renal impairment (creatinine clearance < 15 mL/min), moderate and severe hepatic impairment with elevated INR, or with azole antifungals or HIV-protease inhibitors. These increase blood levels of rivaroxaban and therefore bleeding risk.

PBS listing

Authority required

Preventing venous thromboembolism in patients undergoing total hip or knee replacements.

The listing provides for a dispensed maximum quantity of 40 tablets for hip-surgery patients and 15 tablets for knee-surgery patients.¹

Reason for PBS listing

The PBAC recommended a listing for preventing venous thromboembolism after total hip or knee replacement surgery, after concluding that rivaroxaban has uncertain but acceptable cost-effectiveness compared with that of enoxaparin, the drug most often used for this purpose currently. The decision was based on the RECORD1, RECORD2 and RECORD3 clinical trials along with a cost-effectiveness model incorporating data from these trials.²

The committee observed that oral rivaroxaban is more effective, but possibly less safe, than subcutaneous enoxaparin for this indication. The clinical trials reported a small absolute difference in clinical efficacy between rivaroxaban and enoxaparin.

In the pharmacoeconomic models, the incremental gains in years of life and quality-adjusted life-years were minimal. In these models, the short-term RECORD results were extrapolated to longer term outcomes using data from additional publications of long term risk of recurrent deep vein thrombosis, pulmonary embolism and post-thrombotic syndrome plus quality of life data. These extrapolated, longer-term results accounted for most of the modelled difference in effectiveness between the two drugs.²

During the same meeting the PBAC deferred its consideration of dabigatran (Pradaxa) (another new oral therapy) for a similar indication, to give the applicant an opportunity to submit a comparison with rivaroxaban.³

Place in therapy

Rivaroxaban is an oral factor Xa-inhibitor anticoagulant. It is approved for short-term use to prevent deep vein thrombosis and pulmonary embolism after elective total hip or total knee replacement surgery. Standard duration of therapy is 14 days after knee replacement or 35 days after hip replacement. Efficacy and bleeding risk do not differ greatly from those of enoxaparin, the most common therapy currently. Rivaroxaban was superior

to enoxaparin in preventing a composite of symptomatic and asymptomatic venous thromboembolism but may cause more bleeding (see Safety issues). Trials for other indications have not yet been completed.

Rivaroxaban is an oral anticoagulant

Rivaroxaban is a direct, reversible competitive antagonist of factor Xa (activated factor X) that is active when taken orally. It is the first of this new class of drugs, exhibiting a dose-dependent anticoagulant effect.⁴ Rivaroxaban and dabigatran (Pradaxa) are the first oral anticoagulants to be introduced in Australia since warfarin. Dabigatran is from a different class of drugs (direct thrombin inhibitors) and is currently only available through hospitals or by private prescription.

Rivaroxaban prevents deep vein thrombosis and pulmonary embolism after elective total hip or total knee replacement surgery

Rivaroxaban is approved for short-term use after elective total hip or total knee replacement surgery on the basis of several large clinical trials (RECORD1-3).⁵⁻⁷ There is currently no evidence for using rivaroxaban for any other surgery-related or non-surgery-related indication, pending the completion of additional clinical trials.

The key trials measured the efficacy of rivaroxaban using a composite endpoint.[†] The bulk of the recorded events were cases of venographically detected venous thromboembolism. Fewer cases of venous thromboembolism were detected in participants taking rivaroxaban than were detected in those taking enoxaparin.⁵⁻⁷ While only a fraction of venographically detected cases are clinically significant, the rate correlates with the rate of symptomatic deep vein thrombosis and pulmonary embolism.⁸

Graduated compression stockings are recommended as an adjunct to anticoagulant therapy

Guidelines recommend that surgery patients receive graduated compression/antiembolism stockings from the time of admission, to further reduce the risk of venous

thromboembolism. Patients should continue to wear their stockings after discharge until they return to their usual level of mobility.⁸

Patients using compression stockings should be shown by hospital staff how to wear them correctly. In some cases, intermittent pneumatic compression or foot impulse devices may be used as alternatives to stockings while patients are in hospital.

Participants in the RECORD trials were not permitted to use intermittent pneumatic compression devices, and use of compression stockings was not reported.⁵⁻⁷

Rivaroxaban, low molecular weight heparins, fondaparinux and dabigatran differ only slightly in effectiveness

Evidence-based guidelines from the UK National Institute for Health and Clinical Excellence (NICE) reported broadly similar efficacy for dabigatran, low molecular weight heparins, fondaparinux, or rivaroxaban after elective total hip or total knee replacements.⁸⁻¹⁰ NICE recommended that neither aspirin nor warfarin be used for this indication, because they appear to be less effective than the other agents for preventing venous thromboembolism after elective surgery.⁸

Results from the RECORD1 trial in hip surgery and the RECORD3 trial in knee surgery indicate that the benefits of rivaroxaban and enoxaparin are very similar. While rivaroxaban was superior according to the primary, composite endpoint^{6,7}, the differences in the rates of clinically significant events (symptomatic venous thromboembolism or death from any cause) were small (Table 1).

There have been no clinical trials directly comparing rivaroxaban with dabigatran or fondaparinux for venous thromboembolism prevention. The UK National Institute for Health and Clinical Excellence committee made their assessment on the basis of indirect comparisons and cost-effectiveness modelling.^{9,10}

Table 1. Incidence of symptomatic venous thromboembolism or death from all causes in key trials.¹¹

	Rivaroxaban % with events	Enoxaparin % with events
RECORD1 (hip)	0.5 (10/2209)	0.7 (15/2224)
RECORD3 (knee)	0.7 (8/1220)	2.1 (26/1239)

* Australian approval was based on data from the RECORD1-3 trials. RECORD4 used a dosing regimen of enoxaparin that is not approved in Australia, but safety data from the trial was used in some subsequent pooled analyses.

† Composite endpoint of venographically detected thromboembolism, symptomatic deep vein thrombosis or pulmonary embolism, and death from any cause.

