



# CMV Resistance Sequencing

TEST CODES:  
33125, 33126,  
30722

CPT CODE:  
87910 (with Multiplier)

CATEGORY  
Infectious Disease

## Reportable Mutations - UL54 (DNA Polymerase)<sup>1</sup>

| Viral Phenotype Confirmed by Marker Transfer <sup>2</sup> |           |           |             |                            |
|-----------------------------------------------------------|-----------|-----------|-------------|----------------------------|
| Mutation                                                  | Cidofovir | Foscarnet | Ganciclovir | REFERENCE                  |
| S290R                                                     | S         | R         | S           | 106                        |
| D301N                                                     | R         | S         | R           | 19,33,56                   |
| E303D <sup>4</sup>                                        | R         | S         | R           | 93                         |
| E303G <sup>4</sup>                                        | R         | S         | R           | 93                         |
| N408D                                                     | R         | S         | R           | 9,12,23,31,33,35,56,72     |
| N408K <sup>4</sup>                                        | R         | S         | R           | 13,74,93                   |
| N408S                                                     | R         | S         | R           | 84,88                      |
| N410K                                                     | R         | S         | R           | 19,23                      |
| F412C                                                     | R         | S         | R           | 9,20,23,33,35,65,72        |
| F412L                                                     | R         | S         | R           | 74,111                     |
| F412S                                                     | R         | S         | R           | 25,74,111                  |
| F412V                                                     | R         | S         | R           | 9,23,72                    |
| D413A                                                     | R         | S         | R           | 69,73                      |
| D413E                                                     | R         | S         | R           | 19,23,31,33,52,56,69,72,73 |
| D413N                                                     | R         | S         | R           | 89                         |
| D413Y <sup>4</sup>                                        | R         | S         | R           | 93                         |
| P488R                                                     | R         | S         | R           | 79,111                     |
| K493N                                                     | R         | R         | R           | 118                        |
| N495K                                                     | S         | R         | S           | 73,76,106                  |
| P497S                                                     | R         | S         | S           | 118                        |
| K500N                                                     | R         | S         | R           | 79,11                      |
| L501I                                                     | R         | S         | R           | 2,9,12,23,33,64,72         |
| T503I                                                     | R         | S         | R           | 12,19,33,35,72,73          |
| K513N                                                     | R         | S         | R           | 23,33,35,56,72             |
| K513E                                                     | R         | S         | R           | 9,23,33,34,35,72           |
| K513R                                                     | R         | S         | R           | 35,72,89                   |
| K513T                                                     | R         | S         | R           | 118                        |
| D515E                                                     | S         | S         | R           | 90                         |
| D515Y                                                     | R         | S         | R           | 91,120                     |
| L516P                                                     | R         | S         | R           | 120                        |
| L516R                                                     | R         | S         | R           | 19,33                      |
| L516W                                                     | R         | S         | R           | 92                         |

<sup>1</sup> Most UL54 mutations also have UL97 mutations.

<sup>2</sup> R and S denote resistant and sensitive, respectively. ND indicates Not Determined.

<sup>3</sup> Low-grade or variable resistance.

<sup>4</sup> Also confers resistance to CMX001.

