Common Drug Review
Patient Group Input Submissions

Asfotase Alfa (Strensiq) for Hypophosphatasia, pediatric-onset

Patient group input submissions were received from the following patient groups. Those with permission to post are included in this document.
Soft Bones Canada — permission granted to post.

CADTH received patient group input for this review on or before September 28, 2015.

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Soft Bones Canada

Section 1 – General Information

Name of the drug CADTH is reviewing and indication(s) of interest	Asfotase Alfa
Name of the patient group	Soft Bones Canada
Name of the primary contact for this submission:	[redacted]
Position or title with patient group	[redacted]
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Permission is granted to post this submission	Yes

1.1 Submitting Organization

Soft Bones Canada is a source of education, information, encouragement, and support for Canadian individuals and their families affected by HPP, including interested individuals in the medical community.

The purposes of SBC as set out in the articles of incorporation are:

(a) To advance education by providing courses, seminars, workshops, and educational materials about Hypophosphatasia to the public, patients and medical professionals;

(b) To promote health by providing Hypophosphatasia patients and their caregivers with access to health counseling, information, and group support programs; and

(c) To advance education by supporting and conducting research into the causes and possible treatments of Hypophosphatasia and making the results publicly available

1.2 Conflict of Interest Declarations

a) We have the following declaration(s) of conflict of interest in respect of corporate members and joint working, sponsorship, or funding arrangements: None

b) We have the following declaration(s) of conflict of interest in respect of those playing a significant role in compiling this submission: None

Section 2 — Condition and Current Therapy Information

2.1 Information Gathering

Soft Bones Canada obtained information from patients and caregivers through one-to-one conversations by telephone and email, drawing from our own personal experiences and by meeting with families in a group setting to openly share and discuss. These interactions were with both those on asfotase alfa and those not on medication.

2.2 Impact of Condition on Patients

The impact of HPP is dramatic on patients, often right from birth. The over-arching impacts according to the people we engaged were pain and fatigue.

Pain was the primary issue noted by everyone. Many people described themselves as being in constant, relentless pain that while it may vary in intensity, is always there. In children, joint pain can be so severe that they cannot even walk. One mother told us that in the four months prior to her son taking the ERT, "he would scream every night, and cry saying his legs hurt. We tried pain relief medication, but nothing would work".

Adult patients spoke of the inability to function due to joint pain (shoulders, knees, neck, ankles, wrists, lower back, hands, fingers, feet, toes), as well as inflammation and stiffness. Severe muscular and bone pain is also typical, described by one person as "the bones in my wrists and ankles burn like they're on fire". Headaches are frequent, often due to muscle stiffness and spasm.

The impact of being in chronic pain was frequently mentioned by people, too. Overwhelming frustration, being in a mental fog, impatience with family members, anxiety, fear, depression, and lack of intimacy were just a few noted.

Closely aligned with constant pain amongst the patients we connected with was constant fatigue. Having HPP leaves one physically and emotionally exhausted. More than one parent mentioned that their children with HPP sometimes had a complete inability to move without great fatigue. For adults, fatigue means placing limitations on almost all aspects of their lives. One person told us that she is forced to live a largely sedentary lifestyle, but not by choice. Others spoke of limitations on job opportunities (ones that require standing/walking), job loss and frequent absenteeism. Some even mentioned limitations on housing, needing to live in a single story home with no stairs.

Perhaps most telling, however, is the link between fatigue and the raising of children. Numerous patients spoke about their inability to carry or even play with their kids. One person noted "I can't walk as fast as my toddler". Choosing to not even have children due to the fatigue associated with HPP was mentioned in another case.

The findings from our engagement with patients/families are further expanded upon below.

For children:

- Excessive sleeping
- Craniosynostosis
- Stress fractures in legs and hips

- Poor appetite and failure to gain weight/growth
- Stomach pain and frequent vomiting
- Loss of baby teeth prior to second birthday, meaning some children go up to six years without any teeth (impeding speech development and self-esteem)
- In some cases, baby teeth were small, soft, or deformed
- Requirement of a wheelchair, limiting their independence and ability to fully participate in school activities
- Socially ostracizing (due to inability to run, jump, climb stairs, ride a bike, and play with friends) and disheartening
- Frequent loss of school days
- Accommodation requirements at school
- Unable to dress themselves, go to the bathroom without assistance in severe cases

For adults:

