Asfotase alfa (Strensiq®) for the treatment of hypophosphatasia (HPP)

Summary of recommendations by *Zorginstituut Nederland* (National Health Care Institute, the Netherlands) dated 25 March 2019.

Zorginstituut Nederland carried out an assessment of the medicinal product asfotase alfa (Strensiq®), whereby they came to the following conclusion.

In a letter dated 9 July 2018 (CIBG-18-06564), the Minister of Health, Welfare and Sport (VWS) asked *Zorginstituut Nederland* to assess whether asfotase alfa (Strensiq®) is interchangeable with a medicinal product that is already included in the Medicine Reimbursement System (GVS). The *Zorginstituut* has completed its assessment. The *Zorginstituut* sent the Minister the GVS report and the pharmacotherapeutic report its considerations.

The manufacturer has asked for inclusion on List 1B of the Health Insurance Decree for the registered indication.

Asfotase alfa is an orphan drug and is registered for exceptional circumstances for the indication 'long-term enzyme replacement therapy in patients with paediatric-onset hypophosphatasia to treat bone manifestations of the disease.' Asfotase alfa is available as 40 mg/ml and 100 mg/ml solution for injection. The dose is 2 mg/kg body weight, three times a week, administered subcutaneously; or 1 mg/kg body weight, six times a week, administered subcutaneously. If more than 1 ml is needed, then it has to be administered using several injections.

Assessment of interchangeability
Based on the criteria for interchangeability, asfotase alfa (Strensiq®) is not interchangeable with the other products included in the GVS.

Based on the above, asfotase alfa (Strensiq®) cannot be placed on List 1A. What has to be examined is whether asfotase alfa is eligible for placing on List 1B.

Therapeutic value
Hypophosphatasia is a rare metabolic disorder that can be life-threatening. Young patients with hypophosphatasia whose initial symptoms occurred before birth (HPP with perinatal onset) or before the age of six months (HPP with infantile onset) have a limited chance of survival: the median survival of patients from the historic control group was 8.9 months.

The chance of survival with a milder form of juvenile onset HPP (initial symptoms at the age of between 6 months and 18 years) is significantly higher; in these cases bone manifestations are predominant.

Zorginstituut Nederland concludes, with the advice of the Scientific Advisory Board (WAR), that treatment with asfotase alfa has a therapeutic added value for patients with hypophosphatasia and a perinatal or infantile onset, in comparison with best supportive care alone.
The therapeutic value of asfotase alfa for the treatment of patients with hypophosphatasia and juvenile onset is lower due to insufficient data.

Budget impact analysis
Taking into account the numbers of patients (prevalence and incidence) and the number of new patients per year, including asfotase alfa (Strensiq®) for hypophosphatasia on List 1B for patients from the age of 6 months will be accompanied by additional costs to the pharmacy budget of €1.2 million. Uncertainty exists about the number of patients in the coming years. This is important due to the costs per patient per year: these are for 0-1 years €144,263 per year, for 2-4 years €244,410 per year and they could increase to as much as €1,282,341 per year for 13 years and older.
Furthermore, there is a chance that asfotase alfa will also be used for patients with juvenile onset HPP.

Pharmacoeconomic analysis
As the budget impact for patients with hypophosphatasia and a perinatal or infantile onset is €1.2 million, dispensation can be granted for the pharmacoeconomic analysis.

Advice
Asfotase alfa (Strensiq®) is not interchangeable with any product in the GVS. Based on the above-mentioned consideration, we advise the Minister to include asfotase alfa (Strensiq®) on List 1B and List 2 of the Health Insurance Decree and to stipulate the condition indicated below. Inclusion on List 1B will involve additional costs.

Condition for asfotase alfa
Only for an insured person with hypophosphatasia whose initial symptoms occurred in the womb (before birth) or before the age of 6 months.

For further information, please contact: JBoer@zinl.nl; warcg@zinl.nl

The original text of this excerpt from advice of Zorginstituut Nederland was in Dutch. Although great care was taken in translating the text from Dutch to English, the translation may nevertheless have resulted in discrepancies. Rights may only be derived on the basis of the Dutch version of Zorginstituut Nederland's advice.
Furthermore, Zorginstituut Nederland points out that only the summary of this report was translated. A proper understanding of all relevant considerations and facts would require familiarity with the Dutch version of this report, including all appendices.