CADTH

CADTH REIMBURSEMENT REVIEW

Patient Input

DINUTUXIMAB (Unituxin)

(United Therapeutics Corp.)

Indication: Neuroblastoma

CADTH received patient input from:
Neuroblastoma Canada, Canadian Organization for Rare Disorders (CORD) and Ontario Parents Advocating for Children with Cancer (OPACC) (Joint Submission)

December 10, 2020

CADTH

Patient Input Template for CADTH CDR and pCODR Programs

Name of the Drug and Indication	**Unituxin**
Name of the Patient Group	**Neuroblastoma Canada, Canadian Organization for Rare Disorders (CORD) and Ontario Parents Advocating for Children with Cancer (OPACC)**
Author of the Submission	[redacted]
Name of the Primary Contact for This Submission	[redacted]
Email	[redacted]
Telephone Number	[redacted]

1. About Your Patient Group

Neuroblastoma Canada

Neuroblastoma Canada is a national community-based organization dedicated to uniting Canadian neuroblastoma families. http://www.neuroblastoma.ca

Canadian Organization For Rare Disorders (CORD)

CORD is Canada's national network for organizations representing all those with rare disorders. CORD provides a strong common voice to advocate for health policy and a healthcare system that works for those with rare disorders. CORD works with governments, researchers, clinicians and industry to promote research, diagnosis, treatment and services for rare disorders in Canada. https://www.raredisorders.ca/

Ontario Parents Advocating for Children with Cancer (OPACC)

OPACC will be the leading voice and expert resource for families and organizations navigating the childhood cancer journey. http://www.opacc.org/

2. Information Gathering

Information was gathered through one survey, provided in English and jointly created by Ac2orn, CORD and OPACC. The survey was created and made available to respondents late October and over the whole month of November 2020. The online survey was posted using Survey Monkey and distributed by Ac2orn, CORD, and OPACC through various social media channels and directly by email. The survey asked for input from patients and families who were treated for high-risk (relapsed/refractory) neuroblastoma cancer, and who may or may not have had experience with Unituxin in combination with irinotecan and temozolomide for relapsed/refractory cancer. There were 20 responses to the survey. A total of 11 respondents had direct experience with Unituxin in combination with irinotecan and temozolomide (2 in frontline and 9 in relapse). Of the respondents who identified the location of their primary residence, 3 respondents were from Ontario and 1 from British Columbia. 5 respondents were from the United States of America and 2 respondents were international. The remainder (7 responses)

did not give a residence. The majority of survey respondents were parents of patients (17 responses), 1 respondent was the legal guardian and another was an immediate family member of the patient.

Five one-on-one interviews were also conducted with patients and families who had direct experience with Unituxin in combination with irinotecan and temozolomide. All interviews were conducted by telephone. One interview was conducted with a patient (female, aged 17) and her mother and another with a mother of a patient (female, aged 17), all from Ontario. A third interview was conducted with a mother of a patient (male, aged 10) from the United States of America. A fourth interview was conducted with father of a patient (male, aged 16) from British Columbia. The fifth interview was conducted mother and father of a patient (male, aged 3) from British Columbia.

3. Disease Experience

The age at time of diagnosis for the children in the survey and interviews was representative of the diagnosis age profile for high-risk neuroblastoma. Of those who reported an age of diagnosis (20 survey respondents and 5 interviews), the average age was 4 years old. 80% of patients were aged 5 or under at the time of diagnosis, with 36% at 2 years old. Other participants were 9 years old (3 patients), one at 10 years old, and one at 15 years old at the time of diagnosis, making up the remaining 20%. Almost all children were diagnosed with high-risk neuroblastoma, and only one was diagnosed with intermediate risk neuroblastoma.

Prior to diagnosis, many respondents identified that their child experienced issues of pain, persistent fevers, and uncharacteristic behaviours. Other issues of constipation, low energy levels, pain, weight loss or gain, and loss of appetite were common issues prior to diagnosis. Since most children were quite young at the age of diagnosis, they were unable to articulate what they were feeling and caregivers had to decipher concerning changes in their child.