- Extensive dental issues (bone loss in the jaw, severe gum recession, frequent root canals, missing teeth, abscessed teeth, implants, bridges, crowns) - all at great financial cost
- Unable to participate in many sports (tennis, hiking, golf)
- Walking distances is difficult due to pain
- Sitting for extended periods makes legs and hips sore
- Numbness and tingling
- Twitching limbs, fingers, restless legs
- Difficulty preparing meals, playing the piano, grocery shopping, walking the dog, mowing the lawn, gardening, shovelling snow, cleaning the house, carrying laundry – basic tasks must often be performed in stages
- Difficulty driving and travelling as a passenger in a car
- Poor sleep patterns and difficulty moving in the morning
- Fear of tripping, falling, and becoming permanently debilitated
- Balance problems
- Poor muscle tone due to inability to exercise
- Multiple fractures (tibia/fibula, humerus, femur, ribs, feet) that take a long time to heal
- Multiple surgeries to fix broken bones
- Osteoarthritis
- Osteophytes
- Joint cysts
- Anemia
- Ectopic deposits of CPPD on spine and in soft bones/organs
- Kyphosis of spine
- Nerve damage
- Psychological challenges – being told you ‘look fine’ when you are hurting inside; knowledge that the pain you have will never go away, as you walk on broken bones that will not heal
- Challenges getting good medical help due to the rarity of HPP
- Anger – at delayed diagnosis and poor pain management options
- Knowing that you have a decreased life expectancy

Patients' Experiences With Current Therapy

There are currently no treatments specifically to treat HPP. Nevertheless, a number of adjunctive therapies were mentioned by the people we engaged:

- Physiotherapy – to increase muscle tone
- Massage therapy – although for some patients this was too painful
- Osteopathy – to ensure body alignment
- Bone healing device
- Surgery – to repair broken bones
- Over-the-counter pain relievers (although ones with codeine caused kidney pain in some cases)
- Morphine
- Cortisone injections
- Anti-inflammatory medications/supplements
- Specialist visits (i.e. periodontist, endocrinologist, naturopath, and nutritionist)
- Special footwear/orthotics
- Yoga/meditation

It was also noted by one person that if she stops taking any of her pain management therapies, "the symptoms come back with a vengeance".

Unfortunately, whether the people we engaged were taking one or multiple treatments to help manage their disease, everyone mentioned a lack of effectiveness. Nothing they did really helped with the pain and fatigue of living with HPP.

Some of the hardships associated with these limited adjunctive therapies included running out of money for physiotherapy, long wait times to see a specialist or get an MRI (over a year), extensive travel/overnight accommodations just to see a specialist or have tests done (time away from family) and the costs of maintaining a certain diet to control B6, calcium and phosphate.

2.3 Impact on Caregivers

HPP places a tremendous amount of responsibility on caregivers in virtually all circumstances. The content below focuses on what we heard from parents whose children have the disease.

For parents:

- If diagnosed at birth, children can remain in hospital for months
- Necessity of acting as a full-time caregiver to their children with the disease – meaning an inability to hold a job
- Preparation of only soft food meals because of teeth loss
- Driving their children everywhere due to limited mobility
- Inability to leave even older children alone due to risk of falls
- Need to protect their children and educate others involved in their lives (friends, teachers)
- Unable to enjoy activities as a family (hiking, camping)
- Constant need to accommodate their child with HPP (often at the expense of other siblings)
- Frustration at not being able to do more for their suffering children
- Emotional strain, anxiety, depression, isolation, and exhaustion
- Financial costs – wheelchairs, electric stair climbers, walkers, physiotherapy
- Financial strain – missing/unable to work
- Constantly taking children for tests and other medical appointments
- Difficulty accessing community supports or funding for programs with such a rare condition

Section 3 — Information about the Drug Being Reviewed

3.1 Information Gathering

Soft Bones Canada obtained information from patients and caregivers through one-to-one conversations by telephone and email, and by meeting with families in a group setting to openly share and discuss. These interactions were with those on asfotase alfa.

3.2 What Are the Expectations for the New Drug or What Experiences Have Patients Had With the New Drug?

a) Based on no experience using the drug:

The overwhelming hope is that asfotase alfa will help people with HPP survive. For those diagnosed at birth, they will hopefully survive into adulthood. For those diagnosed as adults, they will ideally survive longer than their current life expectancy.

It will improve mobility and independence. Children and adults will be able to walk, run, play and engage in mainstream physical activities with less fatigue. This, in turn, will lead to a better quality of life and improved emotional well-being.

But more than any expectation, it is the hope that asfotase alfa will finally provide some measure of relief from the debilitating pain.

Additional benefits could be less time away from work (for both patients and caregivers), decreased incidence of fractures, increased muscle tone/bone density, the need for fewer adjunctive therapies, fewer medical appointments and less financial burden.