Standard duration of therapy is 14 days after knee replacement or 35 days after hip replacement

Trials administered rivaroxaban for 14 days after knee replacement surgery or for 35 days after hip replacement surgery, durations consistent with current recommendations for other anticoagulants. A meta-analysis of hip replacement surgery data found that extending the duration of prophylaxis with heparin from 4–17 days to 27–42 days decreased the rate of symptomatic venous thromboembolism from 4.3% to 1.4% (odds ratio 0.33, 95% confidence interval 0.19 to 0.56). The meta-analysis did not demonstrate a corresponding benefit of extended prophylaxis in knee replacement surgery.¹²

Safety issues

As with other drugs used for this indication, managing the risk of bleeding is a primary concern with rivaroxaban. Bleeding risk is dose dependent and anything greater than a twofold increase in rivaroxaban exposure is considered clinically significant. Drug–drug interactions (e.g. with HIV-protease inhibitors or azole antifungals) and drug–disease interactions may increase rivaroxaban concentrations. The incidence of common adverse effects is similar to that for enoxaparin; there are insufficient data to characterise rare or long-term adverse effects.

Report suspected adverse reactions to the Therapeutic Goods Administration (TGA) online (www.ebs.tga.gov.au) [then click 'Adverse reaction to a medicine' at left] or by using the 'Blue Card' distributed with *Australian Prescriber*. For information about reporting adverse reactions, see the TGA website (www.tga.gov.au).

Average risk of serious bleeding in trials was approximately 2%

People with risk factors for bleeding constituting a contraindication for enoxaparin were excluded from trials for postsurgical prevention of venous thromboembolism. A pooled analysis of safety data for the first 2 weeks of treatment found a rate of 1.8% for major bleeds and surgical-site bleeds with rivaroxaban, compared with 1.4% with enoxaparin. Gastrointestinal haemorrhage was the only form of overt extrasurgical bleeding. There was 1 fatal bleed among 6183 people exposed to rivaroxaban across the 4 RECORD trials, and no fatal bleeds among 6200 people exposed to enoxaparin.¹¹

Rivaroxaban is contraindicated for patients with clinically significant active bleeding, spontaneous impairment of haemostasis, or lesions that may spontaneously bleed significantly (e.g. stroke within the previous 6 months). Other patients with bleeding risk factors or who may experience an increased anticoagulant effect should be counselled about the possibility of serious bleeding and to seek prompt medical attention if they exhibit signs.¹³

Combining rivaroxaban with other anticoagulants is not recommended.¹³

Take care combining with antiplatelets or NSAIDs

Aspirin, clopidogrel or NSAIDs prolong bleeding time when combined with rivaroxaban. A subset of patients receiving the combination of clopidogrel and rivaroxaban experienced a greater than additive effect.^{11,13} For the cases when a patient requiring ongoing antiplatelet therapy undergoes elective surgery, an expert should assess the risks and potential benefits of venous thromboembolism prophylaxis and select the appropriate regimen.

Renal or hepatic impairment can increase bleeding risk

Rivaroxaban is eliminated by active renal excretion and hepatic oxidation (by CYP3A4 and CYP2J2). Rivaroxaban is contraindicated in severe renal impairment (creatinine clearance < 15 mL/min) because the exposure to rivaroxaban is increased by more than twofold. Rivaroxaban is also contraindicated for people with moderate or severe hepatic insufficiency when coagulopathy is also present (i.e. abnormally elevated International Normalised Ratio [INR]).¹³

Rivaroxaban may be prescribed with caution for people with creatinine clearance of 15–29 mL/min. Renal impairment in the range 30–49 mL/min may contribute to a clinically relevant increased bleeding risk when there are other factors that increase rivaroxaban levels (e.g. drug interactions).¹³

Strong inhibitors of CYP3A4 or P-glycoprotein increase rivaroxaban levels

Rivaroxaban is contraindicated for people receiving azole antifungals (except fluconazole) or HIV-protease inhibitors. Most of these drugs are strong inhibitors of CYP3A4 and also inhibit P-glycoprotein. Less potent inhibitors or drugs inhibiting only one of these two

pathways (e.g. amiodarone, cyclosporin, clarithromycin, diltiazem, dipyridamole, erythromycin, fluconazole, tamoxifen or verapamil) are not contraindicated but may contribute to a clinically relevant increased bleeding risk when there are other factors that increase rivaroxaban levels.^{13–15}

There is no antidote to rivaroxaban-induced bleeding

Treat bleeding symptomatically and arrange hospital management if warranted. The product information lists possible emergency procoagulant treatments, but their clinical value is uncertain. Stopping or delaying the next dose may be sufficient to manage minor bleeding, given that rivaroxaban has a mean terminal elimination half-life of 5–13 hours and inhibits factor Xa reversibly.¹³

An increased risk of rare adverse events has not been ruled out

There were few serious adverse events in clinical trials. Further data are required to characterise the incidence of hepatotoxicity, renal injury, thrombotic cardiovascular events, pancreatitis or other rare or delayed adverse events.

There were rare cases of hepatic adverse events in registration trials but too few to judge if rivaroxaban was the cause. Analysis of the RECORD1–4 safety database found similar numbers of drug-related liver injury cases with rivaroxaban and enoxaparin.¹¹

There was no significant difference in the number of cardiovascular events for rivaroxaban and enoxaparin. However, too few events occurred in the RECORD trials to rule out the possibility that there is a small increase in event rate after discontinuing rivaroxaban (i.e. a rebound effect).^{11,16}

Dosing issues

The dose is 10 mg once daily, with or without food. Initiate 6–10 hours after wound closure and haemostasis. Continue rivaroxaban for 14 days after knee surgery or 35 days after hip surgery. Do not exceed the dose of 10 mg once daily or the standard duration.¹³

Dose adjustment, dose titration and monitoring of prothrombin time are not required

Rivaroxaban 10 mg once daily rapidly produces an anticoagulant effect in the correct range to prevent venous thromboembolism, without dose titration or adjustment (e.g. for body weight). Monitoring is not required. Even though prothrombin time correlates closely with inhibition of factor Xa, there are no standards to relate prothrombin times to therapeutic or adverse effects, and the INR cannot be used to characterise rivaroxaban's effect.¹³

Some patients will require a GP prescription soon after discharge

Some public hospital patients will be advised to see their GP soon after discharge for a rivaroxaban prescription to cover the remaining duration of therapy.* The average time between surgery and discharge in Australia is 9 days for hip replacements and 7 days for knee replacements.¹⁷ Hospitals that do not provide a PBS prescription on discharge may dispense a small supply of tablets to cover the period until the patient can see a GP.

