



Common Drug Review *Patient Group Input Submissions*

Propranolol oral solution (Hemangiol) for Infantile hemangioma

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

AboutFace Craniofacial Family Society — permission granted to post.

CADTH received patient group input for this review on or before September 16, 2016

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AboutFace Craniofacial Family Society

Section 1 — General Information

Name of the drug CADTH is reviewing and indication(s) of interest	Propranolol oral solution (Hemangirol) for Infantile hemangioma
Name of the patient group	AboutFace Craniofacial Family Society
Name of the primary contact for this submission:	[REDACTED]
Position or title with patient group	[REDACTED]
Email	[REDACTED]
Telephone number(s)	[REDACTED]
Name of author (if different)	[REDACTED]
Patient group's contact information:	
Email	[REDACTED]
Telephone	416-597-2229 x21
Address	1057 Steeles Ave. West, Box 702, Toronto, ON M2R 3X1
Website	www.aboutface.ca
Permission is granted to post this submission	Yes

1.1 Submitting Organization

Every year in Canada more than 10,000 babies are born with facial birth defects; and over 50,000 Canadians will acquire a facial disfigurement through trauma or illness. Living with a facial difference is something you cannot hide. Clinical depression, isolation and anxiety are very common mental health issues among the estimated 1.5 million affected Canadians. AboutFace is the only national charity that empowers individuals with facial differences to develop the confidence, skills and self-esteem to break free from isolation and integrate effectively into society.

- *A visible difference is in fact a “social disability” as it is noticed by other people, and impacts the thoughts, feelings and behaviours of individuals living with one. (Macgregor 1979).*
- *Cultural definitions and social values placed on appearances, differences and disabilities have a profound impact on one’s development of their sense of self. Modern Western society values the “body beautiful” ideal, and therefore, there exists a tendency to judge others based on how they measure up to appearance “standards” and “norms”, which are essentially impossible to attain. (Rice et al., 2003).*

Founded in 1985, AboutFace works to promote and enhance positive mental and emotional well-being of individuals with facial differences and their families through social and peer support, information, educational programs, and public awareness. We offer a variety of support services in-person and through conference calls; experiential programs like camps and retreats to facilitate skill development, socialization and self-awareness which enable the development of positive mental and emotional well-being so that affected individuals can lead productive lives. Our membership is on a voluntary basis without fee, and includes parents of affected children, affected adults, other care-givers like partners and spouses, and health care professionals who work in the craniofacial area including doctors, nurses, surgeons, dentists, orthodontists and other specialists.

We also promote a culture of empowerment and diversity within communities by offering educational and awareness programs in schools, work places, and professional forums especially in the healthcare sector.

More and more research is becoming available on the impact loneliness and isolation have on a person's mental health and self-esteem. We are learning more about the importance of socialization and peer networks to help keep individuals grounded and how bullying, taunting, and negative messaging can have long term, damaging impact on a person even though they may have a positive sense of self. AboutFace is working with affected individuals, parents and professionals to understand the impact, so that we can enhance, improve or create programs and services to address the various psycho-social aspects of living with a facial difference.

- *Individuals with facial differences are often subjected to significant teasing and peer rejection in childhood and adolescence (Snyder, Pope, & Bilboul, 2005; Turner et al., 1997).*
- *They are also susceptible to hurtful name calling, offensive remarks, uncomfortable stares, “double-takes”, whispers, curiosity, personal questions, laughter, manifestations of pity, stereotyping, blatant avoidance in public situations, and even physical violence (Macgregor, 1979, 1990; Renooy, Rice, & Beveridge, 1999).*
- *The experience of these negative interactions may cause affected individuals to withdraw from and avoid social interaction (Snyder et al., 2005), impeding their ability to meet and relate to new people, make friends, and develop long term intimate relationships (Robinson, 1997).*
- *The reactive behaviours of unaffected strangers often generate feelings of shame, weakness, anger and humiliation, which can significantly erode the self-image and self-esteem of an individual with a facial difference. (Macgregor 1990).*
- *Taken together the feelings of worthlessness and embarrassment that result from being stared at or demeaned by strangers are a form of “psycho-emotional disablism”, which can prevent individuals from participating in society. (Reeve, 2004).*
- *About 40 percent of children with facial deformities also have significant social problems. These children have few friends, are reluctant to join organized activities, and are teased almost daily. They don't establish normal relationships with classmates, going to school is very difficult. They don't want to go out at recess. (Kapp-Simon, 1998)*