## Reportable Mutations - UL54 (DNA Polymerase)<sup>1</sup>

| Viral Phenotype Confirmed by Marker Transfer <sup>2</sup> |                     |           |                     |                               |
|-----------------------------------------------------------|---------------------|-----------|---------------------|-------------------------------|
| Mutation                                                  | Cidofovir           | Foscarnet | Ganciclovir         | REFERENCE                     |
| I521T                                                     | R                   | S         | R                   | 66,68,72                      |
| P522A                                                     | R                   | S         | R                   | 33,37,68,72                   |
| P522S                                                     | R                   | S         | R                   | 68,72                         |
| del524                                                    | R                   | S         | R                   | 88                            |
| V526L                                                     | R                   | S         | R                   | 82                            |
| C539G                                                     | R                   | S         | R                   | 89                            |
| C539R                                                     | R                   | S         | R                   | 79,111                        |
| D542E <sup>4</sup>                                        | R                   | S         | S                   | 81                            |
| A543P                                                     | R                   | S         | R                   | 108                           |
| L545S                                                     | R                   | S         | R                   | 9,12,33,72                    |
| L545W                                                     | R                   | S         | R                   | 74,111                        |
| T552N                                                     | S                   | R         | R                   | 79,106,111                    |
| L565V                                                     | S                   | R         | S                   | 118                           |
| Q578H                                                     | R                   | R         | R                   | 24,74,111                     |
| Q578L                                                     | S                   | R         | S                   | 83                            |
| S585A                                                     | S                   | R         | S                   | 79,111                        |
| D588E                                                     | S                   | R         | S                   | 9,12,23,35,72                 |
| D588N                                                     | S                   | R         | R                   | 12,23,27,33,74                |
| F595I                                                     | S                   | R         | S                   | 79,111                        |
| T700A                                                     | S                   | R         | S                   | 5,9,18,33,47,72               |
| V715A                                                     | S                   | R         | S                   | 92                            |
| V715M                                                     | S                   | R         | S                   | 5,9,18,25,33,37,47,72,92      |
| I726T                                                     | S                   | S         | R                   | 83                            |
| E756K                                                     | R or S <sup>3</sup> | R         | R                   | 12,19,23,33,36,74, 82,110     |
| E756D                                                     | S                   | R         | S                   | 12,19,31,33                   |
| E756Q                                                     | S                   | R         | S                   | 12,18,33,37                   |
| L773V                                                     | R                   | R         | R                   | 24,89                         |
| L776M                                                     | S                   | R         | R                   | 67,73                         |
| V781I                                                     | S                   | R         | R <sup>3</sup>      | 9,23,74                       |
| V787A                                                     | S                   | R         | R                   | 91                            |
| V787L                                                     | S                   | R         | R                   | 18,37,48,73                   |
| L802M                                                     | S                   | R         | R or S <sup>3</sup> | 9,12,18,20,23,27,33,35,65,73  |
| K805Q                                                     | R                   | S         | S                   | 9,18,28,35,72                 |
| A809V                                                     | S                   | R         | R                   | 18,25,28,33,47,72,106         |
| V812L <sup>4</sup>                                        | R                   | R         | R                   | 12,18,20,27,28,33,72,73,78,93 |
| T813S                                                     | R                   | R         | R                   | 28,73                         |
| T821I                                                     | S                   | R         | R                   | 9,18,28,33,35,72,73           |
| V823A                                                     | R                   | S         | R                   | 118                           |
| P829S                                                     | S                   | S         | R                   | 79,111                        |

<sup>1</sup> Most UL54 mutations also have UL97 mutations.

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<sup>3</sup> Low-grade or variable resistance.

<sup>4</sup> Also confers resistance to CMX001.

## Reportable Mutations - UL54 (DNA Polymerase)<sup>1</sup>

| Viral Phenotype Confirmed by Marker Transfer <sup>2</sup> |           |           |             |                       |
|-----------------------------------------------------------|-----------|-----------|-------------|-----------------------|
| Mutation                                                  | Cidofovir | Foscarnet | Ganciclovir | REFERENCE             |
| A834P                                                     | R         | R         | R           | 13,73                 |
| T838A                                                     | S         | R         | S           | 27,28,73              |
| G841A                                                     | R         | R         | R           | 28,72,73              |
| G841S                                                     | S         | R         | R           | 83                    |
| V946L                                                     | S         | R         | S           | 79,111                |
| E951D                                                     | S         | R         | R           | 106                   |
| L957F                                                     | ND        | ND        | R           | 79,111                |
| del981 to 982                                             | R         | R         | R           | 11,19,33,63,72,73,108 |
| A987G                                                     | R         | S         | R           | 1,9,22,23,25,43,72    |
| A987V                                                     | S         | R         | S           | 118                   |
| E989D                                                     | S         | R         | R           | 118                   |
| N495K+Q783R                                               | S         | R         | R           | 106                   |
| A543V                                                     | R         | S         | S           | 124                   |
| A928T                                                     | R         | R         | R           | 124                   |
| V787E                                                     | R         | R         | R           | 126                   |
| V787A                                                     | S         | R         | S           | 126                   |

## Reportable Mutations - UL54 (DNA Polymerase)<sup>1</sup>

| Viral Phenotype found in Clinical Isolates (Unconfirmed by Marker Transfer) <sup>2</sup> |           |           |             |                |
|------------------------------------------------------------------------------------------|-----------|-----------|-------------|----------------|
| Mutation                                                                                 | Cidofovir | Foscarnet | Ganciclovir | REFERENCE      |
| M393R                                                                                    | R         | R         | R           | 20,72          |
| M393K                                                                                    | R         | R         | R           | 20,72          |
| T419M                                                                                    | S         | R         | S           | 24             |
| L501F                                                                                    | R         | S         | R           | 23,25,31,56,72 |
| Y(I)722V                                                                                 | R         | S         | R           | 35,72          |
| H729Y                                                                                    | S         | R         | S           | 115            |
| Y751H                                                                                    | R         | S         | R           | 35,72          |
| V787I                                                                                    | S         | R         | S           | 33             |

<sup>1</sup> Most UL54 mutations also have UL97 mutations.