For many respondents, it took time to finally reach the diagnosis of cancer, often requiring multiple visits to family doctors, emergency rooms and specialists. Respondents shared that symptoms were downplayed and classified as transitory or not serious (e.g., constipation). Four respondents stated that their child was initially diagnosed with juvenile arthritis, and that specialist identified the cancer through scans trying to locate the persistent joint and bone pain. When symptoms returned or persisted, caregivers advocated for their child until appropriate tests were ordered which ultimately identified the illness as neuroblastoma cancer. In a few cases, the diagnosis was made directly.

- A parent of a 2 year old patient said, "*My son was finally diagnosed with NB after I continually asked questions and brought my son back in to pediatrician. Saw a different pediatrician who felt mass and sent us to ER where X-ray confirmed a mass and we were admitted*."
- A parent to a 5 year old patient shared, "*She started with intermittent fevers and leg pain. Occasional stomach pain, fatigue, and loss of interest in playing. The fevers became more frequent over the course of 2 months until she ran a consistent 101 fever even on antipyretics. She stopped being able to walk more than a few steps and was experiencing constant leg pain. She was seen by infectious disease for 2 months, we asked and was told it wouldn't be cancer because it was too rare and because her bloodwork didn't show any sign of leukemia. Weekly blood tests only showed mild and then progressively worse anemia, negative for every pathogen she was tested for. When she completely stopped eating and drinking we were referred to hematology, as opposed to waiting 6 weeks to get into rheumatology. A bone marrow biopsy revealed 99% bone marrow involvement, she needed an immediate blood transfusion. Three days later we had confirmation that it was neuroblastoma, she was admitted to the hospital, and we watched as a tumor grew on her skull in a matter of hours*."
- A parent of a 2 year old patient said, "*He complained of pain in his leg and had a hard time walking. Also had fever. It took a couple of trips to the doctor, and on the second trip to the ER was admitted and then diagnosed*."

- A parent of a 2 year old patient shared, "*Child was never sick. Then one day he threw up. It felt unusual so we had it to the ER. In ER they wanted to discharge us thinking that this is just a typical transient sickness but I the father started to probe my son's stomach and hit a hard mass. I brought it to the attention of the doctor and we were admitted to oncology that same night*."

In many cases, respondents shared details about the escalation of symptoms until they reached severe levels before a diagnosis was finally made. It is not uncommon for neuroblastoma to masquerade as other common childhood conditions, and high-risk neuroblastoma being metastatic and advanced at the time of diagnosis.

4. Experiences With Currently Available Treatments

Experiences with Frontline Therapy:

For high-risk neuroblastoma, almost every type of treatment is utilized to address the cancer. Standard of care therapy for frontline includes multiple cycles of chemotherapy, surgery, mega-dose chemotherapy with stem cell transplant, radiation, and immunotherapy. This combination therapy was developed through consortium clinical trials, such as those conducted by the Children's Oncology Group (COG).

From the survey, of the 19 respondents who shared information about their child's frontline treatment, 68% experienced chemotherapy, 58% had radiation therapy, 63% had surgery, 53% had mega-dose chemotherapy, 9% had a stem cell transplant, 8% had immunotherapy or Unituxin, and 32% experienced maintenance therapy (Accutane, cis-retinoic acid). Two respondents stated that their child received Unituxin with irinotecan and temozolomide in frontline therapy and 3 respondents shared that their child received DFMO on the completion of frontline therapy. Of the 9 respondents who stated their child received immunotherapy, 8 shared that their child received chemotherapy, surgery, radiation and stem-cell transplant, which is the standard COG frontline treatment protocol. One respondent shared that their child also received MIBG therapy as part of their frontline treatment, which is a new introduction to the current COG phase 3 clinical trial for high risk neuroblastoma. One respondent noted that their child received Naxitamab, or 3F8, which is an immunotherapy similar to Unituxin.

Respondents were asked to share their child's experience with frontline therapy. Of the 12 respondents who provided comments, three shared that they felt their child's cancer responded well to frontline therapy, with no major complications. Three other respondents shared that frontline treatment was difficult but were able to manage through the expected complications. The remaining five respondents who provided details found various aspects of frontline treatment to be difficult and often overwhelming.

