

Vutrisiran: Use With mRNA COVID-19 Vaccines

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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

- Per the US Prescribing Information, clinical drug-drug interaction studies have not been conducted and there are no known contraindications to vutrisiran.¹
- For additional information about the currently available mRNA COVID-19 vaccines, including efficacy, safety, or drug interactions, please contact the respective manufacturers of the mRNA COVID-19 vaccines.
- The decision to administer mRNA COVID-19 vaccines in patients receiving vutrisiran is at the clinical discretion of the healthcare professional.

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MECHANISM OF ACTION

RNAi Therapeutics

RNAi therapeutics utilize a natural endogenous intracellular catalytic mechanism that potentially enables the specific and potent silencing of any gene by targeting mRNA for degradation, hence reducing the expression of proteins and their function in disease.^{2,3}

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. It is delivered to and primarily acts in the liver.¹

mRNA COVID-19 Vaccines

mRNA COVID-19 vaccines use mRNA corresponding to the target viral antigen. Following an intramuscular injection, the mRNA is expressed in muscle cells and cells of the immune system. This expression drives an immune response to the target viral antigen via a neutralizing antibody and cellular immune response which may contribute to protection against COVID-19 disease.⁴

DRUG INTERACTION/CROSS REACTIVITY

There are no clinical data currently available on the co-administration of vutrisiran, an RNAi therapeutic, and an mRNA vaccine. Drug-vaccine interaction studies have not been formally conducted, and there is no clear biological basis that suggests cross-reactivity between vutrisiran and mRNA vaccines for the following reasons:

- Vutrisiran is delivered to the liver following subcutaneous administration, whereas mRNA vaccines are injected into muscle, and the mRNA is expressed in muscle cells and cells of the immune system.^{1,4-6}
- RNAi therapeutics are specific to their intended target mRNA.^{2,3} Due to the lack of any significant sequence homology between TTR mRNA targeted by vutrisiran and the SARS-CoV-2 spike antigen mRNA present in the COVID-19 mRNA vaccines, it is unlikely that vutrisiran could target this sequence.⁴⁻⁶
- The protective antibodies generated by the vaccine directed towards the SARS-CoV-2 spike antigen are not likely to cross-react with vutrisiran because of the structural dissimilarity of proteins and small mRNA molecules.^{1,5,6}

AMVUTTRA PRESCRIBING INFORMATION – RELEVANT CONTENT

The **CONTRAINDICATIONS** section provides the following information¹:

None.

The **CLINICAL PHARMACOLOGY** section provides the following information¹:

Drug Interaction Studies

No clinical drug-drug interaction studies have been performed with vutrisiran. In vitro studies suggest that vutrisiran is not a substrate or inhibitor of cytochrome P450 enzymes. Vutrisiran is not expected to cause drug-drug interactions by inducing CYP enzymes or modulating the activities of drug transporters.

ABBREVIATIONS

GalNAc = N-acetylgalactosamine; mRNA = messenger ribonucleic acid; RNAi = ribonucleic acid interference; siRNA = small interfering ribonucleic acid; TTR = transthyretin.

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REFERENCES

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