Prescribers will need to take into account the number of tablets the hospital has already provided when selecting the pack size and giving instructions to the patient. As pack sizes will not always match the recommended treatment duration, there may be tablets left over.

* Patients attending public hospitals in ACT, NSW, Tasmania and some hospitals in SA that have not yet implemented PBS prescribing.

Information for patients

Advise patients and carers:

- to take 1 tablet at about the same time each day, with or without food
- that if they miss a dose, to take a tablet immediately and continue the following day with 1 tablet at the same time as usual. Do not take a double dose to make up for a forgotten tablet
- when switching from tablets dispensed by the hospital to tablets prescribed by a GP, to continue taking 1 tablet every 24 hours
- to continue to wear any compression stockings supplied by the hospital until they return to their usual level of mobility, to minimise the risk of developing venous thromboembolism
- to consult a doctor before using non-prescription medicines containing aspirin or nonsteroidal anti-inflammatory drugs. Paracetamol can be used for minor ailments
- to consult a doctor if they have any prolonged or excessive bleeding
- to consult a doctor if symptoms suggesting internal bleeding appear after leaving hospital, such as unexplained bruising, red urine or black faeces
- to tell their doctor, dentist or pharmacist they are taking rivaroxaban at each consultation.¹⁸

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

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The information contained in NPS RADAR is derived from a critical analysis of a wide range of authoritative evidence and is current at the time of publication. Any treatment decisions based on the information provided in NPS RADAR should be made in the context of the clinical circumstances of each patient.

NPS RADAR articles may be updated when there is new evidence about safety or efficacy, or in case of regulatory or PBS listing changes. Please refer to www.npsradar.org.au for the most recent version as well as any supplementary information.

Teriparatide (Forteo) for severe osteoporosis

(ter-i-PAR-a-tide)

Summary

- Teriparatide is subsidised on the Pharmaceutical Benefits Scheme for severe established osteoporosis in people at very high risk of fracture who develop one or more new symptomatic fractures despite at least 12 months of continuous antiresorptive therapy.
- PBS-subsidised treatment must be initiated by a specialist but can be continued by a GP.
- Teriparatide is given as a daily subcutaneous injection using a prefilled multidose delivery device (pen).
- Treatment with teriparatide is limited to a lifetime maximum duration of 18 months because of the possible risk of osteosarcoma. Informed consent is required.
- Some patients may benefit from restarting antiresorptive osteoporosis therapy after stopping teriparatide.
- Common adverse effects include nausea, arthralgia, headaches, dizziness and injection-site reactions.
- Ensure calcium and vitamin D intake are adequate. Supplement if necessary.

PBS listing

Authority required

Initial treatment

Treatment as the sole PBS-subsidised agent for severe established osteoporosis in patients with a very high risk of fracture who have:

- a bone mineral density (BMD) T-score of -3.0 or less, AND
- 2 or more fractures* due to minimal trauma, AND
- at least one new symptomatic fracture after at least 12 months of continuous treatment with antiresorptive therapy at adequate doses.†

Treatment must be initiated by a specialist or consulting physician and can be continued by a general practitioner.

Only 18 months of treatment (a maximum of 18 pens) will be subsidised on the PBS.

The authority application must include:

- details of previous osteoporosis therapy
- fracture history, including the date(s), site(s) and symptoms associated with the fracture that developed during antiresorptive therapy
- qualifying BMD score.

Details of any contraindication to antiresorptive therapy, as described in the relevant Therapeutic Goods Administration (TGA) approved product information, must be provided at the time of application.

Continuing treatment

For patients who previously received PBS-subsidised teriparatide for severe established osteoporosis.

Patients who were prescribed teriparatide before the PBS listing date are now subsidised to receive teriparatide if they have severe established osteoporosis and a very high fracture risk.

Teriparatide must only be used for a lifetime maximum of 18 months of therapy.

* A vertebral fracture is defined as a $\geq 20\%$ reduction in height of an anterior or mid-portion vertebral body relative to the posterior height of that body, or a $\geq 20\%$ reduction in any vertebral height compared with vertebral height above or below the affected vertebral body.

† Antiresorptives and doses accepted for the purposes of this restriction: alendronate 10 mg daily or 70 mg weekly, risedronate 5 mg daily or 35 mg weekly, raloxifene 60 mg daily (women only), etidronate 200 mg with calcium carbonate 1.25 g daily, strontium 2 g daily and zoledronic acid 5 mg once a year. If severe intolerance occurs that requires permanent withdrawal of one antiresorptive agent, an alternative antiresorptive agent must be trialled so that a minimum of 12 months of continuous therapy is achieved.

Reason for PBS listing


The Pharmaceutical Benefits Advisory Committee (PBAC) recommended teriparatide for listing on the basis of acceptable cost-effectiveness compared with alendronate in the context of a very high clinical need (for patients who continue to experience fracture despite the availability of antiresorptives).¹

The PBAC recommended restricting use to people who experience new symptomatic fractures, because loss of quality and quantity of life in osteoporosis is expected to be associated with fracture symptoms rather than asymptomatic fracture.

Place in therapy


Teriparatide is recombinant human parathyroid hormone, given as a daily subcutaneous injection. In contrast to antiresorptive agents, which inhibit bone loss, teriparatide is an anabolic agent that activates osteoblasts and stimulates bone formation.²

Teriparatide is TGA approved for treating postmenopausal osteoporosis in women and primary osteoporosis in men (hypogonadal or idiopathic osteoporosis) when other treatments are considered unsuitable and there is a high risk of fracture.² It is also approved for the treatment of osteoporosis associated with sustained systemic glucocorticoid therapy in people at high risk of fracture.² The PBS listing restricts use to people with severe established osteoporosis and a very high risk of fracture, in whom at least one new symptomatic fracture develops despite antiresorptive therapy (see PBS listing).