- A caregiver whose child was diagnosed at 9 years old shared, "*My daughter's experience with frontline therapy was difficult, she suffered severe nausea and diarrhea through every admission for chemotherapy. My daughter is neuroblastoma did not respond very well to front-line treatment we did not see much response until she reached immunotherapy*."
- A caregiver of a child who was diagnosed at 3 years old said, "*Frontline chemo was hard but we took it one day at a time and made it through. She got infections between every round and spent the majority of her time inpatient. Stem cell was tough but easier than expected for us. She engrafted quickly and spent just 5 weeks in hospital. Radiation was relatively easy she was tired and nauseous every 3 to 4 days but tolerated it well. Immunotherapy was awful for her as we had a difficult time staying ahead of the pain. By round 4 we had a good routine set to tolerate it as well as possible*."

Two interviewees shared the following:

- Said one dad, "*After two years of chemotherapy which was very difficult, he received surgery followed by radiation was really brutal because we had to travel to Calgary and stay there. He was 12 years old and missed his school and friends."*
- *A father of a 3 year old, "18 months of chemotherapy, 2 bone marrow transplants, then radiation and more radiation. It was horrendous for a three-year old. And none of it worked; he was refractory to all."*

Respondents also shared specific comments about their child's experience with Unituxin. Because many hospitals do not see high-risk neuroblastoma patients as frequently as other pediatric cancers, specialized treatments such as immunotherapy can be difficult to administer because every child has a different experience to the therapy. Each cycle for each child is a learning experience, as stated by two survey respondents. One said, "*Unituxin was difficult for my daughter, she was in a great deal of pain and suffered a few episodes of very low blood pressure. But once we added pre meds prior to starting immunotherapy things were much better and more tolerable*." If a hospital does not have a great deal of experience with Unituxin, the steep learning curve can be challenging, as one respondent shared, "*Our experience with Unituxin was very hard on our son, this was the first time our hospital had administer this medicine, gauging his pain and treating it was difficult, side effects after treatment were very hard*."

Overall, neutropenia, nausea, vomiting, hair loss, fatigue, and weight loss were the most significant side-effects faced in frontline therapies. Fevers, pain, neuropathic pain, and constipation were also challenging but manageable side-effects. Mobility challenges, infections, eye sight changes, and damage to organs were side-effects that were considered to have lower impact for most respondents; however, for one or two, they had extremely large impacts. Caregivers were asked to share their feelings on their child's quality of life. "Eating challenges" (46%), "changes in physical activity" (46%), "social development" (69%) and "educational development" (54%) all had large or extremely large impacts on the child's quality of life during frontline treatment. There were also significant changes in "mental health and overall happiness" (39%) for children experiencing treatment for high-risk neuroblastoma. In all categories at least one respondent answered that they experienced an "extremely large impact".

The family as a whole also experiences significant quality of life issues. Overall, respondents stated that they had a large or extremely large impact for all categories of "mental health and overall happiness" (62%) of the family, "parenting other children" (46%), "ability to participate in activities with family and friends" (77%), "ability to work" (85%), "ability to manage financial responsibilities" (69%), and "manage responsibilities at the home" (62%). In terms of the impact on the marriage of the caregivers, half responded that it had a small or medium impact and the other half responded that it had a large or extremely large impact.

- One caregiver of a 2 year old child noted, "*The trauma my son carries as a result of us having to hold him down for dressing changes and procedures negatively impacted his relationship with us, where there is trust issues that result in him trying to control everything all the time*."
- Another respondent shared, "*My daughter was unable to continue with gymnastics and horseback riding due to compression fractures in her spine from treatments of chemotherapy, still to this day she is no longer able to do gymnastics because of weakened spinal cord*."
- A caregiver of a 2 year old said, "*My son had tube feeds running at night, so one of us had to sleep in his bed with him for the entire duration of treatment. He puked a lot at night. My son had to relearn to walk, he was fearful of other children who looked at him funny with his feeding tube. His friends moved away while he was sick and because of his issues after treatment we were unable to make new ones, so he lost his social circle. He still struggles with eating, weight gain, social skills, trust, and control. He has no friends and is obsessed with technology like iPads because it was all he had for a long time. He is developmentally behind his peers by quite some margin due to delayed frontal cortex development. He can t manage being in crowds, in public, he has difficulty relating to people*."