Over the years, AboutFace has established core programs that focus on psycho-social support, interactive learning, and education for parents, children and adults, such as:

- An informative DVD and workbook to address the top 5 challenges of raising a baby with a facial difference
- Camp Trailblazers – offered across Canada: British Columbia, Manitoba, Ontario, Nova Scotia, Newfoundland and Labrador
- Leadership & Life Skills Retreat for young adults with facial differences ages 19 to 24;
- Adult Retreat for affected adults ages 25 and older
- Two educational programs for primary and elementary school aged children
- Annual National Scholarships to encourage continued education
- Monthly support conference calls for affected adults and parents of affected children
- Access to care information and support to help parents and adults advocate on their own behalf
- In-service presentations to educate healthcare professionals

1.2 Conflict of Interest Declarations

None.

Section 2 — Condition and Current Therapy Information

2.1 Information Gathering

About Face collected people's experiences living with infantile hemangioma through various forms of communication and social media outreach to both our membership and online community members. One core element was our database which identifies members and their various conditions. Through that we connected with people directly through personal email outreach and/or phone call discussions, one-on-one. Through social media, we posted questions and inquiries on specific Facebook groups and forums on social media from people who are either affected individuals or caregivers of affected children. We spoke to families who have used Propranolol as a treatment for infantile hemangioma, as well as many who had different forms of treatment that were available over the years.

2.2 Impact of Condition on Patients

It is said that 'the face is the mirror of the soul' and when one's appearance is different, unusual and perhaps distorted, it is seen as a deficiency in character. Looking different in a society that idolizes and rewards physical perfection can create discomfort, awkwardness and in many cases draws negative and unwanted attention from others like staring, whispering, name calling and even verbal, physical and attitudinal violence for those who look different. Living with a facial difference is something you can't hide and often causes barriers to socialization, communications, relationships, employment and aspirations. Hemangiomas in particular can be visually striking depending on the location, severity and extent of the hemangioma. For adults living with hemangioma, when they were younger they received little or no treatment and for the treatment that did exist, much of it was experimental. Adults with hemangiomas describe that many of the treatments that were available during their infancy and/or childhood, were risky, invasive and painful. Yet, many feel that the psycho-social impact of living with a large hemangioma can be far more damaging than the condition itself.

When children meet someone with an unusual appearance they may stare out of curiosity and often use direct blunt language not necessarily to be mean, but because of their simplicity, concern and anxiety. However, the most hurtful and damaging of interactions comes from other adults. Their captivation, interest and most often, fascination with someone's difference creates an uncomfortable experience for the affected person. Adults are more direct and intrusive with their questions, comments and stares. They are more expressive and uninhibited by their curiosity and in many cases voice their disapproval and repulsion. Adults with hemangiomas often face ridicule, humiliation and suffering in public and/or in the workforce by other adults. Kids can be unkind, but adults can be malicious, cruel and ruthless, making life for a person with a facial difference, like a hemangioma, very difficult and unforgiving.

An affected adult shared the following:

"I think that playing all the sports I played and sometimes not with the proper equipment I am lucky to be alive. I never realized what I had and it was never explained to me that my cheek was full of pumping blood under a lot of pressure. The smallest facial injury could have been devastating. For example when I was in my late teen I was eating a toasted tomato sandwich and a piece of the toast nicked the corner of my mouth and boy did I ever bleed. It took over two hours for the bleeding to stop and that was when I was at rest, not participating in sports with my cheek puffed up full of blood and under pressure."