As with other therapies for osteoporosis, adequate calcium and vitamin D should be ensured.² [www](#) 

Antiresorptive therapies should be stopped before starting teriparatide, and can be resumed after treatment with teriparatide has finished.

The duration of treatment with teriparatide is limited to a lifetime maximum of 18 months (see Safety issues).

[www](#)  Refer to this review at www.npsradar.org for more information on vitamin D deficiency and supplementation.

Teriparatide reduces the risk of vertebral and non-vertebral fractures in women but data on men are limited

In a trial of postmenopausal women with severe established osteoporosis (i.e. at least one previous vertebral fracture), teriparatide 20 micrograms daily increased BMD and reduced the risk of new vertebral and non-vertebral fractures compared with placebo (see Table 1).³ The trial was not designed to investigate the effect of teriparatide on specific types of non-vertebral fracture (e.g. hip, wrist, humerus).

There are limited data on fracture outcomes in men. Compared with placebo, teriparatide increases BMD in men with primary osteoporosis.⁴ Men in trials were generally young (mean age < 60 years) and recruited on the basis of BMD scores rather than a history of fracture.⁴

Teriparatide's effect on fracture rates has not been compared as a primary outcome with that of other established osteoporosis treatments. Some trials have shown greater increases in BMD with teriparatide compared with bisphosphonates, but the clinical significance of this has not been determined.⁵⁻⁷

Data from follow-up observational studies in women suggest that, compared with placebo, the risk of radiographically detected vertebral and all non-vertebral fractures is reduced for up to 18 months after stopping teriparatide.^{8,9}


Table 1: Effect of teriparatide (20 micrograms daily) on vertebral and non-vertebral fracture rates in postmenopausal women with severe osteoporosis^{3,10}

Fracture type	Relative risk: teriparatide versus placebo (95% confidence interval)	Numbers needed to treat (NNT) [‡]
New radiographically detected vertebral fracture ^{**}	0.35 (0.22 to 0.55)	11
New non-vertebral fracture	0.65 (0.43 to 0.98)	25
Hip fracture	0.50 (0.09 to 2.73)	NA
Wrist fracture	0.54 (0.22 to 1.35)	NA

^{**} Defined as a $\geq 20\%$ reduction in vertebral height in previously normal vertebrae.

[‡] NNT: number of patients who would need to be treated for 21 months (median trial duration) with teriparatide instead of placebo to prevent one additional fracture.

Ensure adequate calcium and vitamin D intake

Patients in all teriparatide clinical trials received supplemental calcium 1000 mg and at least 400 units vitamin D daily.^{3–5,11} Use supplements for all patients who cannot obtain adequate amounts of calcium and vitamin D through diet and sunlight exposure alone (see Table 2).^{2,12} [www](#) 

Some patients taking calcium supplements with teriparatide may develop hypercalcaemia (see Safety issues) and require less calcium.

Table 2: Recommended daily intakes of calcium and vitamin D for adults^{12,13}


Calcium	At least 1000 mg daily (1300 mg for women > 50 years and men > 70 years)
Vitamin D	At least 400–800 units (10–20 micrograms); higher (800–2000 units daily [20–50 micrograms]) in people with limited sun exposure

Stop antiresorptive therapies before starting teriparatide

Combining teriparatide with a bisphosphonate does not improve BMD compared with teriparatide alone^{6,7}; both these drugs may even act antagonistically¹⁴ and their combination is not PBS subsidised.

The anti-fracture efficacy of teriparatide in patients previously treated with antiresorptive therapy has not been established. Participants from trials were excluded if they had received medications that alter bone metabolism (such as bisphosphonates) in the lead-up to trials (up to 24 months).^{3,4}

There is no requirement for a washout period between stopping antiresorptive therapy and starting teriparatide.² A recent small unblinded study suggested that teriparatide improves BMD and markers of bone formation regardless of previous long-term antiresorptive therapy (at least a year), or the lag-time between stopping previous therapy and starting teriparatide.¹⁵

[www](#)  Refer to this review at www.npsradar.org for more information on vitamin D deficiency and supplementation.

Consider antiresorptive therapy after stopping teriparatide

After stopping teriparatide, additional antiresorptive therapy may help to maintain or enhance gains in BMD.^{9,14,16,17} Women who did not receive subsequent treatment with a bisphosphonate lost total hip and femoral neck BMD over 30 months after withdrawal of teriparatide.⁹ Similarly in men, total hip BMD levels had reverted to near baseline levels at 30 months after the withdrawal of teriparatide, without subsequent osteoporosis drug therapy.¹⁷

Safety issues

Common adverse effects in patients treated with teriparatide include nausea, arthralgia, headache, dizziness and injection-site reactions.² Consider measuring baseline serum levels of calcium, vitamin D, creatinine, uric acid and parathyroid hormone to ensure that they are within acceptable limits before starting teriparatide.¹⁴ See Forteo product information for a complete list of adverse effects, interactions and precautions.²

Report suspected adverse reactions to the TGA online (www.ebs.tga.gov.au [then click 'Adverse reaction to a medicine' at left]) or by using the 'Blue Card' distributed with *Australian Prescriber*. For information about reporting adverse reactions, see the TGA website (www.tga.gov.au).

Possible risk of osteosarcoma with long-term treatment

The TGA-approved product information for teriparatide contains a boxed warning concerning the increased incidence of osteosarcoma in rats that were exposed to between 3 and 60 times the normal human exposure over a significant portion of their lives. In Australia the lifetime maximum duration of therapy is 18 months, to mitigate the theoretical risk of osteosarcoma in humans.²

Avoid use of teriparatide in patients at increased risk of bone cancers, including people with:^{2,18,19}

- Paget's disease
- hyperparathyroidism
- bone disorders other than osteoporosis (including primary or secondary bone cancers)
- open epiphyses
- a history of skeletal radiation therapy
- unexplained increases in serum alkaline phosphatase concentration.

Avoid use of teriparatide in patients with pre-existing hypercalcaemia or urolithiasis.