The only category where there were "no impact" responses was in the "parenting of other children" (4 of the 13, or 31%).

Experiences with Relapsed/Refractory Therapy:

Five respondents shared that their child relapsed during frontline therapy.

- A caregiver of a 2 year old patient shared, "*He had a MIBG scan after surgery and five cycles of frontline treatment. We were told that while his condition had improved, he had not responded well enough to the chemotherapy to continue to bone marrow transplant. He was then put on a study ANBL 1221*."

- A caregiver of a 9 year old said, "*My daughter has progression during Frontline therapy, she has a neuroblastoma tumour grow just weeks after having her tumour removal surgery. Once my daughter completed Frontline therapy and was declared NED she remained NED for 3 years before relapsing*."
- A caregiver of a 3 year old boy with neuroblastoma shared, "*My son has relapsed 3 times - once during frontline treatment (technically progression after surgery) then 3.5 years from end of treatment and the again 3 years later. He has ATRX gene mutation*."

Other respondents shared that their child's relapse was found during routine follow-up scans, with some children relapsing multiple times. One respondent shared, "*Scans showed that after 4 1/2 years of being stable, that her NB had progressed*." Another respondent shared, "*Relapse. Not refractory. Clear for 1 1/2 years. Then again 2 years later then again 2 1/2 years later*." Two sets of parents reported their children had been refractory to all treatment. One parent reported, *"When the scans came back and showed the last round of chemo had done nothing, we decided it was time to just stop. It wasn't fair to [our son]. The oncologist had a hard time convincing us to give immune therapy a try."* According to another father whose 10-year-old son also did not respond to any of the traditional chemotherapy, surgery, and radiation, *"We asked about clinical trials but were told there was nothing available here. We researched the option of going to the states where there were experimental therapies. That's when the oncologist came back and said we were approved for compassionate access to immune therapy. That was our first break in two years."*

Patients received a variety of therapies that included chemotherapy (7), radiation (9), surgery (3), high dose chemotherapy (1), immunotherapy (3), maintenance therapy (1), Unituxin with irinotecan and temozolomide (9) and DFMO (2). Neutropenia (small to medium), fevers (small, 1 extremely large impact), nausea (medium, 1 extremely large impact), vomiting (medium to large), pain (large), neuropathic pain (large), constipation (small), hair loss (large, 3 extremely large impact), organ damage (small), hearing loss (mixed, 1 extremely large impact), eye sight changes (mixed), mobility changes (mixed, 2 extra large impact), infections (medium), weight loss (mixed, 3 extremely large impact), and fatigue (mixed, 2 extremely large impact).

Accessing Treatment:

For almost all of the respondents, accessing frontline treatment for high risk neuroblastoma was not an issue. Some respondents were very happy about the care that their child received. One caregiver shared, "*Our experience with our hospital team was very satisfying. We had a good relationship with our team and felt free to discuss issues and felt our voices were heard*."

5. Improved Outcomes

When a child's neuroblastoma relapses, the caregivers and care team work closely together to determine the best treatment pathway for the child based on previous therapies, co-morbidities, and many other health based determinants. Caregivers and patients must also weigh their own priorities to determine what therapies to access. All caregivers stated that they select a treatment with quality of life in mind and 82% stated that it is selected based on possible impact on the disease. Other factors are physician recommendation (36%), closeness to home (27%), treatment in the out-patient setting (27%) and religious considerations (8%).

