Canada's Drug Agency
L'Agence des médicaments du Canada

CDA-AMC REIMBURSEMENT REVIEW

Patient and Clinician Group Input

vutrisiran (Amvuttra)

(**Alnylam Canada ULC**)

Indication: Amvuttra (vutrisiran) is indicated for the treatment of wild-type or hereditary transthyretin-amyloidosis in adult patients with cardiomyopathy.

July 18 , 2025

This document compiles the input submitted by patient groups and clinician groups for the file under review. The information is used by CDA-AMC in all phases of the review, including the appraisal of evidence and interpretation of the results. The input submitted for each review is also included in the briefing materials that are sent to expert committee members prior to committee meetings. **If your group has submitted input that is not reflected within this document, please contact Formulary-Support@cda-amc.ca.**

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Patient Input Template for CADTH Reimbursement Reviews

Name of Drug: *AMVUTTRA*
Indications: Amvuttra (vutrisiran) is indicated for the treatment of wild-type or hereditary transthyretin-amyloidosis in adult patients with cardiomyopathy
Name of Patient Group: Transthyretin Amyloidosis Canada (TAC), previously known as Hereditary Amyloidosis Canada (HAC)
Author of Submission: Anne Marie Carr, President and Founder, Transthyretin Amyloidosis Canada

1. About Your Patient Group

Transthyretin Amyloidosis Canada is a not-for-profit organization that was established in 2019 to support individuals living with all forms of transthyretin amyloidosis, including hereditary (hATTR) and wild-type (wt-ATTR) amyloidosis, through community support, research, and education. TAC was inspired by the journey of our founder, Anne Marie Carr, who is living with hATTR amyloidosis. At the time of her diagnosis, Anne Marie realized the lack of community, support groups, information and resources available to her and her family, and thus began TAC.

Transthyretin Amyloidosis Canada is a patient-led advocacy group supporting individuals and families affected by hereditary and wild-type ATTR amyloidosis. We rely on volunteer efforts and limited funding. Our submissions have highlighted the high morbidity of untreated ATTR and the need for timely access to therapies. Challenges include gathering robust patient data due to small population size and lack of staff dedicated to reimbursement processes.

Website – www.madhattr.ca

2. Information Gathering

We engaged with Canadian patients and caregivers (2024) from both a qualitative and quantitative information gathering perspective. From a quantitative standpoint, TAC issued a 23-question online survey which was completed by 30 patients and caregivers from different provinces, including Ontario, Quebec, British Columbia, Alberta, Manitoba and Nova Scotia. From a quantitative perspective, TAC held 12 individual interviews with patients, based off a 25-question questionnaire. Each interview lasted between 45 to 60 minutes in length and the respondents were asked questions pertaining to their pre-diagnosis odyssey, duration of illness, hereditary and family history and experience with different therapies. Additionally, TAC held a 2-hour roundtable discussion with patients and caregivers from across Canada. The main topics of discussion during the roundtable included health literacy of therapies for hATTR, shared-decision making / patient choice and tools, resources and support for patients and caregivers living with hATTR. In total, 51 patients and

caregivers provided their input in either a qualitative or quantitative fashion. Because of the nature of transthyretin amyloidosis and the typical profile of patients diagnosed with the illness, all respondents were over the age of 65, with a near-even split between male (n=23) and female (n=28) patients.

3. Disease Experience

As the founder of TAC, I created this organization as a means to assist Canadians patients like myself who had no support or information upon diagnosis. My journey and experience in living with transthyretin amyloidosis is, unfortunately, not anomalous, but instead a pattern of doctor's visits, tests, hardship, pain, suffering and frustration.

I first noticed neuropathy symptoms and initially dismissed them, attributing them to time spent at my keyboard or simply carpal tunnel syndrome. I developed cardiac symptoms within a few years of noticing my neuropathy.

These symptoms eventually developed into heart failure, including tightness, palpitations, lightheadedness, shortness of breath, low energy, trouble sleeping, tiredness, low blood pressure, autonomic dysfunction, fluid retention and feelings of being full all the time despite not having eaten much. I have a heart murmur, and my echocardiograms sometimes vary drastically. My ejection fraction can vary from 20%-33%. My cardiac walls are often thicker.

I have trouble eating, often choke on food, my liver is distended, and I experience gastrointestinal symptoms, particularly diarrhea. At times, I have lost control of my bowels.

One leg often trails behind the other when climbing stairs, leading to a fall often.

I had a cardiac arrest in 2017, and had a dual pacemaker and defibrillator implanted.

