The ClinGen Evidence Repository is an **FDA-recognized human genetic variant database** containing expert-curated assertions regarding variants' pathogenicity and supporting evidence summaries. [Disclaimer]

Variant: NM_001204.7(BMPR2):c.1217T>G (p.Met406Arg)

Version: 2.0

CA350341879

812826 (ClinVar)

Gene: BMPR2 (HGNC:659)
Condition: pulmonary arterial hypertension (MONDO:0015924)
Inheritance Mode: Autosomal dominant inheritance
UUID: 8a65ebc3-d1be-4d36-9da9-18d84d0c66dc
Approved on: 2026/4/9
Published on: 2026/4/9

HGVS expressions

NM_001204.7(BMPR2):c.1217T>G (p.Met406Arg)
NM_001204.7:c.1217T>G
NC_000002.12:g.202532673T>G
CM000664.2:g.202532673T>G
NC_000002.11:g.203397396T>G
CM000664.1:g.203397396T>G
NC_000002.10:g.203105641T>G
NG_009363.1:g.161347T>G
ENST00000374580.10:c.1217T>G
ENST00000638587.1:c.1148T>G
ENST00000374574.2:c.1217T>G
ENST00000374580.8:c.1217T>G
NM_001204.6:c.1217T>G

Likely Pathogenic

Met criteria codes 5

PM2_Supporting PM1 PS4_Supporting PP2 PP3

Not Met criteria codes 5

PVS1 BS2 BS1 BP4 BA1

Evidence Links 0

Expert Panel

Pulmonary Hypertension VCEP

Criteria Specification Information

Criteria Specification: *ClinGen Pulmonary Hypertension Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for BMPR2 Version 2.0.0*
Criteria Specification Approval History
Criteria Specifications for this VCEP

Evidence submitted by expert panel

Pulmonary Hypertension VCEP

The c.1217T>G (p.Met406Arg) variant is a missense variant located in exon 9 of the BMPR2 gene, predicted to cause substitution of methionine to arginine encoding the functionally relevant catalytic kinase domain but without functional evidence indicating a critical or non-critical amino acid residue (PM1_moderate). This variant is absent from gnomAD v2.1.1 and v4.1 (PM2_supporting). BMPR2 has a low rate of benign missense variation and missense variants are a common mechanism of pulmonary hypertension (PP2). The REVEL prediction algorithm score is 0.96 and AlphaMissense is 0.9818 indicating pathogenicity (PP3_supporting). The variant has been reported in four

studies based on 2 unrelated probands (PMIDs: 29650961, 33066286, 32581362, and 27537724) (PS4_supporting). PS2 was not assessed due to lack of paternity data. Functional studies have not been conducted for this variant (PS3 not assessed). In summary, this variant meets the criteria to be classified as a likely pathogenic for pulmonary arterial hypertension based on the ACMG/AMP criteria applied, as specified by the ClinGen Pulmonary Hypertension VCEP: PM1_moderate, PM2_supporting, PP2, PP3_supporting, PS4_supporting (VCEP specification version 2.0, 1/30/2026).

Met criteria codes

PM2_Supporting	✔	Variant is absent in gnomAD v2.1.1 & v4.1.
PM1	✔	Variant changes an amino acid in the kinase domain without functional evidence indicating critical or non-critical
PS4_Supporting	✔	The variant ass reported in 2 probands (PMID: 29650961 & PMID: 27537724). Additional reports (PMID: 33066286 & PMID: 32581362) refer to the same individual as in PMID: 29650961.
PP2	✔	BMPR2 has a z-score of 3.28 for missense variants which is above the threshold of 3.09 (PMID: 40496714) for constraint.
PP3	✔	REVEL score is 0.96 which is ≥0.75 cutoff and AlphaMissense score is 0.9818, predicted to be likely pathogenic.

Not Met criteria codes

PVS1	✖	The variant is a missense variant.
BS2	✖	Variant absent in gnomAD v2.1.1 & v4.1
BS1	✖	Variant is absent in gnomAD v2.1.1 & v4.1.
BP4	✖	REVEL score is 0.96 which is ≥0.75 cutoff and AlphaMissense score is 0.9818, predicted to be likely pathogenic.
BA1	✖	Variant is absent in gnomAD v2.1.1 & v4.1.

Curation History

Showing 1 to 2 of 2 rows

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