When asked about trade-offs, one caregiver shared "*If my daughter relapsed we would do whatever we could to save her regardless of the risks. I could not live with myself if we did not try everything we could*." For the parents of children with refractory neuroblastoma, their intense desire was to find an effective treatment for their child. There was also frustration that more advanced or experimental therapies were not available to them, even as options. *"I can't say that we would have agreed to all of the experimental treatments that we were hearing about and we knew from other parents that there was no guarantee, but we felt we should at least have the chance."*

6. Experience With Drug Under Review

Accessing Immunotherapy During Relapse:

For relapsed therapy, there were more challenges accessing Unituxin with irinotecan and temozolomide for treatment. 4 respondents accessed immunotherapy through clinical trials, 2 through special access and 3 unknown (9 total). One caregiver shared, "*I fought very hard for this treatment because in my gut I knew it was the only treatment my daughter had favorable response to drink Frontline therapy. Our doctor wasn't completely convinced that this was the right decision to do as it had not been done yet for secondary relapse of neuroblastoma but he honoured my wishes and fought for the treatment and it worked again*." 3 respondents (27%) stated that it was difficult or extremely difficult to access immunotherapy and the remaining respondents (8, 73%) shared that it was normal or not difficult to access. 10 respondents were able to access immunotherapy at their home hospital, with only one having to travel for treatment within their state/province. For refractory patients, the option to access Unituxin with irinotecan and temozolomide was due to the efforts of their oncologist who made the request for compassionate access. *"We were considering something else when she came back and suggested the immunotherapy combination [with Unituxin] with maybe a 50-50 chance of success. We thought these were good odds."* Another parent said*, "We initially refused. Another 17 weeks seemed too much."*

Impact on Cancer:

Respondents were unsure as to the degree to which Unituxin, irinotecan and temozolomide impacted their child's cancer since it was too soon post therapy to be able to assess the long-term success of the treatment. One caregiver shared that "*It cleared residual disease in combination with the previous treatment with Naxitamab with irinotecan/temozolomide*." One caregiver noted that it even though her child's cancer has continued to progress through treatment, it may be at a slower rate because of the combination immunotherapy. Parents of both patients with refractory neuroblastoma patients reported their scans were clear, as soon as three months after the completion of the cycles and still in remission.

Side-Effects from the Combination Immunotherapy:

Overall, the majority of side-effects from the combination immunotherapy were manageable and comparable to those experienced in frontline therapy. Pain (manageable overall, 2 very serious side-effect), fever (manageable overall), nausea and vomiting (combination of serious and manageable, 1 very serious), allergic reaction (mixed, 1 very serious), breathing issues (manageable overall), headache (mixed, 2 very serious), low platelet count (mixed, 1 very serious), low red blood cell count (manageable to minor overall), low white blood cell count (manageable to minor overall), low or high blood pressure (serious), fluid retention (serious), dehydration (manageable), fatigue (manageable), vision changes (did not experience, 2 serious), sleepiness (manageable), allergic reaction to GM-CSF (4 very serious or serious, others did not experience), Reaction to IL-2 (2 very serious, others did not experience), diarrhea (manageable, 2 very serious) and constipation (manageable to minor). The following were some comments provided by caregivers:

- "*The chemo causes issues with gastric system so had to be stopped*."
- "*Once pre-meds were figured out and nausea diarrhea vomiting and pain were under control this treatment was extremely tolerable*."
- "*It was manageable - harder than outpatient Naxitamab with irinotecan and temozolomide. Her pain was well-controlled but the morphine made her vomit and created a full-body rash with intense itching which did not resolve completely with antihistamines. We switched to a dilaudid drip and those symptoms resolved. She showed signs of withdrawal for several days after the pain medication was stopped. She received neurontin prior and after treatment, so did not have issues with lingering neuropathic pain. She developed a fever in response to the treatment and had minor issues with constipation while on the drip for pain. It resolved once the medication stopped. She did not need prophylactic antibiotics for irinotecan, instead using probiotics which prevented diarrhea. Her main symptoms were vomiting and fatigue. She suffered some hair loss from the chemo as well as fatigue and mild weight loss after treatment*."