Some of the patients we engaged specifically told us they would take asfotase alfa if it improved their quality of life, even with extensive side effects. As one person stated “I would use this therapy because the alternative is a life of pain, dependence on the health care system and long term disability”. Another simply said that any improvement would be beneficial – even as low as 10% improvement.

b) *Based on patients’ experiences with the new drug as part of a clinical trial or through a manufacturer’s compassionate supply:*

The results for patients who have been on asfotase alfa are resoundingly positive. It was described as both life-changing and life-saving.

The following is a representative example from a parent whose child was put on the medication at five months old (the child is now 16 months old):

Before asfotase alfa	After asfotase alfa
• At four weeks old, child stopped eating due to muscle weakness • Little growth or weight gain in the first five months • Not able to hold head up • Hip fracture found on x-ray • Bones appeared translucent on x-ray	• Child began to grow, but still small for age • Eats without tiring • Able to hold head up, roll around • Walking by 12 months old/walking normally (no waddling gate) • Bones appear solid on x-ray • All baby teeth are in place/not loose • No pain, no new fractures

Other positive effects expressed by parents included:

- Much less pain
- An almost immediate and significant improvement in strength and physical abilities
- Children feel and look 'normal', like the rest of their friends
- Able to walk, run, jump, climb stairs, play sports, ride a bike
- Some children are performing normally for their age group
- Improved overall quality of life
- Emotional improvement – more confident
- Bones are now 100% dense
- Ability to come off all other medications
- Limitations on the child/family have been removed

The positive effects expressed by adults included:

- Walk without pain
- Walking taller, straighter, faster
- No more waddling gait
- Decreased use of walker
- Hiking (for as long as three hours)
- No longer need to 'pull' themselves up the stairs
- After six months on the drug, improved stamina and mobility
- No more broken bones
- Emotional improvement - no longer sees the world through the eyes of pain

The negative effects expressed were few and able to be well managed, including:

- Dark/purple spots on the skin (at the injection sites), but they are generally mild
- Saggy skin (at the injection sites), which has made some children self-conscious
- The need for some to self-administer an injection
- Abdominal/thigh pain (at injection sites)
- Fatigued for the first three months on treatment
- Low grade fever for the first month on treatment

However, all of the people we engaged said that the negative effects were far outweighed by the benefits of the treatment.

Patients and their families noted that overall, asfotase alfa was easy to use. With the need for three injections a week, a couple said that their schedules were somewhat disrupted and if they travelled, they needed to ensure that the medication was properly packed and kept at a temperature of between 2°C-6°C. Another person did not like the fact that she could receive only two months' supply of the drug and that she had to be home when it was delivered.

One adult patient stated that unfortunately, asfotase alfa doesn't retroactively repair bones and teeth to non-HPP levels. Another noted that despite being on the drug, she will always have some pain because she has osteoarthritis in most of her joints.

Based on the experiences that we gathered from people on asfotase alfa, below are some perspectives on the impact of the new medication and how it is expected to change a patient's long-term health and well-being:

"If I had the chance to change anyone's mind on how powerful asfotase alfa has been for us (as a family), I would plead and fight it until the day I die. It's that life-changing for her (their daughter)."

"This medication is a miracle. My child is no longer the same. It has changed his life. He can live and not just survive suffering."

"Everything is better because of asfotase alfa."

"I expect to live many years able to walk without pain, a cane or a wheelchair and to participate in life as a normal person, to visit galleries and museums, to go hiking with friends on long trails, to travel freely - all the things that other people take for granted, but which I was unable to do outright or without a great deal of pain."

"I expect it will keep me walking the rest of my life."

One particular experience with the new medication really captured the need for access to asfotase alfa:

"I am the mother of a child with HPP. It was discovered by ultrasound when I was pregnant that something was very wrong with his bones and it became clear that he likely had HPP. I was devastated to hear that something was so wrong with my baby, but at the same time I was given hope by knowing that there was a treatment in trial that had already helped others. Our son was born on December 20, 2011 and it was confirmed he did in fact have HPP and was started treatment the very next day. He was our first child, and our newborn experience was far from normal but again, because of the asfotase alfa, we had hope that at some point our life would become somewhat close to normal. If the medication did not exist when our son was born, we would have had to take him off life support. He would have not have had any chance of survival because he had close to zero bones in his body. It took some time but after a month of our son being on asfotase alfa, we began to see improvement. We could feel his skull beginning to harden and his x-rays showed bones beginning to form, lengthen and even straighten! It was so amazing to see and gave us so much hope! Unfortunately our son's lungs never developed properly and at 14 months old he passed away. Although we never got to take him out of the hospital, without asfotase alfa instead of 436 days with our child, I'm sure it would have been just a few days. Because of the treatment, we have so many wonderful memories with our son that we wouldn't trade for anything. I am unbelievably grateful for this drug. It gave me time with my son and I love seeing what it's doing for others with HPP. They are living and thriving thanks to asfotase alfa.