

## New drugs

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### Asfotase alfa

**Approved indication: hypophosphatasia**

**Strensiq (Alexion)**

**Vials containing 18 mg, 28 mg, 40 mg, 80 mg**

**Australian Medicines Handbook section 10.3.3**

Hypophosphatasia is a rare disorder that causes defective mineralisation of bone. It is caused by genetic mutations which result in reduced activity of (tissue non-specific) alkaline phosphatase. Hypophosphatasia can present in a variety of ways. In children it can cause failure to thrive, short stature, fractures, rickets, muscle weakness and loss of teeth. Renal function can be impaired, but respiratory failure is the main cause of death. There is no effective treatment and the mortality in infants is at least 50%.

Asfotase alfa is a genetically engineered glycoprotein. It has been designed to have enzymatic activity in bone, to address the lack of alkaline phosphatase, with the expectation that mineralisation will improve.

The enzyme has to be given by subcutaneous injection. Doses are determined by the weight of the patient and given three or six times a week. Asfotase alfa is catabolised as a protein and has an elimination half-life of 2.28 days. No studies have been done in children with renal or hepatic impairment.

As hypophosphatasia is a rare disease there are limited numbers of patients to participate in clinical trials. The trials of asfotase alfa have mostly been open-label, phase II studies.

One study enrolled 11 children under three years old with life-threatening hypophosphatasia. After 24 weeks of treatment there was a radiological response in all but one patient. The bony abnormalities continued to improve over 48 weeks. On the 10-point rickets severity scale the median score fell by 8.8 points from a baseline of 9.5 points. At the start of the study 10 children required ventilatory support. Six of the nine patients treated for 48 weeks were able to breathe without ventilatory support.<sup>1</sup>

Another study compared the outcomes for 13 children, 6–12 years old, with those of 16 historical controls. Treatment with asfotase alfa resulted in changes on skeletal radiographs after six weeks. This improvement persisted for five years. The rickets

severity score reduced from a median of 2.75 points at baseline to 1 after a year and 0 at five years.

Although not all the children had complete healing, there was no change at all in the historical controls. There were also improvements in physical function and reduced disability.<sup>2</sup>

When asfotase alfa was approved for use in Australia the safety analysis was based on a total of 71 patients. Some of these patients were adults, but 68 had paediatric-onset hypophosphatasia. Injection site reactions, such as erythema, are very common, so it is important to rotate where the drug is injected. Most patients will develop antibodies to asfotase alfa, but these do not predict who will have a hypersensitivity reaction. Approximately 1% of patients have an anaphylactic reaction. Fever, irritability and headache are very common. With such small numbers of patients it is difficult to be certain if adverse events such as ectopic calcification and craniosynostosis are related to the treatment or the disease. Calcium and parathyroid hormone should be checked during treatment.

Asfotase alfa appears to have some benefit, but hypophosphatasia is a lifelong condition. To assess if the drug has an effect on survival, data from two studies were compared with historical outcomes for patients with perinatal or infantile hypophosphatasia. Compared with 48 historical controls, survival at the age of one year was significantly better (42% vs 95%) in the 37 children given asfotase alfa. At five years the corresponding figures were 27% and 84%.<sup>3</sup> As there are limitations in using historical controls, the patients prescribed asfotase alfa will need monitoring to see if the effect of treatment is sustained. If the child lives into adulthood, there are few data to guide whether treatment is effective in patients over 18 years old.

**T** [manufacturer provided some information](#)

### REFERENCES

- Whyte MP, Greenberg CR, Salman NJ, Bober MB, McAlister WH, Wenkert D, et al. Enzyme-replacement therapy in life-threatening hypophosphatasia. *N Engl J Med* 2012;366:904-13. <https://doi.org/10.1056/NEJMoa1106173>
- Whyte MP, Madson KL, Phillips D, Reeves AL, McAlister WH, Yakimoski A, et al. Asfotase alfa therapy for children with hypophosphatasia. *JCI Insight* 2016;1:e85971. <https://doi.org/10.1172/jci.insight.85971>
- Whyte MP, Rockman-Greenberg C, Ozono K, Riese R, Moseley S, Melian A, et al. Asfotase alfa treatment improves survival for perinatal and infantile hypophosphatasia. *J Clin Endocrinol Metab* 2016;101:334-42. <https://doi.org/10.1210/jc.2015-3462>



Some of the views expressed in the following notes on newly approved products should be regarded as preliminary, as there may be limited published data at the time of publication, and little experience in Australia of their safety or efficacy. However, the Editorial Executive Committee believes that comments made in good faith at an early stage may still be of value. Before new drugs are prescribed, the Committee believes it is important that more detailed information is obtained from the manufacturer's approved product information, a drug information centre or some other appropriate source.

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The Transparency Score is explained in [New drugs: transparency, Vol 37 No 1, Aust Prescr 2014;37:27.](#)

At the time the comment was prepared, information about this drug was available on the websites of the [Food and Drug Administration in the USA](#), the [European Medicines Agency](#) and the [Therapeutic Goods Administration](#).