

## Feedback from the field

bpac<sup>nz</sup> has been working with local practices to help identify areas where potential savings could be made in pharmaceutical expenditure, without compromising patient care or safety. The following feedback on selected topics has been received from doctors and nurses in primary care in the southern region:

### Bone health

- *Low levels of awareness of the availability of risedronate – a fully subsidised bisphosphonate*
- *Some general practitioners identified the opportunity to prescribe risedronate to patients with osteopenia and those taking corticosteroids long-term, as subsidy is not subject to Special Authority approval*
- *The concept of a “five-year holiday” for patients taking a bisphosphonate is gaining more traction*
- *Some practices have set up the facility to offer zoledronic acid infusions to patients, and therefore these practices are higher prescribers of this bisphosphonate. Most other practices do not promote zoledronic acid due to the cost.*

Risedronate has been fully subsidised, without restriction, on the Pharmaceutical Schedule since September, 2013. In November 2013, an article was published in Best Practice Journal outlining its place in practice.

Risedronate is indicated for the treatment of osteoporosis and for the prevention of osteoporosis in people taking corticosteroids long-term. Risedronate is superior to etidronate for preventing fracture, with a simpler once-weekly dosing regimen. Risedronate is considered to be equally effective as alendronate, with a similar adverse effect profile and the

same dosing regimen, but is not subject to Special Authority approval for subsidy. In addition, the cost of risedronate is \$1.00 per tablet compared to \$4.43 per tablet for alendronate.

When making the decision to initiate a patient on a bisphosphonate, risedronate is a reasonable first-line choice. Zoledronic acid is a once-yearly infusion and is considerably more expensive (\$600 per 100 mL) than either risedronate or alendronate. Zoledronic acid should be reserved for patients who meet the criteria for Special Authority approval and are unable to tolerate an oral bisphosphonate.

There are two main factors that determine the clinical effectiveness of bisphosphonates – their affinity to bind to bone and the extent to which they inhibit a key enzyme. When these two factors are considered the ranking for the three more potent bisphosphonates is:


- For bone binding affinity – zoledronic acid > alendronate > risedronate
- For potency of inhibition of the enzyme, farnesyl pyrophosphate synthase – zoledronic acid > risedronate > alendronate

There are no restrictions on the prescribing of risedronate, however, clinical judgement applies. Risedronate is specifically indicated for the prevention of osteoporosis in patients taking corticosteroids, e.g. patients aged 65 years or over, taking  $\geq 7.5$  mg prednisone (or equivalent) daily, for more than three months. Osteopenia is not a listed indication for risedronate, therefore this use would be “off-label” and informed consent from the patient must be obtained.

Prior to being prescribed a bisphosphonate, the patient’s diet should be reviewed to ensure they have an adequate calcium intake and that they are not at risk of vitamin D deficiency, e.g. frail elderly people who are house-bound. Vitamin D supplementation can be prescribed without laboratory testing of vitamin D levels. Calcium supplementation is appropriate if dietary intake is inadequate.

Risedronate should be prescribed for an initial period of three to five years. After that time, re-assessment with bone mineral density and fracture history is recommended. There is increasing evidence that the majority of the benefit from bisphosphonate treatment occurs within the first five years of treatment. The

concept of a “drug holiday” applies to treatment with all bisphosphonates and is thought to allow bone resorption to recover and aims to reduce the risk of rare adverse effects. Patients who are expected to benefit most from a period of discontinued treatment are those with bone density T-scores above -2.0 who have been receiving treatment for three to five years. A dose reduction, rather than a drug holiday, may be appropriate for some patients who have received treatment for five years or more, e.g. reducing the dose of risedronate from 35 mg weekly to 35 mg fortnightly. Regular reassessment is required for patients taking drug holidays or those taking reduced doses – the suggested interval for reassessment for risedronate is one year (alendronate one to two years, zoledronic acid two to three years, as it is based on the bone-binding affinity of the medicine).

 For further information see: “Risedronate now fully subsidised: what is its place in practice? BPJ 56 (Nov, 2013).

### Infant formula for cows’ milk protein allergy

- *Lack of awareness of the high cost of infant formula, particularly amino acid formula*
- *A common scenario is for a formula to be initiated by a paediatrician, and continued by the general practitioner, without regular review of the ongoing need for specialised formula*
- *Parental pressure to continue with specialised formula is a barrier to reducing prescription*

Cows’ milk protein allergy (CMPA) has a prevalence of approximately 2% in children aged under two years. It should not be confused with lactose intolerance. Symptoms of CMPA can vary and diagnosis can be challenging, therefore it is recommended that children with suspected CMPA are referred to a paediatrician for assessment.