Transient post-dose hypercalcaemia (serum calcium concentration > 2.6 mmol/L) occurred in 3–11% of trial participants who received teriparatide 20 micrograms daily, which usually returned to normal within 24 hours.¹¹ For patients at risk of hypercalcaemia, consider monitoring serum calcium levels before dosing, or at least 16 hours after the most recent injection.² If persistent hypercalcaemia occurs, withhold teriparatide, calcium and vitamin D supplements until the cause of hypercalcaemia is established.^{2,11}

Avoid in people with severe renal impairment

The safety and efficacy of teriparatide has not been evaluated in people with severe renal impairment.² In trials, elevation in serum uric acid concentration was more common in participants who received teriparatide than for those who received placebo (2.8% versus 0.7%).²

Circulating antiparathyroid hormone antibodies have been detected in teriparatide-treated patients; however, the clinical significance of this remains unknown.^{2,3}

Dosing issues

The recommended dose of teriparatide is 20 micrograms daily, administered as a once-daily subcutaneous injection into the thigh or abdomen. Teriparatide can be administered at any time of the day, but subsequent doses should be administered at or around the same time each day.²⁰

Teriparatide is available in a multi-dose prefilled delivery device (pen). Each pen contains enough teriparatide to deliver 28 daily doses. Instruct patients on the proper injection technique and ensure that they understand how to use and store the device and dispose of needles safely. Calcium and vitamin D supplements can be taken at the same time as teriparatide.²

Before starting treatment, the TGA-approved product information states that patients are required to provide informed consent regarding the lifetime maximum duration of treatment with teriparatide (18 months).

Teriparatide should be refrigerated at between 2 and 8 degrees Celsius.

Information for patients and carers

Advise patients of the following.^{2,20}

- Stop taking bisphosphonates or other antiresorptive medications before starting teriparatide.
- Do not stop taking daily calcium and vitamin D if these have been prescribed.
- The lifetime maximum duration of therapy is 18 months because of the possible risk of osteosarcoma with long-term use.
- Teriparatide needs to be kept refrigerated (but not frozen).
- Report any side effects to their doctor; nausea, arthralgia, headache, dizziness and injection-site reactions are common.
- Dizziness when standing up can occur, especially in the first few hours after the initial doses; sit or lie down until it passes.

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

References

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Updated August 2009: approved for the treatment of osteoporosis associated with sustained systemic glucocorticoid therapy in people at high risk of fracture.

First published: May 2009

The information contained in NPS RADAR is derived from a critical analysis of a wide range of authoritative evidence and is current at the time of publication. Any treatment decisions based on the information provided in NPS RADAR should be made in the context of the clinical circumstances of each patient.

NPS RADAR articles may be updated when there is new evidence about safety or efficacy, or in case of regulatory or PBS listing changes. Please refer to www.npsradar.org.au for the most recent version as well as any supplementary information.

In Brief

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

Hydromorphone prolonged-release tablets (Jurnista) for chronic severe disabling pain

Hydromorphone prolonged release (Jurnista), a once-daily long-acting opioid, was listed on the Pharmaceutical Benefits Scheme (PBS) on 1 May 2009. It is available as a restricted benefit for chronic severe disabling cancer or non-cancer pain not responding to non-opioid analgesics. Other oral formulations of hydromorphone available on the PBS are immediate-release tablets and oral liquid (both with the brand name Dilaudid).

A maximum quantity of 10 hydromorphone prolonged-release tablets can be supplied under the PBS, with an authority required for supply of increased maximum quantities and/or repeats.

The Pharmaceutical Benefits Advisory Committee (PBAC) recommended listing on the basis of cost minimisation compared with oxycodone controlled-release tablets (that is, no less effective and at a similar price).¹

Hydromorphone prolonged-release tablets are an option for chronic severe pain not responding to non-opioid analgesics. In the absence of adequate, published head-to-head trials there is no evidence that hydromorphone is more effective than equivalent doses of other modified-release opioids with established clinical experience.

The risk of toxicity is high

Hydromorphone is a strong opioid that is approximately 5 times more potent than morphine.² The once-daily tablets are available in 8 mg, 16 mg, 32 mg and 64 mg strengths. The 32 mg and 64 mg tablets equate to about 160 mg and 320 mg oral morphine respectively and so would be suitable only for patients who are highly opioid tolerant. Prescribers are reminded of the risks of toxicity with inappropriate use or accidental overdose.

Opioid-naïve patients should start treatment with an immediate-release preparation, titrating upwards until an adequate level of analgesia is achieved, before converting to the appropriate total daily dose of hydromorphone prolonged-release tablets.³

If switching to hydromorphone from another opioid, switch to between one-third and one-half of the equianalgesic total daily dose of hydromorphone prolonged-release tablets to allow for incomplete cross-tolerance.^{3,4}

Provide patients and carers with clear instructions on how to take hydromorphone prolonged-release tablets

Advise patients and carers that hydromorphone prolonged-release tablets²:

- should only be taken **once daily**, at or around the same time each day
- must be swallowed whole; do not crush or chew hydromorphone prolonged-release tablets, as this can cause absorption of a large dose over a short time
- may cause adverse effects, including constipation, nausea, vomiting, sedation, somnolence, dizziness, headache, sweating, mood swings, dry mouth and pruritus
- can increase the risk of adverse effects, including sedation and potentially fatal respiratory depression if taken incorrectly or more often than prescribed
- have a non-dissolvable outer coating that may be visible in the patient's stool.

Avoid concomitant use with other CNS depressants, including alcohol

As with any slow-release opioid, concomitant use of hydromorphone prolonged-release tablets with other central nervous system depressants (e.g. other opioids, sedatives or alcohol) can increase the risk of adverse effects, including sedation, hypotension, respiratory depression and coma.^{2,3}

Intentional misuse may cause serious toxicity

Hydromorphone is a potential drug of abuse. The excipients in hydromorphone prolonged-release tablets may cause fatal complications when crushed and injected. In animals intravenous administration caused anaemia, damage to myocardial and renal tubular cells and death.²

Ensure a genuine medical need for hydromorphone. If in doubt, consider seeking management advice from a drug and alcohol specialist advisory service. Referring the patient to a drug and alcohol service (see www.ancd.org.au/links/aod-information/) is usually appropriate.

