



HCV NS3 Protease Drug Resistance

TEST CODES:
10001,
30600, 30601

CPT CODE:
87902

CATEGORY
Infectious Disease

HCV genotype 1a					
CODON	Glecaprevir 1a	Grazoprevir 1a	Paritaprevir 1a	Simeprevir 1a	Voxilaprevir 1a
V36A		S 13	R 10	comment	
V36L		S 13	R 10		
V36M		S 13	R 10, 16	comment	
Q41R		comment			
F43I				comment	
F43L			R 4, 10, 16		
F43S		comment		comment	
F43V				comment	
T54S			S 10		
V55A		S 13			
V55I			S 10		
Q80H				comment	
Q80K		S 13	R 4, 10, 16	R 6, 11, 15	
Q80L			R 10	S 15	
Q80R		S 13	R 10	R 11, 15	
S122R				R 15	
S138T				comment	
R155G		comment	R 4, 10	comment	
R155K		R 13, 14, 16	R 4, 10, 16	R 11, 14, 15	
R155Q		R 14	R 14	R 14	
R155S			R 4, 10		
R155T			R 10	comment	
R155W			R 10		
A156G		R 14	R 14	R 14	
A156L					R 2
A156S		R 14	R 14	S 14	
A156T	R 1, 3, 16	R 16	R 4, 10, 16	comment	R 2
A156V	R 1, 3			comment	
D168A	R 16	R 13, 14, 16	R 4, 10, 14, 16	R 14, 15	
D168E		R 13, 16	R 4, 10, 16	R 11, 15	

HCV genotype 1a					
CODON	Glecaprevir 1a	Grazoprevir 1a	Paritaprevir 1a	Simeprevir 1a	Voxilaprevir 1a
D168F	R 1, 3		R 4		
D168G		R 13		comment	
D168H			R 4, 10	comment	
D168I				comment	
D168K		comment			
D168N			R 4, 10	comment	
D168Q				comment	
D168T			comment	comment	
D168V	R 16	R 16	R 4, 10, 16	R 15	
D168Y	R 1,3	comment	R 4, 10	comment	
I170T		R 13		comment	
Y56H		R 16	R 16		

*Low-grade or variable resistance.

**Resistance to boceprevir has been noted in genotype 1b, however this substitution is not commonly found in genotype 1a.

For the most up-to-date list of assays, please visit our website at www.Viracor-Eurofins.com. This test was developed and its performance characteristics determined by Viracor Eurofins. It has not been cleared or approved by the U.S. Food and Drug Administration.

The CPT codes provided are based on Viracor Eurofins' interpretation of the American Medical Association's Current Procedural Terminology (CPT) codes and are provided for informational purposes only. CPT coding is the sole responsibility of the billing party. Questions regarding coding should be addressed to your local Medicare carrier. Viracor Eurofins assumes no responsibility for billing errors due to reliance on the CPT codes illustrated in this material.

HCV genotype 1b					
CODON	Glecaprevir 1b	Grazoprevir 1b	Paritaprevir 1b	Simeprevir 1b	Voxilaprevir 1b
V36A		R 12	comment	R 8	
V36L		S 13	comment	S 8	
V36M		S 13	comment	R 7, 8	
Q41R		R 12		S 5, 8	
F43I				R 5, 8	
F43L			comment		
F43S		R 13		R 5, 8	
F43V				R 5, 8	
T54A			S 10	S 7, 8	
T54S				S 8	
V55A		S 13	S 10		
Q80H				R 5, 8	
Q80K			comment	R 5, 8, 9, 11, 15	
Q80L			comment	S 11, 15	
Q80R		R 13	comment	R 5, 8, 11, 15	
S122R				R 5, 9, 15	
S138T				R 8	
R155G		R 13	comment	R 8	
R155I				S 8	
R155K		R or S* 12, 13, 14	R 10, 16	R 5, 7, 8, 11, 15	
R155M				S 8	
R155Q		comment	comment	S 8	
R155S			comment		
R155T			comment	R 8	
R155W			comment		
A156G		comment	comment	R 5, 8	
A156S		comment	S 10	S 7, 8	
D168A		R 24	R 5, 16	R 1, 6, 12	
A156T	R 1, 3, 16	R 12, 13, 16	R 4, 10, 16	R 5, 7, 8	R 2
A156V	R 1, 3, 16	R 16	R 16	R 5, 8	R 2
D168A		R 13, 16	R 4, 10, 16	R 5, 8, 15	
D168E		R 13, 16	R 10, 16	R 5, 8, 11, 15	
D168F	R 1, 3		comment		
D168G		R 13		R 8	
D168H			R 4, 10	R 5, 8	
D168I				R 5, 8	
D168K		R 13			
D168N			comment	R 5, 8	

HCV genotype 1b					
CODON	Glecaprevir 1b	Grazoprevir 1b	Paritaprevir 1b	Simeprevir 1b	Voxilaprevir 1b
D168Q				R 9	
D168T			R 10	R 5, 8	
D168V	R 16	R 16	R 4, 10, 16	R 5, 8, 15	
D168Y	R 1, 3	R 12	R 10	R 5, 8	
I170A			S 10	S 8	
I170T		S 13		R 6, 8	
I170V				S 9	

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Comment:

Patient genotype (1a/1b) displayed a mutation that has shown resistance to (drug name) in genotype (1a/1b).