A parent said:

“Our daughter has multiple large infantile hemangiomas on both shoulders and the right side of her neck. At their largest, the right side of her neck expanded past her shoulder and pushed her ear up folding her earlobe approximately the dimensions of a large apple. The mass was impeding on her posture in that she had to compensate for the pressure it was putting on her neck tilting her head to the left. She was also unable to lift her arm much higher than roughly 50 degrees. If left untreated, she would not have been able to maintain a good balance and learn to walk with good posture thus creating an array of other complications, aches, and pains.

“As a parent having a child who developed a hemangioma shortly after birth, the world is a scary place where other children don't understand and concerned adults point and whisper. Our daughter's hemangiomas appeared during our stay at the NICU and though the nurses and medical staff were extremely professional and reassuring, I couldn't help but panic when I overheard them say a word that ended with 'angioma' during shift change. I quickly Googled it and even quicker yet shut down my computer. Tumor. Birth defect. Vascular anomaly. Ulceration. Development delays. Complications. Internal hemangiomas. Liver function. Blood disorders. The truth is that there is very little reliable information sources out there when it comes to the treatment and care of hemangiomas. It is terrifying.”

Although these daily difficulties can be limiting, many individuals with a Hemangioma will agree that much worse than any physical limitation, is the reaction they get in society because of the way they look. People with Hemangioma experience bullying and discrimination their whole lives. Continued bullying can often seriously affect their mental health and well-being. Research shows that repeated experiences of bullying, isolation, negative attention like staring and harsh comments and judgements by peers and others can cause long term damage to the person's self-confidence, self-esteem and socialization. Left unaddressed, these issues can develop into serious health and social problems such as anxiety disorders, depression, isolation, substance use and abuse, which ultimately affects their ability to find and/or hold employment, relationships and overall become a social and financial burden on society.

An affected adult said:

“There are “normal” kids that are bullied so much that they commit suicide, what must it be like for someone with a facial difference to get by? If there was some way to give these kids a chance to not have to go through any more than they absolutely have to I hope they get that chance. Life can be hard enough so they do not need any more hardship if they do not need to.”

2.3 Patients' Experiences With Current Therapy

Currently there are a few types of treatment available to children with hemangioma that are covered by provincial health care or private insurance. They include: oral systemic corticosteroids; laser therapy; and surgical removal. Adults with hemangioma have usually tried several different types of treatment when they were children with minimal results. More often than not, the hemangioma grew back or there was no difference. Unfortunately, many times, especially several years ago, surgical removal became a common treatment that often did not have a positive outcome. Surgical removal is invasive, can be quite painful, it is high risk, has a longer recovery period, and unfortunately has a much lower success rate for patient satisfaction.

One of the hardships is the unpredictability of the current treatments. There is little or no treatment for adults living with hemangiomas who may or may not have had treatments in the past. Having access to

Propranolol would prevent a child from having to grow up with a hemangioma and the health and mental health issues that can come with it.

An affected adult shared:

“I spent a good deal of my childhood having surgeries to stop the advancement of my hemangioma with limited success at best. I have averaged a surgery almost every two years of my life using a wide range of treatments. None of these have proven particularly successful. These surgeries have been painful both physically and emotionally, not to mention, extremely expensive for the medical system.”

2.4 Impact on Caregivers

Being a caregiver of a child with a Hemangioma can be very difficult. There are two key areas of concern: making the decision to pursue treatments that are painful and do not guarantee success; and making the decision to opt out of treatment and what long term consequences this may have. Parents struggle with these decisions because they are most concerned about the impact of their child having a facial difference. They anticipate the psycho-social impact of living with a difference. Often it negatively impacts their social network, their self-esteem and aspirations with impacts to their mental health. It can be very difficult to watch your child endure repeated painful treatments with little or no success. It's difficult to watch children at play and see your child being neglected, ignored or avoided all together. Parents often take on the role of their child's social network and friend to minimize the impact of having no friends. Parents also have to educate themselves on the condition and its various characteristics. They need to understand the treatment options, risks, benefits and limitations. Often, they can become overwhelmed with conflicting information from doctors, peers and the internet, which combined can create much stress and anxiety at a time when they need clarity and support to make informed decisions.