Be aware of common drug-seeking behaviours related to hydromorphone prolonged-release tablets, such as requests for injectable opioids or opioids in more than one form (injectable and oral), or being asked for hydromorphone by name.⁵

If you suspect that a patient is obtaining multiple PBS prescriptions for hydromorphone ('doctor-shopping') consider contacting Medicare Australia's Prescription Shopping Information Service for more information.^{3,6}

References

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Oxybutynin patch (Oxytrol) PBS listed as an alternative for overactive bladder

Oxybutynin transdermal patches (Oxytrol) were PBS listed as a restricted benefit on 1 August 2009. Each patch is applied twice weekly and releases approximately 3.9 mg of oxybutynin per 24 hours.¹

The PBAC recommended the listing of oxybutynin patches on the basis of acceptable cost-effectiveness compared with placebo.² The listing is restricted to patients with detrusor overactivity who cannot tolerate or swallow oral oxybutynin.² There is no evidence to suggest that transdermal oxybutynin has an efficacy advantage over oral oxybutynin.³

Oxybutynin patches may cause less anticholinergic side effects, but skin reactions are common and may be intolerable for some people

Anticholinergic side effects such as dry mouth and constipation are less likely with transdermal oxybutynin than with the oral formulation.³ Application-site reactions occur in at least 10% of patients, and include redness, rash, itching, macule or vesicle formation.^{1,3,4} Such reactions are usually transient and mild in severity, but were the most common reason for stopping the patches in trials.^{1,3}

Information for patients about proper use and disposal of patches

Instruct patients to apply one patch twice a week (every 3-4 days).¹ To help minimise skin reactions, a new application site should be used for each new patch, avoiding the same site for at least 7 days after patch removal.¹

Advise patients to discard used patches safely by disposal in household refuse that is out of reach of children, pets or others.¹ Folding a patch in half so that the adhesive layers evenly stick together can also help to prevent accidental application.

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Praziquantel (Biltricide) tablets PBS listed for schistosomiasis

Praziquantel tablets (600mg) have been listed as an authority-required (streamlined) benefit on the PBS as of 1 August 2009. In the light of government initiatives to address the health care needs of refugees, the PBAC recommended listing for the treatment of schistosomiasis (bilharzia) on the basis of acceptable cost-effectiveness.¹

Schistosomiasis is caused by parasitic worms inhabiting the gastrointestinal or renal tract

Larvae released into fresh water by infested snails penetrate the skin of people coming into contact with the contaminated water. Even brief exposure can lead to infestation. After entering the body, the adult worms live in blood vessels and the females release eggs. Some eggs are passed out of the body in the urine or faeces but others become trapped in body tissues, causing an immune reaction.² Adult worms can live for decades in the body.^{2,3}

Schistosomiasis is often asymptomatic

Schistosomiasis is often asymptomatic. A pruritic rash may develop soon after the larvae penetrate the skin.

In the following months an individual may develop Katayama fever (sudden fever, fatigue, myalgia, malaise, cough, weight loss, eosinophilia, abdominal pain, diarrhoea and haematuria).^{2,4} Katayama fever is more common in travellers; it is rare among those living in endemic areas.²

Chronic untreated schistosomiasis progressively damages the bladder, ureters and intestines as well as causing enlargement of the liver and spleen. It may eventually lead to kidney failure or bladder cancer.^{2,3,5}

Schistosomiasis is endemic in Africa and parts of south-east Asia

Schistosomiasis occurs throughout tropical and subtropical regions (Table 1) but the greatest burden of illness is in Africa.³ Up to 41% of recently arrived African refugees have positive serology for schistosomiasis.³

Table 1: Areas of endemic schistosomiasis^{6,7}

Region	Endemic areas	Schistosome species
Africa	Throughout Africa: highest risk in southern and sub-Saharan Africa	<i>S. haematobium</i> <i>S. mansoni</i> <i>S. intercalatum</i>
Asia	Cambodia, Laos, Philippines, Southern China	<i>S. japonicum</i> <i>S. mekongi</i>
Middle East	Egypt, Iran, Iraq, Oman, Saudi Arabia, Yemen	<i>S. haematobium</i> <i>S. mansoni</i>
South America & Caribbean	Brazil, Dominican Republic, Suriname, Venezuela	<i>S. mansoni</i>

Diagnosis of schistosomiasis

The diagnostic 'gold standard' for schistosomiasis is the examination of the faeces or urine for eggs. However, this may require multiple samples and on its own may not detect a light-to-moderate worm burden. For this reason, diagnosis often relies on serology.³

Positive serology does not distinguish between current and past infection. However, most new arrivals to Australia with positive serology are probably infected, as the worms can survive for decades and individuals in endemic areas are repeatedly infected.³

For travellers returning from endemic regions, a positive antibody response will only be detected more than 6 weeks after initial infection.⁸

In people with equivocal serology the specimen should be re-tested using a different serological method.³ If the result remains equivocal, treat the individual as if it was positive.

Treat with 2 doses of praziquantel 4 hours apart

Current Australian guidelines recommend 2 doses of praziquantel 4 hours apart in people with positive serology. For people infected anywhere except south-east Asia, each dose should be praziquantel 20 mg/kg.^{3,9} This dosage regimen has been shown in systematic reviews to be effective and well tolerated.³ For people infected in south-east Asia, each dose should be praziquantel 30 mg/kg.³

Each dose should be taken after food. The tablets can be broken into four pieces to ensure accurate dosing but should not be chewed because of their bitter taste.^{10,11}

The praziquantel product information recommends an alternative dosage regimen of 3 doses of praziquantel, 20 mg/kg, 4 hours apart.¹¹ This dosage regimen is the same irrespective of country of infection.

