

Variant: *NM_000531.6(OTC):c.42del (p.Phe14fs)*

Version: 1.1

CA224593 [↗](#)

97194 (ClinVar) [↗](#)

Gene: OTC ([HGNC:5009](#))

Condition: ornithine carbamoyltransferase deficiency ([MONDO:0010703](#))

Inheritance Mode: X-linked inheritance

UUID: 9d6f02c6-831e-44b8-9349-2a7fc5e88e20

Approved on: 2026/5/19

Published on: 2026/9/10

HGVS expressions

NM_000531.6:c.42del

NM_000531.6(OTC):c.42del (p.Phe14fs)

NC_000023.11:g.38352738del

CM000685.2:g.38352738del

NC_000023.10:g.38211991del

CM000685.1:g.38211991del

NC_000023.9:g.38096935del

NG_008471.1:g.5256del

ENST00000039007.5:c.42del

ENST000000643344.1:c.42del

ENST00000039007.4:c.42del

ENST000000465127.1:c.172-313383del

ENST000000488812.1:n.134del

NM_000531.5:c.42del

Pathogenic

Met criteria codes **3**

PP4_Moderate

PM2_Supporting

PVS1

Not Met criteria codes **2**

BA1

BS1

Evidence Links **0**

Expert Panel

Urea Cycle Disorders VCEP [↗](#)

Criteria Specification Information

[↗](#) **Criteria Specification:** ClinGen Urea Cycle Disorders
Expert Panel Specifications to the ACMG/AMP Variant
Interpretation Guidelines for OTC Version 1.0

[↗](#) **Criteria Specification Approval History**

[↗](#) **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

Urea Cycle Disorders VCEP

The NM_000531.6:c.42del (p.Phe14LeufsTer24) variant in OTC is a frameshift variant predicted to cause a premature stop codon in biologically relevant exon 1/10 leading to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1; GeneReviews). At least one heterozygous female individual with this variant displayed elevated ammonia, low/normal citrulline and elevated urine orotic acid, which is highly specific for Ornithine Transcarbamylase (PP4_Moderate, PMID:14976564). This

variant is absent from gnomAD v41.0 (PM2_Supporting). In summary, this variant meets the criteria to be classified as Pathogenic for X-linked ornithine carbamoyltransferase deficiency. ACMG/AMP criteria met, as specified by the ClinGen Urea Cycle Disorders VCEP (OTC specifications version 1.0.0): PVS1, PP4_Moderate, PM2_Supporting

Met criteria codes

PP4_Moderate			At least one heterozygous female individual with this variant displayed elevated ammonia, low/normal citrulline and elevated urine orotic acid, which is highly specific for Ornithine Transcarbamilase (PP4_Moderate, PMID:14976564).
PM2_Supporting			This variant is absent in gnomAD v4.1.0 (PM2_Supporting).
PVS1			The NM_000531.6:c.42del (p.Phe14LeufsTer24) variant in OTC is a frameshift variant predicted to cause a premature stop codon in biologically relevant exon 1/10 leading to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1)

Not Met criteria codes

BA1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Curation History



 

 

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