

# I643= — WFS1 Molecular Atlas Card

**Variant type:** Synonymous (silent)

**Codon:** position 643 (Isoleucine, I) — amino acid unchanged

**Domain context:** C-terminal ER-luminal (calcium binding, calmodulin, chaperone)

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

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No amino-acid change (I643 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:** Benign/Likely benign
- **Review status:** criteria provided, multiple submitters, no conflicts
- **Associated conditions:** Wolfram syndrome 1; Cataract 41; Wolfram-like syndrome; Autosomal dominant nonsyndromic hearing loss 6; Type 2 diabetes mellitus
- **cDNA change:** c.1929C>T
- **ClinVar accession:** VCV000386434
- **Last evaluated:** 2025/10/29 00:00
- **Submissions:** 1

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Card generated by *wolfram-atlas-batch* (synonymous pipeline) on 2026-06-08T02:55:22.336002Z.

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