Praziquantel is available as 600 mg tablets, with a maximum of 8 tablets. This will be sufficient for most individuals. However, if prescribing for a person infected in south-east Asia who weighs ≥ 80 kg, you will need to request an increase in the maximum quantity.*

Praziquantel is only active against adult worms.^{2,8} In recently infected people, who are likely to have immature worms, a second round of treatment with praziquantel several weeks later may be necessary.⁸

Check for eggs in all people with positive serology

In addition to treatment with praziquantel, all people with positive (or equivocal) serology should be examined for eggs to identify those with a high worm burden.³

If eggs are present in the faeces, check for indicators of end-organ damage[†] and refer to a specialist if necessary. Repeat the faecal examination in 3 months and prescribe another dose of praziquantel if eggs are still present.³

* If using the 3-dose regimen specified by the product information, any individual who weighs ≥ 80 kg will require an increase to the maximum quantity.

† History of chronic liver disease, gastrointestinal haemorrhage, hepatomegaly, splenomegaly, ascites, positive hepatitis B or C serology, thrombocytopenia, low albumin or raised liver enzyme concentration.

Perform a urinalysis to check for blood and, if positive, request urine microscopy to check for eggs. If eggs are present in the urine check for a history of recurrent urinary tract infections, evidence of genital lesions or hydronephrosis, and perform a renal ultrasound. Refer to a urologist if necessary. Repeat the urine examination in 3 months and prescribe another dose of praziquantel if eggs are still present.³

If there are no eggs but the individual has eosinophilia, perform a full blood count after 3 months and investigate further if eosinophilia is still present.³

Adverse effects are mainly caused by dying worms

Common adverse effects with praziquantel include dizziness, headache, malaise, drowsiness, nausea, vomiting, abdominal pain and diarrhoea.^{2,3,10} Many are thought to be caused by immune responses to the dying worms.^{3,10} Symptoms are usually mild and transient. However, there have been occasional reports of acute colic with bloody diarrhoea in heavy infections.^{2,12,13}

There is limited information on use of praziquantel in pregnant and lactating women.^{3,10} In endemic areas the WHO advises that the health advantages of treating pregnant women outweigh the risks to their health and to the health of their babies.¹⁴ Withhold treatment during the first trimester but offer it in the second or third trimester or during lactation, after discussing its risks and benefits with the patient.^{3,10}

The federal government provides 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.³ 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.¹⁵

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Update on PBS listings for Aboriginal and Torres Strait Islander peoples

Since August 2006 a number of medicines have been listed on the PBS specifically for people who identify as Aboriginal or Torres Strait Islander. The PBAC recommended these authority-required listings to improve the capacity of the PBS to meet the particular healthcare needs of these people. Most are streamlined authority listings.

Box 1 lists the medicines currently subsidised on the PBS for treating common conditions in Aboriginal and Torres Strait Islander peoples.

To keep up to date with future listings, go to the health professionals' site at www.pbs.gov.au, click on 'PBS publications' and scroll to the 'PBS listings for Aboriginal and Torres Strait Islander people' fact sheet.

Box 1: Authority-required PBS listings* for Aboriginal and Torres Strait Islander peoples (as at 1 July 2009)

Treating condition	Subsidised medicine
Fungal or yeast infection	Bifonazole cream, 1% Clotrimazole cream, 1% Ketoconazole cream, 1%; shampoo, 2% Miconazole nitrate cream, powder, lotion, 2% Miconazole tincture, 2% Nystatin cream, 100 000 units per gram Terbinafine hydrochloride cream, 1%
Thiamine deficiency (prophylaxis)	Thiamine hydrochloride tablet, 100 mg
Whipworm infestation	Albendazole tablet, 200 mg
Chronic suppurative otitis media (age ≥ 1 month)	Ciprofloxacin ear drops, 0.3%
Dermatophyte infection when topical treatment has failed	Terbinafine hydrochloride tablet, 250 mg
Nicotine dependence as the sole PBS-subsidised therapy	Nicotine transdermal patch, releasing approximately 15 mg per 16 hours
Nasal colonisation with <i>Staphylococcus aureus</i>	Mupirocin nasal ointment, 2%

* Authority-required listings are streamlined except for ciprofloxacin ear drops and terbinafine hydrochloride tablets.

Sitagliptin with metformin (Janumet) fixed-dose combination tablets PBS listed for type 2 diabetes mellitus

Sitagliptin with metformin tablets (Janumet) in fixed-dose combinations of 50/500 mg, 50/850 mg and 50/1000 mg are available on the PBS as of 1 August 2009. The authority required (streamlined) listing is for the treatment of type 2 diabetes when:

- HbA_{1c} is > 7% despite use of metformin, and when a combination of metformin and a sulfonylurea is contraindicated or not tolerated, or
- people are stabilised on a PBS-subsidised regimen of oral medicines for diabetes that includes metformin and sitagliptin.

The fixed-dose combination tablets are **not** TGA approved or PBS subsidised for use as initial drug therapy, or in combination with a sulfonylurea or a thiazolidinedione (glitazone) as part of triple oral therapy.

The authority-required listing for sitagliptin (Januvia) has been revised and is now streamlined to be consistent with the listing for Janumet.¹

Starting or switching to the fixed-dose combination tablets

Sitagliptin with metformin fixed-dose combination tablets should be taken twice daily with meals.² If necessary, increase the dose gradually so as to minimise gastrointestinal side effects with metformin.²

Individualise the starting or switching dose according to the patient's current regimen, level of glycaemic control and tolerability, while maintaining a daily dose of sitagliptin of 100 mg/day.²

The initial dose for patients who are inadequately controlled on metformin is sitagliptin 50 mg twice daily plus the previous dose of metformin.²

For patients who are already taking sitagliptin and metformin, a fixed-dose combination tablet may be prescribed at the dose of each medicine that was used separately.²

Advise patients who are switching to the combination tablets to return their separate medicines to a pharmacy for disposal.

Consider prescribing metformin and sitagliptin as separate medicines for some patients

Sitagliptin with metformin fixed-dose combination tablets provide metformin at a total daily dose of 1000 mg, 1700 mg or 2000 mg. However, some patients may be taking other doses of metformin, such as 1500 mg or 3000 mg daily.

For patients who are less flexible to changes in their current metformin regimen — for example, because of tolerability — it may be preferable to start or continue with sitagliptin and metformin as separate medicines. In doing so, side effects with either drug can also be identified and assessed more easily.

