

# I421= — WFS1 Molecular Atlas Card

**Variant type:** Synonymous (silent)

**Codon:** position 421 (Isoleucine, I) — amino acid unchanged

**Domain context:** Transmembrane helix 4

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## SCHEMA CATEGORY: SILENT — SILENT — NO AMINO-ACID CHANGE

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No amino-acid change (I421 is unchanged): the codon is altered but the protein sequence is identical to wild-type. No structural, stability or AlphaMissense effect applies. Synonymous variants are typically benign unless they affect splicing or regulatory elements; this one is not adjacent to an exon boundary.

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## CLINICAL EVIDENCE

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- **Classification:** Conflicting classifications of pathogenicity
- **Review status:** criteria provided, conflicting classifications
- **Associated conditions:** WFS1-Related Spectrum Disorders; Wolfram syndrome 1; Autosomal dominant nonsyndromic hearing loss 6
- **cDNA change:** c.1263C>T
- **ClinVar accession:** VCV000761794
- **Last evaluated:** 2024/10/16 00:00
- **Submissions:** 1

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*Card generated by wolfram-atlas-batch (synonymous pipeline) on 2026-06-08T02:53:12.799085Z.*

*WFS1: UniProt O76024, AlphaFold v6. Synonymous variants carry no protein-structural effect.*