As ATTR is a progressive illness, my symptoms are progressing and will not ever return to normal. In addition to the symptoms listed above, I have difficulty sleeping and am often fatigued during the day. I have also noticed my energy is decreasing over time and I am not able to do the things I was able to do even a few years ago. I struggle to walk, have numbness & foot pain, which makes it extremely difficult to navigate stairs or even regular walking. When I do attempt any walking, it requires rest often and for an extended period.

Due to my ATTR, I do not visit easily with friends or family outside of our home - it takes a significant amount of time to get ready and thoughtful planning. I will not have my granddaughter visit when I am home alone.

My neuropathy is also getting worse; I have increasing difficulty with fine motor skills. I constantly drop things and struggle to pick them up. I get severe cramps from my elbows to my wrists, and my

fingers often lock. I struggle to write or type. One of my legs often trails behind the other, this results in balance issues causing me to fall.

Overall, there is not a single aspect of my life – physical, financial or emotional – that has not been affected by amyloidosis. As mentioned previously, this is unfortunately the norm for many patients, especially those who are inadequately treated.

4. Experiences With Currently Available Treatments

There are currently 2 (two) treatments available to treat the different forms of cardiac transthyretin amyloidosis. These treatments include:

TAFAMIDIS, VYNDAQEL

Tafamidis is used in the treatment of adult patients, with cardiomyopathy due to transthyretin-mediated amyloidosis, wild-type or hereditary, to reduce cardiovascular mortality and cardiovascular-related hospitalization.

It is characterized by the deposition of amyloid fibrils throughout the body including in nervous tissue and can have a devastating impact on patients' quality of life.

AMVUTTRA

AMVUTTRA (Vutrisiran)is a prescription medicine that is indicated for the treatment of wild-type or hereditary transthyretin-amyloidosis in adult patients with cardiomyopathy. AMVUTTRA is used by adults only.
It is characterized by the deposition of amyloid fibrils throughout the body including in nervous tissue and can have a devastating impact on patients' quality of life.

AMVUTTRA is administered once every 3 months by subcutaneous injection. This is administered into the fatty layer below the skin. Common injection sites include the back of the upper arms, front outer area of thighs, and the top of the buttocks. These areas offer a good layer of subcutaneous fat for injection and are easily accessible. AMVUTTRA targets the cardiac hATTR amyloidosis at its source by reducing production of the Transthyretin protein.

Both therapies are approved by Health Canada and have varying degrees of public reimbursement in different provinces. Both therapies have their benefits and also their side effects.The costs of medications are also prohibitive, and I could never pay for these personally. I am no longer able to work due to this illness, which makes the additional costs of treatment even that much harder to bear.

5. Improved Outcomes

Currently available therapies to treat hATTR are great and may be preferred and in fact needed by some. However, given the age of patients affected by hATTR, along with the already significant dependency challenges brought about by the disease, AMVUTTRA does have some unique advantages that can lead to meaningfully improved outcomes for some patients. These advantages may include:

- Mode of Administration and Convenience - 1 x 3 months
- According to patients and caregivers surveyed in TAC's qualitative analysis, 83.3% of respondents (25/30) felt travelling for medical appointments and/or treatment infusions was highly or somewhat invasive. Additionally, 80.0% of respondents (24/30) felt home administration was an important attribute for a therapy. Since this is 1 x 3 months makes this an easy decision.
- AMVUTTRA is given once every 3 months, thereby further alleviating the burden of treatment on our already overburdened health care system.

- As a core pillar of TAC's patient support efforts, TAC's Founder, Anne Marie Carr, has held individual non-therapeutic discussions with hundreds of hATTR and wt-TTR patients since its inception. Empirically, the overwhelming majority of patients speak about the fear of amyloidosis and how it will impact their Quality of Life. In particular, patients are concerned about their ability to manage amyloidosis, including the continuous medical visits and the burdensome medical regimens. A therapy that is administered once every 3-months has the ability to assuage fears and greatly reduce stress and anxiety for patients.

- As a ubiquitous disease, the location of TTR patients is not isolated to urban centres. As such, patients who live in rural, remote areas in Canada may have challenges in accessing therapies that require continuous visits to their clinic. A therapy that is administered once every 3-months has the ability to balance health equity for those patients who would otherwise not have access to medical intervention, as they do not have the financial means to travel far distances for sustained periods. In Canada, health equity should be an important consideration for rural and marginalized communities.