Moreover, as the child grows and begins to understand and can articulate their feelings and concerns, it makes the treatments that much harder for parents as well. Children may be afraid and not want to go, so they may cry, scream, and/or fight every time they go to treatment. Conversely, children and particularly youth may struggle with their feelings about why more was not done when they were younger, they may be sad because of negative peer and social pressures, and they may feel overwhelmed to try and do more to 'fix it' or 'cover it up' to minimize the negative attention they receive.

A parent said:

“The only thought I can imagine to be any more terrifying than this is knowing that the effective treatment is out there and available but for whatever reason, I couldn't afford it because of my financial situation. Because I couldn't afford to pay for a treatment for my child, they could be severely affected for the rest of their lives. Though I would give the world to her if it was mine to give, in this situation cost would be a factor and because of that, she may not get the best treatment possible.”

3.1 Information Gathering

During the Summer and Fall of 2014, AboutFace reached out to affected adults and parents of affected children via Facebook, social media, email and telephone, using our database. AboutFace also spoke to medical specialists to invite any of their patients (or their family members) to share any relevant information they may have.

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

Based on no experience using the drug:

Some AboutFace clients indicated that since they did not have access to Propranolol as a treatment in their infancy, they do not therefore know directly what the impact might have been for them had they been treated with this drug. However, some members have had to undergo invasive, costly treatments. In some cases multiple surgeries or repeated laser treatments or were given oral cortico-steroids that did not ultimately result in permanent or significant reduction in the advance of their hemangioma. In many cases, clients chose to stop treatments because of the many disruptions in their life, the excessive pain and healing time, costs of treatment, or traveling to various locations, and the disappointment of little or no results.

As a result, many clients without access to this drug also endured and learned to live with both the physical, psychological and social impacts of living with a hemangioma that is active, invasive and in many cases, un-concealable. In many cases, members endured the ‘wait and see’ option, which can result in negative and unwanted attention; it raises many concerns for parents and caregivers too. Parents often worried about their child and their well-being. Are they in pain? Is there discomfort? When will it stop growing? How bad might it get? What other aspects might it affect both physically, functionally, and emotionally? And, most importantly, what psycho-social impact will living with the hemangioma have on them?

It is clear from parent feedback today, the results are very impressive and they are very happy. Should Propranolol be accessible to treat infants with hemangiomas early on, it could minimize, reverse or diminish the negative impacts of the condition, thus avoiding many of the related negative medical, physical and psycho-social aspects.

An affected adult shared:

“I spent a good deal of my childhood having surgeries to stop the advancement of my hemangioma with limited success at best. I have averaged a surgery almost every two years of my life using a wide range of treatments. None of these have proven particularly successful. These surgeries have been painful both physically and emotionally, not to mention, extremely expensive for the medical system.”

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

Much of the feedback we received came from parents who were using the drug outside of Canada. USA and Australia seem to be very advanced in the usage of Propranolol and they are very pleased with the treatment and outcomes.

Parents said:

“It has worked very well for us so far with absolutely no side effects. He growing well and gaining weight like a champ. His pediatrician says he is farther ahead in mental development than other babies his age too so it has not had any side effects.”

“In two weeks we started noticing a change. The swelling has gone down, it has gotten lighter. We are very happy with the results to date.”

“Same thing here after a month or so of treatment and it's a wonderful feeling!”

“I know I share a lot but I hope to instill hope for other parents that medicine does work. My son has only been on treatment for a little over 2 months and his hemangiomas are almost gone. When we started his eye was starting to swell shut and now you can hardly tell in pictures that he has them. We still have a ways to go but he's going well and has had no side effects.”

When discussing side effects and concerns with this group of parents, it was clear that most did not experience any severe or concerning side effects. Some of the parents reported on restlessness of the child, and in some cases insomnia for the first few weeks, but nothing unmanageable. Several parents said that after weaning their child off the Propranolol they noticed that the hemangioma started to re surge.

Parents said:

“My daughter started propranolol at 3 months and I weaned her off it at about 18 months as it was completely flat and all colour had gone. She is now 2.5 years old and over the last month or so it's raised by only about a millimetre or two and some light red colouring has come back.”