<sup>2</sup> R and S denote resistant and sensitive, respectively. ND indicates Not Determined.

<sup>3</sup> Low-grade or variable resistance.

<sup>4</sup> Also confers resistance to CMX001.

## Reportable Mutations - UL56 (Terminase)

| Viral Phenotype Confirmed by Marker Transfer <sup>1</sup> |            |                |
|-----------------------------------------------------------|------------|----------------|
| Mutation                                                  | Letermovir | REFERENCE      |
| S229F                                                     | R          | 104            |
| V231A                                                     | R          | 102            |
| V231L                                                     | R          | 98,102,104,108 |
| N232Y                                                     | R          | 105            |
| V236A                                                     | R          | 108            |
| V236L                                                     | R          | 102            |
| V236M                                                     | R          | 97,98,104,110  |
| E237D                                                     | R          | 102,105        |
| L241P                                                     | R          | 98,102,103,104 |
| T244K                                                     | R          | 102            |
| L254F                                                     | R          | 104            |
| L257F                                                     | R          | 104            |
| L257I                                                     | R          | 102,104        |
| K258E                                                     | R          | 105            |
| F261L                                                     | R          | 102,104,105    |
| Y321C                                                     | R          | 102            |
| C325F                                                     | R          | 102            |
| C325W                                                     | R          | 108            |
| C325R                                                     | R          | 102            |
| C325Y                                                     | R          | 98,102         |
| M329T                                                     | R          | 102,105        |
| A365S                                                     | R          | 108            |
| N368D                                                     | R          | 104            |
| R369G                                                     | R          | 98             |
| R369M                                                     | R          | 98,104         |
| R369S                                                     | R          | 98,103         |
| E237D, T244K, F261L                                       | R          | 102            |
| V236L, L257I                                              | R          | 102            |
| V236M, L257I, M329T                                       | R          | 102            |
| S229F, L254F, L257I                                       | R          | 104            |

<sup>1</sup> R denotes resistance.

## Reportable Mutations - UL97 (Phosphotransferase)

| Viral Phenotype Confirmed by Marker Transfer <sup>1</sup> |           |                |                                          |
|-----------------------------------------------------------|-----------|----------------|------------------------------------------|
| Mutation                                                  | Maribavir | Ganciclovir    | REFERENCE                                |
| F342S                                                     | ND        | R              | 94,95,96                                 |
| F342Y                                                     | R         | R              | 112,114                                  |
| V356G                                                     | ND        | R              | 95,96                                    |
| K359E                                                     | ND        | R              | 112,114                                  |
| K359Q                                                     | ND        | R              | 112,114                                  |
| K359N                                                     | ND        | R              | 114,116                                  |
| E362D                                                     | ND        | R              | 116                                      |
| L405P                                                     | ND        | R              | 75                                       |
| T409M                                                     | R         | ND             | 114,119                                  |
| H411L                                                     | R         | ND             | 117,118                                  |
| H411N                                                     | R         | ND             | 117                                      |
| H411Y                                                     | R         | ND             | 114,117                                  |
| M460I                                                     | ND        | R              | 3,5,6,7,8,10,12,23,25,33,109             |
| M460T                                                     | ND        | R              | 75,109                                   |
| M460V                                                     | ND        | R              | 6,7,8,10,11,17,24,33,43,50,109           |
| V466G                                                     | R         | R              | 73,77,96                                 |
| C480F                                                     | R         | R              | 112,118                                  |
| C518Y                                                     | ND        | R              | 84,85                                    |
| H520Q                                                     | ND        | R              | 6,7,10,25,33,43,109                      |
| P521L                                                     | R         | R              | 96,112                                   |
| del590 to 593                                             | ND        | R              | 12,72                                    |
| del591 to 594                                             | ND        | R              | 8,10,33,34,35,72,107                     |
| del591 to 607                                             | ND        | R              | 51,72                                    |
| A591V                                                     | ND        | R              | 107                                      |
| C592G                                                     | ND        | R <sup>2</sup> | 6,8,10,11,20,23,27,33,51,106,107,109,114 |
| A594E                                                     | ND        | R              | 73,75                                    |
| A594G                                                     | ND        | R              | 84,86                                    |
| A594P                                                     | ND        | R              | 6,25,59,72                               |
| A594T                                                     | ND        | R              | 10,25,33,36,50,51,54,92                  |
| A594V                                                     | ND        | R              | 5,6,8,10,11,17,25,27,33,50,107,109,113   |
| A594S                                                     | ND        | R              | 113                                      |
| L595F                                                     | ND        | R              | 10,33,41,72                              |
| L595S                                                     | ND        | R              | 5,6,8,10,11,12,17,23,25,33,109           |
| L595W                                                     | ND        | R              | 6,10,25,33,51,72                         |
| del595                                                    | ND        | R              | 4,10,17,72,107                           |
| del595 to 603                                             | ND        | R              | 14,33,48,72,107                          |
| del596                                                    | ND        | R              | 107                                      |
| E596G                                                     | ND        | R              | 10,20,33,35,36,51,72                     |
| E596Y                                                     | ND        | R              | 90                                       |
| del597 to 599                                             | ND        | R              | 92,107                                   |