- Analysis Presented at the Heart Failure 2025 Congress Supports Primary Findings, Highlighting Impact of AMVUTTRA, which Delivers Rapid Knockdown of Transthyretin –
- Additional 42-Month Data Reinforced AMVUTTRA Impact on the Risk of All-Cause Mortality and further Underscore the Effect on Cardiovascular Mortality –
- Vutrisiran (AMVUTTRA) Demonstrated Substantial Benefit Across a Range of Cardiovascular Events, Notably Reducing Urgent Heart Failure Visits by **46%** in the Overall Patient Population During the Double-Blind Period, huge reduction in health care costs

- **Quality of Life** – In a multi-system disease such as hATTR, autonomy goes beyond the necessity to attend clinical and infusion appointments. According to the qualitative interviews, loss of autonomy is one of the single greatest quality of life losses felt by patients and caregivers alike. This loss of autonomy permeates through every activity and has an immeasurable impact on many facets of a patient's life including:
    - Ability to maintain a career – 66.7% of respondents (20/30) from the patient survey have had to either stop working, retire early or scale back to less than 15 hours per week due to hATTR;
    - Travel – 80% of respondents (24/30) feel hATTR has a significant or somewhat significant impact on their ability to travel
    - Social life – in all qualitative interviews, patients feel hATTR has had a significant impact on their ability to maintain a social life. Patients relayed that their psyche and whole identity is engrossed in hATTR & wtATTR and this is partially due to the need to constantly be planning their whole lives around medical and infusion appointments.

- **Treatment Options** – It is well-documented that not every therapy works equally as well in every patient. As such, allowing patients and physicians access to different treatment options, particularly in a rare- multi-system disease such as hATTR, is paramount in ensuring no patient is left behind. Given that AMVUTTRA is only administered once every 3 months further adds to its importance as a unique treatment option for patients.
- **Hospital admissions** may be decreased significantly with patients on correct therapy, which decreases the pharmacoeconomic burden of illness related to TTR-amyloidosis. At a time where hospitals remain over-burdened due to the pandemic, keeping patients who are typically elderly and already have frail immune systems, away from hospital centres is a key impetus for maintaining optimal health.

6. Experience With Drug Under Review

Due to privacy laws protecting patients' identities in Canada, we were unable to obtain any patient input directly from Canadians who participated in the AMVUTTRA clinical trials. However, all respondents from the qualitative interviews, as well as feedback obtained during the 2-hour roundtable meeting, spoke to the void of AMVUTTRA can satiate as the only therapy that can be administered once every 3 months subcutaneous injection in your upper arm, thigh, or abdomen

It is important to remember that hATTR is a disease highly characterized by its psychological impact on patients, in addition to the vast physical co-morbidities. This psychological impact is primarily associated with a lack of autonomy and a total loss of independence. A therapy that has the ability to remove the shackles of dependence on infusion centres, can be conveniently stowed and carried with a patient anywhere they go and can be administered simply and easily goes a long way in helping return a measure of control in their lives.

Overall, there are many ways in which the symptoms and co-morbidities of ATTR can impact a patient's life. Current therapeutic intervention is extremely important in limiting the symptoms, progression and co-morbidities of ATTR, but are also often associated with inconveniences that patients suffer through in order to experience the therapeutic benefits. With AMVUTTRA, patients can attain the therapeutic benefit without the limiting inconveniences.

8. Anything Else?

Transthyretin amyloidosis is a disease characterized by high phenotype variability, primarily due to the fact that amyloid deposits can be found in almost every part of the body. This, of course, leads to expressivity that is different in almost every patient; patients can demonstrate an infinite combination of symptoms including neurological, cardiac, gastrointestinal, ophthalmologic, fatigue, urologic, muscular, and so on. In the quantitative patient questionnaire, patients identified 18 different symptoms they experience on a regular basis, which is consistent with a multi-system disease like ATTR. As such, due to this phenotype variability and expressivity, it is paramount to have as many therapies approved and accessible for patients, in order to ensure no patient is left without appropriate treatment.

Appendix: Patient Group Conflict of Interest Declaration

To maintain the objectivity and credibility of the CADTH reimbursement review process, 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.

   No

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 2 years AND who may have direct or indirect interest in the drug under review.

Table 1: Financial Disclosures

Check Appropriate Dollar Range With an X. Add additional rows if necessary.

Company	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Astra Zeneca				X
Pfizer				X
Bridge Bio				X
Alnylam				X
SOBI		X		
Johnson & Johnson			X	
Intellia		X		

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: Anne Marie Carr
Position: Founder & Executive Director
Patient Group: Transthyretin Amyloidosis Canada
Date: June 28 2025