“After weaning her off it for 2 weeks and then completely off medication for another 2 weeks, we noticed the nasal tip starting to get darker with a few red spots. We thought about it and have now put her back on it again.”

“After we weaned him off, he becomes very grumpy and clingy and not his normal happy self. It is worse if we don't do the transition slowly. Also we noticed that if we forgot his dose then he would be up during the night and very unsettled. At first I hated propranolol and what it was doing to my child however once we were consistent with it he was fine and I am so glad we stuck with it as it has almost gone and lessened his chance of needing surgery.”

The only other issue that seemed to resonate with many parents was the taste of Propranolol. It appears that parents are having a hard time ensuring that their baby will keep the medicine down. There was many questions about what others do to make sure their child ingests the medication. However, there seemed to be some discrepancy on how to administer the drug, i.e. with or without. Interestingly parent shared creative ways to administer the drug effectively with each other.

Given the feedback on the effectiveness of treatment with propranolol in infantile hemangiomas, it is safe to say that this will go a long way in alleviating many of the long term health, social and emotional well-being of both the child and family. With effective treatment like Propranolol, children born with hemangiomas can live full active lives. Many children with large hemangiomas are often limited or avoid completely in engaging in group sports or physical activities, socialization and other peer-focused programs. This limitation will have long term consequences as well and often is a pre-cursor for adults to be isolated, un-involved or engaged in family and community. It is estimated that over 80% of individuals with facial differences struggle with mental health issues as a result of daily taunting, staring, bullying and social rejection. The reality is we live in a society where people are judged based on their physical appearance. Starting at a very young age, we are taught through fairy-tales, comic books, television and films, to be wary of those who look different. For affected individuals this reinforcement can have a negative impact on self-esteem, impedes confidence in social settings, and diminishes the enjoyment of making new friends.

If by making this treatment accessible will help even one child minimize and/or avoid the negative aspects of living with a facial difference, then it is worth it.

Section 4 — Additional Information

The issue in this process is access to a drug or treatment that could change, minimize, reverse or diminish the effects of a facial difference. Parents of newborn babies are overwhelmed with experience of having a child with a facial difference for both medical reasons and psycho-social reasons. Watching your helpless child develop this unmanageable condition before your eyes with little or no control is daunting and gravely worrisome. Parents are open, eager and determined to find the best treatments options and alternatives to help their baby. They want their baby to have the best start in life that they possibly can. Knowing that there is a drug that may in their case provide significant remedial care to their situation with minimal side-effects is short of a miracle. Not having access to that treatment would be unconscionable. Without access to treatment, parents may have to make serious financial compromises to ensure that their child will get the treatment they need. Or in some cases, they may choose to not pursue the treatment at all, creating an unfair advantage for their child and increasing the social and financial burden of care on the health care system and in society as a whole.

A parent shared:

“We are very fortunate in Canada to have such a wide coverage in health care and affordable private insurance. We are most fortunate for the access we have to health care. Though the system isn't without flaws, as a Canadian we can rely on the expertise of many specialists and specialized centers regardless of our income or social status. It is of utmost importance that, when investigating possible treatment options for their children, parents are informed on all possible avenues and are able to discuss the risk associated with a medication or treatment with qualified medical professionals before electing a course of action. Cost should not be a factor in this decision making process when a child's life, well-being, or development is at play. We are fortunate enough that the type of treatment that was best for our daughter was covered as were all other associated costs. If there was any part of the treatment that was not covered, we would have had to make a very difficult decision which may have had an impact on her physical development by delaying her ability to sit up, roll, and even walk.

In my opinion, determining the very best course of action is undeniably the most important decision you can make for your child. The most benefit you can get while running as little risk as possible. For us, the most practical and most efficient medicine was not the best course of action. Though it seems to be the most popular choice, the risk simply outweighs the benefits of the medicine so we have opted for a different treatment. Cost was not even discussed once and for that I am thankful. The treatment that my daughter receives is at no cost to us but is significantly more costly than many other treatments. I cannot imagine the distress of knowing that this treatment exists and having to settle for another more common medication that would put her life at risk because of cost.”