<sup>1</sup> R denotes resistance. ND indicates Not Determined.

<sup>2</sup> Alone confers modest resistance. When found in conjunction with UL54 del 981 to 982, there is a much higher level of resistance.

## Reportable Mutations - UL97 (Phosphotransferase)

| Viral Phenotype Confirmed by Marker Transfer <sup>1</sup> |           |             |                              |
|-----------------------------------------------------------|-----------|-------------|------------------------------|
| Mutation                                                  | Maribavir | Ganciclovir | REFERENCE                    |
| del597 to 598                                             | ND        | R           | 107                          |
| G598S                                                     | ND        | R           | 33,58,72                     |
| del599                                                    | ND        | R           | 107                          |
| k599T                                                     | ND        | R           | 60,72                        |
| del600                                                    | ND        | R           | 10,33,36,51,72,107           |
| del600-601                                                | ND        | R           | 107                          |
| del601                                                    | ND        | R           | 107                          |
| del601-602                                                | ND        | R           | 107                          |
| del601 to 603                                             | ND        | R           | 69,107                       |
| C603R                                                     | ND        | R           | 73,77,109                    |
| C603W                                                     | ND        | R           | 6,8,10,20,23,25,33,35,72,109 |
| C607F                                                     | ND        | R           | 8,50,51,72                   |
| C607Y                                                     | ND        | R           | 10,25,33,34,35,39,51,72      |
| I610T                                                     | ND        | R           | 90                           |
| A613V                                                     | ND        | R           | 84,87                        |
| L397R                                                     | R         | R           | 125                          |

<sup>1</sup> R denotes resistance. ND indicates Not Determined.

<sup>2</sup> Alone confers modest resistance. When found in conjunction with UL54 del 981 to 982, there is a much higher level of resistance.

## Reportable Mutations - UL97 (Phosphotransferase)

| Viral Phenotype found in Clinical Isolates (Unconfirmed by Marker Transfer) <sup>1</sup> |           |             |                              |
|------------------------------------------------------------------------------------------|-----------|-------------|------------------------------|
| Mutation                                                                                 | Maribavir | Ganciclovir | REFERENCE                    |
| M460L                                                                                    | ND        | R           | 49,72                        |
| A590T                                                                                    | ND        | R           | 10,49,72                     |
| del590 to 600                                                                            | ND        | R           | 17,72                        |
| del590 to 603                                                                            | ND        | R           | 56,72                        |
| A591D                                                                                    | ND        | R           | 10,49,72                     |
| C592F                                                                                    | ND        | R           | 72                           |
| del594 to 601                                                                            | ND        | R           | unpublished clinical isolate |
| L595T                                                                                    | ND        | R           | 10,35,72                     |
| N597I                                                                                    | ND        | R           | 10,49,72                     |
| del597 to 603                                                                            | ND        | R           | 25                           |
| G598V                                                                                    | ND        | R           | 10,49,72                     |
| K599M                                                                                    | ND        | R           | 10,49,72                     |
| C603Y                                                                                    | ND        | R           | 6,10,49,72                   |
| A606D                                                                                    | ND        | R           | 10,49,72                     |

<sup>1</sup> R denotes resistance. ND indicates Not Determined.

<sup>2</sup> Alone confers modest resistance. When found in conjunction with UL54 del 981 to 982, there is a much higher level of resistance.

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