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Variant: NM_000277.3(PAH):c.1076C>G (p.Ser359Ter)

Version: 1.0

CA229330

626 (ClinVar)

Gene: PAH (HGNC:5053)
Condition: phenylketonuria (MONDO:0009861)
Inheritance Mode: Autosomal recessive inheritance
UUID: 66e267b0-cf6d-463d-9f0e-6510e335ebb6
Approved on: 2020/6/26
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HGVS expressions

NM_000277.3(PAH):c.1076C>G (p.Ser359Ter)
NM_000277.3:c.1076C>G
NC_000012.12:g.102843769G>C
CM000674.2:g.102843769G>C
NC_000012.11:g.103237547G>C
CM000674.1:g.103237547G>C
NC_000012.10:g.101761677G>C
NG_008690.1:g.78834C>G
NG_008690.2:g.119642C>G
ENST00000553106.6:c.1076C>G
ENST00000307000.7:c.1061C>G
ENST00000549247.6:n.835C>G
ENST00000551114.2:n.738C>G
ENST00000553106.5:c.1076C>G
ENST00000635477.1:c.180C>G
ENST00000635528.1:n.591C>G
NM_000277.1:c.1076C>G
NM_000277.2:c.1076C>G
NM_001354304.1:c.1076C>G
NM_001354304.2:c.1076C>G

Pathogenic

Met criteria codes 3

PVS1 PP4_Moderate PM2

Evidence Links 2

Expert Panel

Phenylketonuria VCEP

Criteria Specification Information

Criteria Specifications for this VCEP

Evidence submitted by expert panel

Phenylketonuria VCEP

The c.1076C>G (p.Ser359Ter) variant in PAH has been reported in an individual with PKU; BH4 deficiency excluded (PP4_Moderate; PMID: 8097261; (PMID: 9634518). This variant is absent in population databases (PM2). It is a nonsense variant in exon 11 of 13 in PAH,

predicted to undergo nonsense mediated decay with the truncated region critical to protein function (PVS1). In summary, this variant meets criteria to be classified as pathogenic for PAH. PAH-specific ACMG/AMP criteria applied: PVS1, PM2, PP4_Moderate.

Met criteria codes

PVS1	✔	Nonsense variant in exon 11 of 13 in PAH, predicted to undergo nonsense mediated decay with the truncated region critical to protein function
PP4_Moderate	✔	S359X was identified in a PKU patient. PMID: 8097261; BH4 deficiency excluded as part of study inclusion criteria (PMID: 9634518) A new nonsense heterozygous C-->G transversion within exon 11 (S359X) was identified in a PKU patient. PubMed:8097261 PubMed:9634518
PM2	✔	Absent from controls in ExAC, gnomAD, 1000 Genomes, ESP

Curation History

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