- "*My daughter had fevers, pain, neuropathy, blurred vision, diarrhea, and itchy feet. Her hair did grow back and she wasn't neutropenic and didn't have any organ damage. She did not get IL-2*."
- "*The first cycle was the hardest due to hospital protocols on getting to the right pain dosage. Once we got to the right level, pain was manageable but hard to see child so "doped up" all day. He had periodic allergic reactions but managed this by pausing/slowing infusion*."
- One respondent felt that treatment with Unituxin, irinotecan and temozolomide was not the right therapy for her daughter and if she had a different therapy, like MIBG therapy, she would not have died.

Caregivers noted that it took time to figure out how to manage the side-effects from the immunotherapy and chemotherapy combination. However, they were able to figure out the right combination of medications to help to help their child and ease the side-effect burden:

- "*First round is hard but once you have the pain under control it's fairly smooth sailing. Beware of fluid retention and diarrhea causing dehydration*."
- "*Stay on top the pain, every cycle kids react differently*."
- "*Getting in front of the symptoms is much easier than trying to catch up from behind them. Advocate for your children ask questions keep trying different pre-meds so that your child is as comfortable as possible during their treatment*."
- "*It is a very effective treatment. The standard supportive medications do need to be adjusted for the specific patient, so the first few days can be rough. Pre-treatment with gabapentin (neurontin) for neuropathic pain, with antiemitics, and pro-biotics (for irinotecan induced diarrhea) made a big difference in controlling side-effects*."

Comparison to Previous Therapies:

In an interview with a caregiver, she shared that her daughter did not have a great response to any of the chemotherapy in frontline treatment and that immunotherapy was the only treatment that drastically addressed the disease for two different relapses, resulting in complete responses. She felt that this was "*really tailored and really works*". She also said that going through this treatment was "*worth it and with every crap situation, it is worth it and would do it again if needed*." In a different interview with a caregiver, she shared that when her son relapsed during frontline therapy, and they were able to access Unituxin with irinotecan and temozolomide, the response was "miraculous", leaving her son's oncologist stunned. She felt that the "*quality of life was way better than the harder chemotherapies and very effective overall*." She felt that stem-cell transplant "*was hands down the worst*" and that "*all of the long term side-effects are because of transplant*" (e.g., compression fractures, growth issues, etc.). She did not feel that there were these same long-term side-effects from the immunotherapy and chemotherapy combination. In between treatments, her son had good energy, he went to school and felt good overall.

One parent whose son had been refractory to previous treatments felt that Unituxin with irinotecan and temozolomide should be the first-line therapy. Like others, chemotherapy was not only harsh during treatment but had long-term effects. The short-term side-effects of combination immunotherapy are worth the long-term benefits. Two caregivers noted that recovery from Unituxin with irinotecan and temozolomide is different from traditional therapies in terms of the quality of life in between treatment cycles, unlike traditional therapies.

- "*It seems overwhelming treatment to get your head around but it's really effective in treating disease, doesn't have long term side effects like chemo and offers good quality of life in between cycles*."
- "*This treatment provides better quality of life between treatments. The side effects are unpredictable though*."

Caregivers felt that treatment with Unituxin, irinotecan and temozolomide did not come with the long-term side-effects of traditional therapies such as stem cell transplant, harsher chemotherapies, and radiation.

- "*My daughter does not suffer any long-term side effects of this treatment*."
- "*Unituxin with irinotecan and temozolomide made her feel sicker for longer than Naxitamab with irinotecan and temozolomide. But it was not any worse than side-effects from frontline chemotherapy,*

and less severe than side-effects from cisplatin and etoposide chemo rounds. Also, there were no long term side-effects, like the organ damage often suffered from transplant."

- "*I think unituxin IT combo changed trajectory of our journey with Neuroblastoma - we finally found treatment that worked, allowed better quality of life while on it and caused fewer long term issues*."
- "*The side-effects were not long term (unlike hearing loss and organ damage from chemo) and there were options to manage them. Her team worked at finding the best supportive medications for her. She did not get neutropenic which is very comforting given the risk of serious or fatal infections with regular chemo. And the treatment worked well, clearing soft-tissue disease. We would do almost anything to save her life, it's not a pleasant treatment but it's worth it to do something difficult in order to see her grow up, and without this treatment the OS for relapsed neuroblastoma is abysmal*."