1. Product Insert, Glecaprevir (Mavyret)[®], HIGHLIGHTS OF PRESCRIBING INFORMATION. 2017.
2. Product Insert, Voxilaprevir (Vosevi)[®], HIGHLIGHTS OF PRESCRIBING INFORMATION. 2017.
3. Ng et al. Abbvie poster number THU-305 Apr 2017.
4. Product Insert, Paritaprevir (VIEKIRA PAK)[®], HIGHLIGHTS OF PRESCRIBING INFORMATION. Dec 2014.
5. DRC Forum for Collaborative HIV Research, Clinically Relevant HCV Drug Resistance Mutations, appendix linked in <http://www.hivforum.org/projects/hcv-drug-development-advisory-group/hcv-drug-resistance-mutations>.
6. Berger KL, Triki I, Cartier M, et al. Baseline hepatitis C virus (HCV) NS3 polymorphisms and their impact on treatment response in clinical studies of the HCV NS3 protease inhibitor faldaprevir. *Antimicrob Agents Chemother*. 2014;58(2):698-705.
7. Jiang M, Mani N, Lin C, et al. In vitro phenotypic characterization of hepatitis C virus NS3 protease variants observed in clinical studies of telaprevir. *Antimicrob Agents Chemother*. 2013 Dec;57(12):6236-45.
8. Lenz O, Verbinnen T, Lin TI, et al. In vitro resistance profile of the hepatitis C virus NS3/4A protease inhibitor TMC435. *Antimicrob Agents Chemother*. 2010 May;54(5):1878-87.
9. Lenz O, Vijgen L, Berke JM, et al. Virologic response and characterisation of HCV genotype 2-6 in patients receiving TMC435 monotherapy (study TMC435-C202). *J Hepatol*. 2013 Mar;58(3):445-51.
10. Pilot-Matias T, Tripathi R, Cohen D, et al. In Vitro and In Vivo Antiviral Activity and Resistance Profile of the Hepatitis C Virus NS3/4A Protease Inhibitor ABT-450. *Antimicrob Agents Chemother*. 2015 Feb;59(2):988-97.
11. Lenz O, Verbinnen T, Fevery B, et al. Virology analyses of HCV isolates from genotype 1-infected patients treated with simeprevir plus peginterferon/ribavirin in Phase IIb/III studies. *J of Hepatology*. 2015 May;62:1008-14.
12. Summa V, Ludmerer SW, McCauley JA, et al. MK-5172, a selective inhibitor of hepatitis C virus NS3/4a protease with broad activity across genotypes and resistant variants. *Antimicrob Agents Chemother*. 2012 Aug;56(8):4161-7. doi: 10.1128/AAC.00324-12. Epub 2012 May 21. Erratum in: *Antimicrob Agents Chemother*. 2014 Aug;58(8):4995. Huang, Qian [added]
13. Howe AY, Black S, Curry S, et al. Virologic resistance analysis from a phase 2 study of MK-5172 combined with pegylated interferon/ribavirin in treatment-naive patients with hepatitis C virus genotype 1 infection. *Clin Infect Dis*. 2014 Dec 15;59(12):1657-65.
14. Jensen SB, Serre SB, Humes DG, et al. Substitutions at NS3 Residue 155, 156, or 168 of Hepatitis C Virus Genotypes 2 to 6 Induce Complex Patterns of Protease Inhibitor Resistance. *Antimicrob Agents Chemother*. 2015 Dec;59(12):7426-36.
15. Product Insert, Simeprevir (Olysio)[®], HIGHLIGHTS OF PRESCRIBING INFORMATION. Nov. 2013.
16. Ng TI, Tripathi R, Reisch T, et al. *In Vitro* Antiviral Activity and Resistance Profile of the Next-Generation Hepatitis C Virus NS3/4A Protease Inhibitor Glecaprevir. *Antimicrob Agents Chemother*. 2017 Dec 21;62(1). pii: e01620-17. doi: 10.1128/AAC.01620-17. Print 2018 Jan.