For more information on starting dual oral therapy with sitagliptin, see the *NPS RADAR* review on Sitagliptin (Januvia) for type 2 diabetes mellitus.

References

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Risedronate (Actonel Once-a-month) and summary of anti-resorptive drug listings

A new once-monthly tablet formulation containing risedronate sodium 150 mg (Actonel Once-a-month) was listed on the PBS on 1 July 2009. The authority-required (streamlined) listing is for treatment as the sole PBS-subsidised anti-resorptive agent for osteoporosis in people¹:

- with a fracture due to minimal trauma
- aged 70 years or older with a bone mineral density (BMD) T-score ≤ -3.0
- on long-term high-dose corticosteroid therapy (at least 7.5 mg/day of prednisolone or equivalent for ≥ 3 months) with a BMD T-score ≤ -1.5 .

These restrictions are in line with other currently listed risedronate products (Actonel, Actonel Once-a-week, Actonel Combi, Actonel Combi D).

Update on PBS-listed anti-resorptive drugs and their restrictions

Since 2006 several new medicines, formulations and indications for anti-resorptive drugs have been listed on the PBS. Table 1 lists the anti-resorptive drugs currently subsidised for osteoporosis.

For more information about prescribing anti-resorptive drugs, go to the NPS Health Professional webpage at www.nps.org.au/health_professionals and search for 'osteoporosis'.

References

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Table 1: PBS listings of anti-resorptive drugs for osteoporosis (as at 1 July 2009)

Anti-resorptive drug	PBS listing restriction		
	Established osteoporosis with fracture due to minimal trauma	70 years of age or older with BMD T-score ≤ -3.0	Long-term high-dose corticosteroid therapy with BMD T-score ≤ -1.5
Alendronate sodium (<i>Adronat, Alendrobell, Alendro Once Weekly, Fosamax Once Weekly, Fosamax Plus, Ossmax</i>)	✓	✓	✗
Disodium etidronate with calcium carbonate (<i>Didrocal</i>)	✓	✗	✗
Raloxifene hydrochloride (<i>Evista</i>)	✓*	✗	✗
Risedronate sodium (<i>Actonel, Actonel Once-a-month, Actonel Once-a-week, Actonel Combi, Actonel Combi D</i>)	✓	✓	✓
Strontium ranelate (<i>Protos</i>)	✓*	✓*	✗
Zoledronic acid (<i>Aclasta</i>)	✓ [†]	✓*	✗

* Postmenopausal women only.

[†] Use in men only subsidised if they have had a hip fracture due to minimal trauma.

Clopidogrel (Iscover, Plavix) PBS listing extended to cardiac stent insertion

From 1 August 2009 clopidogrel can be prescribed in combination with aspirin as an authority (streamlined) PBS benefit after coronary artery stent insertion.¹ Previously a PBS subsidy was available for the treatment of acute coronary syndrome (ACS), and for prevention of recurrence of ischaemic stroke, transient cerebral ischaemic events, myocardial infarction or unstable angina. The extended PBS listing allows patients who require a stent to have equitable access to clopidogrel therapy.

The PBAC noted that there is evidence that prescribing clopidogrel, in combination with aspirin, is best clinical practice to prevent blood clots reforming after cardiac stent insertion.¹

Clopidogrel was PBS listed for ACS on 1 February 2009. For further information refer to the March 2009 *NPS RADAR* In Brief Item: Clopidogrel PBS listing extended to include acute coronary syndrome (ACS) in combination with aspirin.

References

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Lanthanum (Fosrenol) tablets for adults with chronic kidney disease who are on dialysis

Lanthanum (Fosrenol) was listed on the PBS on 1 May 2009. The authority listing allows prescribing for the treatment of hyperphosphataemia in adults with chronic kidney disease who are on dialysis*, but **not** in combination with sevelamer.¹ Until this listing, lanthanum had been available only on private prescription.

Lanthanum is a rare earth element that reduces serum phosphate concentration by binding phosphate in the gut.^{2,3} Calcium-based phosphate binders are first line for the treatment of hyperphosphataemia (unless serum calcium concentration is > 2.4 mmol/L),⁴ Lanthanum may

be an alternative for people taking calcium carbonate (Caltrate, Cal-Sup), for whom hypercalcaemia is a problem.^{2,4} Other available phosphate binders include aluminium hydroxide (Alu-tab), which is not PBS listed, and sevelamer (Renagel), which has the same PBS authority listing as lanthanum.⁵

Monitor serum phosphate concentrations every 2-3 weeks (adjust lanthanum dose as needed) until stable, then at regular intervals.^{2,3} Although only a very small amount is absorbed, it is distributed into bone.³ Lanthanum often causes gastrointestinal adverse effects (e.g. nausea). As with any new drug, the full toxicity profile and long-term effects of lanthanum are unknown.

A 6-month unblinded randomised trial (n = 777) showed similar efficacy for lanthanum and calcium carbonate in reducing serum phosphate concentrations.⁶ This was maintained for those who remained in the extension trial: 46 people for 2.5 years⁷ and 22 people for 6 years.⁸ Another randomised unblinded trial (2 years, n = 1359) showed similar efficacy for lanthanum and other phosphate binders (including calcium [carbonate and acetate] and sevelamer).⁹

References

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4. Caring for Australians with Renal Impairment (CARI). Use of phosphate binders in chronic kidney disease. The CARI Guidelines. Sydney: CARI, 2006. http://www.cari.org.au/CKD_bone_list_published/The%20use%20of%20phosphate%20binders%20in%20CKD.pdf (accessed 9 January 2009).
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7. Hutchison AJ, et al. *Nephron* 2006;102:c61-71.
8. Hutchison AJ, et al. *Nephron Clin Pract* 2008;110:c15-23.
9. Finn WF, on behalf of the S.P.D. Lanthanum Study Group. *Clin Nephrol* 2006;65:191-202.

* Hyperphosphataemia in an adult with chronic kidney disease who is on dialysis and whose serum phosphate level is not controlled with other products and when:
(a) serum phosphate concentration is > 1.6 mmol/L, or
(b) the serum calcium (mmol/L) × phosphate (mmol/L) product is > 4.0 mmol²/L²

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