If CMPA is suspected, diagnosis is usually confirmed by complete elimination of cows’ milk protein from the diet (the mother’s diet if breast feeding) for two to four weeks and observing if symptoms resolve. Depending on the severity of the CMPA, a re-challenge to see if symptoms recur may be indicated to confirm diagnosis.

For infants with CMPA who are breastfed, cows’ milk should be eliminated from the mother’s diet. For infants who are not

breastfed (or if restricting the mother’s diet is not possible), a specialised milk formula can be prescribed.

Soy, extensively hydrolysed and amino acid formulas are options for children with CMPA. Selection of which depends on the allergy syndrome and the age of the infant:

- For non-anaphylactic CMPA in infants aged under six months **extensively hydrolysed** formula, e.g. Pepti-Junior Gold, Karicare Aptamil, is recommended as first choice (Special Authority approval for subsidy; \$15.21 per 450 g)
- For non-anaphylactic CMPA in infants aged over six months, **soy formula** can be trialled as first choice (not subsidised)
- For infants with anaphylaxis due to CMPA or eosinophilic oesophagitis, **amino acid formula**, e.g. Neocate, Elecare, Vivonex Paediatric, is recommended as first choice (Special Authority approval for subsidy; \$53.00 per 400 g)
- Amino acid formula is also appropriate if the infant has trialled extensively hydrolysed formula and it is unable to be tolerated

If the first choice is not tolerated, an alternative formula can be trialled. If none of these formulae are tolerated, an elemental feed may be trialled; these are the most costly option.


Other formulas such as goats’-milk based, lactose-free and partially hydrolysed formula are not suitable for infants with cows’ milk protein allergy.

Children with cows’ milk protein allergy may develop tolerance to cows’ milk as they get older. Approximately 50% of affected children develop tolerance by age one year, > 75% by the age of three years and > 90% are tolerant at age six years.<sup>1</sup>

There is limited evidence about the optimal interval before re-evaluation but Special Authority renewals for specialised formulas are required every six months. Tolerance development may be assessed by a history of accidental exposure, skin prick test, measurement of cows’ milk specific IgE, or food challenges depending on the severity of cows’

milk protein allergy. This is important to avoid continuing a restrictive diet for an unnecessarily long time which could result in growth impairment of the child.<sup>1</sup>

1. Koletzko S, Niggeman B, Arato A, et al. Diagnostic approach and management of cows'-milk protein allergy in infants and children: ESPGHAN GI committee practical guidelines. *J Pediatr Gastroenterol Nutr* 2012;55(2):221-9.


 For further information see: "Allergy to cows' milk protein and the appropriate use of infant formula", *BPJ Special Edition* (May, 2011).

## Oxycodone

- *Most clinicians noted that they had observed a decrease over the past six months in patients discharged from hospital on oxycodone*
- *All general practitioners reported having at least one patient with possible addiction issues with oxycodone*
- *All general practitioners also reported having difficulty "weaning" patients off oxycodone*

The overall volume of oxycodone dispensed in the community is beginning to decrease. Between the last quarter of 2011 and the first quarter of 2014, there has been a 19% decrease in the number of patients dispensed oxycodone. However, the number dispensed morphine increased by 23%, so there has not been a decrease in the overall dispensing of strong analgesics. The proportion of oxycodone being initiated in secondary care (72%) compared to primary care (28%) has remained relatively constant over the past 12 months.

The article in this month's edition on managing patients with addiction to opioids gives practical information about methods to withdraw patients from oxycodone. Some patients will be able to be ceased abruptly, whereas others will have to undergo a slower tapering process, with additional support. Patients who are resistant to stopping, are unable to stop, or have mental health co-morbidities may need to be referred to specialist addiction services for opioid substitution treatment.

 For further information, see: "Identifying and managing addiction to opioids", Page 16, and "Oxycodone update", *Prescribing Report*, Aug 2014. Available from: [www.bpac.org.nz/Report/2014/August/OxycodoneUpdate.aspx](http://www.bpac.org.nz/Report/2014/August/OxycodoneUpdate.aspx)

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