One caregiver felt that her child had a specific mutation that resulted in immunotherapy causing a "florid relapse" and commented that children with certain cancer mutations should not receive this therapy.

Overall Feelings Toward Unituxin

Overall, parents were willing to tolerate the access challenges and the side-effects associated with Unituxin, especially if this treatment could address the disease burden, help to deter relapse, and potentially be life-saving. For the most part, respondents noted that the side effects were temporary, and although they were challenging at the time, they could be managed by supportive medications. A caregiver in an interview said that she is "*willing to accept that risks. It is an evolution. I want there to be data but if there is something promising in the long term, I will take it. It is all relative to your other choices." She feels that "immunotherapy is a path to less toxic treatments*", "*ground-breaking*" and that "*relapsed neuroblastoma is no longer a death sentence*." In an interview with a patient and her mother, the patient said that "*pain is an acceptable side-effect*" and that the immunotherapy/chemotherapy combination "*gave me 33 months that I might not have had."* She said *"none of the treatments have been pleasant but it is necessary. I have friends who have passed away who haven't had access to treatment. We need more treatments to be cancer free*." This patient was diagnosed with high-risk neuroblastoma at 5 years old, and has been fighting the cancer for almost 13 years.

7. Anything Else?

The treatment for high-risk neuroblastoma cancer is long, intensive, and full of challenges since almost every type of treatment is attempted to address the disease – chemotherapy, surgery, mega-dose chemotherapy with stem cell transplant, radiation, immunotherapy and maintenance therapy,. For relapsed neuroblastoma, the pathway is less clear; however, therapies like Unituxin with irinotecan and temozolomide are changing the stories for children. The once held belief that a neuroblastoma relapse is uncurable is changing quickly, and because of the chemotherapy/immunotherapy combination.

- "*I strongly believe that chemotherapy in combination with immunotherapy is what cured my daughter's neuroblastoma. My daughter was a unique case she did not respond well to Frontline therapy she had progression during Frontline therapy, she went into bone marrow transplant with 50% of her disease. I am a strong and firm believer that irinotecan and temozolomide in combination with immunotherapy is what cured my daughter's cancer. And if she were to suffer another relapse that would be her third relapse I would again choose to do this therapy*."
- "*For us, immunotherapy was the easiest part of the whole frontline treatment, and was most effective at cleaning up residual disease. We didn t experience too many issues during immunotherapy and it was nice to be predictable on when we would get to go home, unlike with chemo where we had to wait for puking to stop which was always an unknown*."
- "*High dose chemo and stem cell transplant should be re-evaluated as a standard for all patients, especially Stage 3 high risk, given that patients still relapse and can suffer severe long term side-effects or death. Immunotherapy with low dose chemo is an excellent and effective treatment for relapsed neuroblastoma and will possibly be even more effective if it is preceded by regular chemo, radiation / surgery as necessary*."
- "*I wish we were a lot further in developing drugs for this cancer*."

Appendix: Patient Group Conflict of Interest Declaration

To maintain the objectivity and credibility of the CADTH CDR and pCODR programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest. This Patient Group Conflict of Interest Declaration is required for participation. Declarations made do not negate or preclude the use of the patient group input. CADTH may contact your group with further questions, as needed.

1. Did you receive help from outside your patient group to complete this submission? If yes, please detail the help and who provided it.

Childhood Cancer Canada provided Neuroblastoma Canada with the use of their Survey Monkey account to administer the English survey. They only provided access to Survey Monkey and Neuroblastoma Canada did all of the English survey set-up and analysis.

2. Did you receive help from outside your patient group to collect or analyze data used in this submission? If yes, please detail the help and who provided it.

No

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000

I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

Name: Antonia Palmer
Position: Founder
Patient Group: Neuroblastoma Canada
Date:

Name: Durhane Wong-Rieger
Position: President and CEO
Patient Group: Canadian Organization for Rare Disorders (CORD)
Date:

Name: Sarai Porretta
Position: Administrative Coordinator
Patient Group: OPACC
Date: