

Patisiran: Mechanism of Action

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SUMMARY

- 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.¹⁻³
- Patisiran is a double-stranded siRNA, formulated as a lipid complex for delivery to hepatocytes. It specifically binds to a genetically conserved sequence in the 3' UTR of mutant and wild-type TTR mRNA. Patisiran 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.⁴

ABBREVIATIONS

3'UTR = 3' untranslated region; AGO2 = argonaute RISC catalytic component 2; mRNA = messenger RNA; RISC = RNA-induced silencing complex; RNA = ribonucleic acid; RNAi = RNA interference; siRNA = small interfering ribonucleic acid; TTR = transthyretin.

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