Vutrisiran: Mechanism of Action

The following information is provided in response to your unsolicited inquiry. It is intended to provide you with a review of the available scientific literature and to assist you in forming your own conclusions in order to make healthcare decisions. This document is not for further dissemination or publication without authorization.

The full Prescribing Information for AMVUTTRA® (vutrisiran) is provided here. Alnylam Pharmaceuticals does not recommend the use of its products in any manner that is inconsistent with the approved Prescribing Information. This resource may contain information that is not in the approved Prescribing Information.

If you are seeking additional scientific information related to Alnylam medicines, you may visit the Alnylam US Medical Affairs website at RNAiScience.com.

SUMMARY

- Vutrisiran is a double-stranded siRNA-GalNAc conjugate that causes degradation of variant and wild-type TTR mRNA through RNAi, which results in a reduction of serum TTR protein and TTR protein deposits in tissues.[1]

INDEX

RNA INTERFERENCE

RNAi is a natural endogenous intracellular catalytic mechanism for the control of gene expression that utilizes siRNAs loaded onto the cytoplasmic RISC to cleave and degrade specific mRNA targets through AGO2, the catalytic component of the RISC. This results in reduced production of the target protein.[2–4]

AMVUTTRA PRESCRIBING INFORMATION – RELEVANT CONTENT

The **DESCRIPTION** section provides the following information[1]:

AMVUTTRA contains vutrisiran, a chemically modified double-stranded small interfering ribonucleic acid (siRNA) that targets mutant and wild-type transthyretin (TTR) messenger RNA (mRNA) and is covalently linked to a ligand containing three N-acetylgalactosamine (GalNAc) residues to enable delivery of the siRNA to hepatocytes.

The **CLINICAL PHARMACOLOGY** section provides the following information[1]:

Mechanism of Action

Vutrisiran is a double-stranded siRNA-GalNAc conjugate that causes degradation of mutant and wild-type TTR mRNA through RNA interference, which results in a reduction of serum TTR protein and TTR protein deposits in tissues.

ABBREVIATIONS

AGO2 = argonaute 2; GalNAc = N-acetylgalactosamine; mRNA = messenger RNA; RNAi = RNA interference; RISC = RNA-induced silencing complex; siRNA = small interfering ribonucleic acid; TTR = transthyretin.

Updated 7 July 2025

REFERENCES

1. AMVUTTRA (vutrisiran) Prescribing Information. Cambridge, MA: Alnylam Pharmaceuticals, Inc.
2. Elbashir SM, Harborth J, Lendeckel W, Yalcin A, Weber K, Tuschl T. Duplexes of 21-nucleotide RNAs mediate RNA interference in cultured mammalian cells. *Nature*. 2001;411(6836):494-498. doi:10.1038/35078107
3. Fire A, Xu S, Montgomery MK, Kostas SA, Driver SE, Mello CC. Potent and specific genetic interference by double-stranded RNA in Caenorhabditis elegans. *Nature*. 1998;391(6669):806-811. doi:10.1038/35888
4. Agrawal N, Dasaradhi PVN, Mohmmed A, Malhotra P, Bhatnagar RK, Mukherjee SK. RNA interference: Biology, mechanism, and applications. *Microbiol Mol Biol Rev*. 2003;67(4):657-685. doi:10.1128/MMBR.67.4.657-685.2003