

Variant: *NM_000132.4(F8):c.6276G>A (p.Val2092=)*

Version: 1.0

CA10567876 [↗](#)

810971 (ClinVar) [↗](#)

Gene: F8 ([HGNC:2157](#))

Condition: hemophilia A ([MONDO:0010602](#))

Inheritance Mode: X-linked inheritance

UUID: e80c8575-b191-4040-8304-608ff545db13

Approved on: 2026/4/10

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HGVS expressions

NM_000132.4:c.6276G>A

NM_000132.4(F8):c.6276G>A (p.Val2092=)

NC_000023.11:g.154896230C>T

CM000685.2:g.154896230C>T

NC_000023.10:g.154124505C>T

CM000685.1:g.154124505C>T

NC_000023.9:g.153777699C>T

NG_011403.1:g.131494G>A

NG_011403.2:g.131494G>A

ENST00000360256.9:c.6276G>A

ENST00000360256.8:c.6276G>A

NM_000132.3:c.6276G>A

Benign

Met criteria codes **2**

BA1 **PP3**

Not Met criteria codes **3**

BS1 **BP7** **PS4**

Evidence Links **0**

Expert Panel

[Coagulation Factor Deficiency VCEP](#) [↗](#)

Criteria Specification Information

[↗](#) **Criteria Specification:** *ClinGen Coagulation Factor Deficiency Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for F8 Version 2.0.0*

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

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

Evidence submitted by expert panel

Coagulation Factor Deficiency VCEP

The c.6276G>A (p.Val2092=) variant is a synonymous variant that is predicted to impact splicing. The Grpmax FAF in gnomAD v4.1.0 is 0.0006600 which is higher than the ClinGen Coagulation Factor Deficiency VCEP threshold (≥ 0.000333) for BA1, and therefore meets this criterion (BA1). The computational predictor Splice AI gives a score of 0.46 for acceptor gain, which is above the CFD VCEP threshold of ≥ 0.2 , evidence that correlates with impact to F8 function meeting PP3. Due to conflicting evidence, this variant is classified as benign for Hemophilia A based on the ACMG/AMP criteria applied, as specified by the ClinGen Coagulation Factor Deficiency VCEP F8 Version 2.0.0 specifications: BA1, PP3.

Met criteria codes

BA1			The Grpmax FAF in gnomAD v4.1.0 is 0.0006600 which is higher than the ClinGen Coagulation Factor Deficiency VCEP threshold (≥ 0.000333) for BA1, and therefore meets this criterion (BA1). (Discrepant frequencies in gnomAD v4. Meets PM2 by gnomAD v2.1.1 Grpmax FAF 0.00002897 (< 0.000333) and absent in males)
PP3			The computational predictor Splice AI gives a score of 0.46 for acceptor gain, which is above the CFD VCEP threshold of ≥ 0.2 , evidence that correlates with impact to F8 function [PP3].

Not Met criteria codes

BS1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP7			The c.6276G>A (p.Val2092=) variant is a synonymous (silent) variant. BP7 was not applied because the splice predictor tool, Splice AI, gives a score of 0.46, which is above the CFD VCEP threshold of ≤ 0.1 , predicts an impact on splicing, meeting PP3.
PS4			There are no cases in the EAHAD or CHAMPS databases.

Curation History



 

 

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