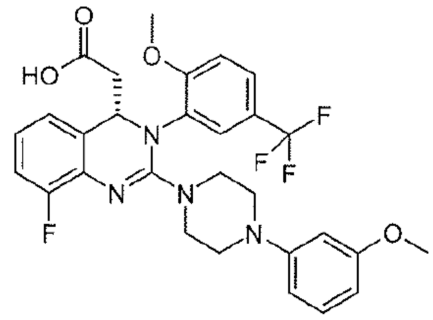
CLAIMS

1. Letermovir according to Formula (I),



Formula (I),

which is in the amorphous state, obtainable by a precipitation process for isolating amorphous Letermovir, **characterized by**

precipitation of said amorphous Letermovir from the water miscible solvents acetone or acetonitrile into excess stirred water, following isolation via filtration or centrifugation of the Letermovir obtained.

2. Letermovir according to claim 1, wherein said process has a subsequent drying step *in vacuo*.

3. Letermovir according to any of the claims 1 and 2, wherein said Letermovir in the amorphous state is not isolated by precipitation using alcohols, particularly methanol, or ethanol, or using THF or MEK.

4. Letermovir according to any of the claims 1 to 3, wherein the Letermovir obtained is processed by dry granulation.

5. Letermovir according to any of the claims 1 to 4, wherein said Letermovir in the amorphous state is further characterized by:

i) an impurity content of mesityl oxide of < / = 31 ppm; and /or

ii) an impurity content of 3-methoxyaniline of < 20 ppm, preferably < 15 ppm, more preferably < 10 ppm, even more preferably < 5 ppm and most preferred < 1.5 ppm.

6. Letermovir according to any of the claims 1 to 5, wherein said Letermovir in the amorphous state is further characterized by having > 99% present Letermovir in one enantiomeric form of the R/S system when determined by

Chiral HPLC assay:

Operating Conditions:

Column:	Chiralpak AD-H, 5µm; 250 x 4.6 mm
Mobile Phase:	Mix 900 ml of n-heptane with 100 ml of 2-propanol and with10 ml of diethyl amine
Isocratic:	50 min
Detection wavelength:	UV detection 260 nm, BW +/- 4 nm
Column temperature:	45ºC
Injection volume:	20 µL
Flow rate:	1.0 ml/min.

7. Letermovir according to any of the claims 1 to 6, wherein said Letermovir in the amorphous state is further characterized by having a content of acetone below 5000 ppm or a content of acetonitrile below 410 ppm, and a content of water < 2.0%, when said acetone or acetonitrile content is determined by static headspace gas chromatography, having the following operating conditions:

Apparatus	Gas Chromatograph, e.g. Agilent 6890
Column	DB-WAXetr: 30 m length, 0.32 mm inner diameter, 1 µm thickness of film
Carrier gas, flow rate	Nitrogen, 0.9 mL/min (constant flow) 120 kPa vial pressure at the headspace sampler
Injector temperature	250°C
Split flow rate	4.5 mL/min

Detector/temperature	FID/250°C
Burning gases:	
Hydrogen	40 mL/min
Air	450 mL/min
Make-up gas (N_2)	25 mL/min
Oven temperature program:	
Starting temperature	40°C
Holding time	8 min
Heating rate	20 K/min
Final temperature	70°C
Holding time	3 min
Cooling rate	20 K/min
Final temperature	50°C
Holding time	3 min
Heating rate	15 K/min
Final temperature	220°C
Holding time	3 min
Period of analysis	30.8 min

Equipment	Headspace Autosampler, e.g. G1888	
Sample temperature	100°C	
Needle temperature	220°C	
Transfer temperature	230°C	
GC cycle time	40 min	
Equilibration time	30 min	
Equilibration time before the 1st run	1 min	
Number of extractions	1	
Shaking during equilibration time	1 (slow)	
Valve times	Pressurization time	0.25 min
	Loop fill time	0.20 min
	Loop equilibration time	0.05 min
	Inject time	0.50 min
Injections volume	1 mL;	

and when said water content is determined by PhEur 2.5.12.

8. Solid pharmaceutical formulation comprising Letermovir in the amorphous state as defined in any of the claims 1 to 7, wherein said solid pharmaceutical formulation is orally administrable.

9. Solid pharmaceutical formulation according to the claim 8, further comprising povidone, croscarmellose sodium, microcrystalline cellulose, colloidal anhydrous silica and magnesium stearate.

10. Solid pharmaceutical formulation according to claim 9, wherein said Letermovir in the amorphous state is comprised in an amount of 30.0% to 50.0% (w/w), said povidone is comprised in an amount of 2.0% to 10.0% (w/w), said croscarmellose sodium is comprised in an amount of 2.0% to 10.0% (w/w), said microcrystalline cellulose is comprised in an amount of 20.0% to 70.0% (w/w), said colloidal anhydrous silica is comprised in an amount of 0.5% to 5.0% (w/w), and said magnesium stearate is comprised in an amount of 0.1% to 5.0% (w/w).

11. Solid pharmaceutical formulation according to the claims 8 to 10, which is effective to achieve an absolute bioavailability of 70% ± 30% of Letermovir when administered orally in said formulation comprising at least 5 mg of Letermovir in the amorphous state.

12. Solid pharmaceutical formulation according to any of the claims 8 to 10, wherein Letermovir in the amorphous state exhibits a dissolution of > 50% within 30 minutes, preferably > 60% within 30 minutes, more preferably > 70% within 30 minutes, even more preferably > 80% within 30 minutes, most preferred > 90% within 30 minutes, when tested for dissolution of Letermovir in the amorphous state using Ph. Eur. method 2.9.3, Apparatus 2, with a paddle speed of 50 rpm at 37.0 ºC ± 0.5ºC in 1000 ml 0.1 N HCl / 0.2% sodium lauryl sulphate medium and measuring by reverse phase HPLC at point in time 30 minutes as follows:

HPLC Operating Conditions:
Column: Waters Symmetry Nucleosil 100 C18, 40 mm x 4.0 mm, 10 µm
Detection wavelength: 256 nm

Approximate runtime:	4 minutes
Approximate retention Time:	1.3 minutes
Column temperature:	40°C
Injection volume:	20 µL
Flow rate:	1.5 ml/min
Mobile phase:	Buffer pH 4.0/Acetonitrile; 55/45 v/v.

13. Solid pharmaceutical formulation according to any of the claims 8 to 12, wherein said solid pharmaceutical formulation is an immediate release formulation, characterized in that not less than 85% amount of the Letermovir in the amorphous state is dissolved within 30 min using USP Apparatus I at 100 rpm or USP Apparatus II at 50 rpm in a volume of 900 ml or less of each of the following media:

(1) acidic media, such as USP simulated gastric fluid without enzymes;
(2) pH 4.5 buffer; and
(3) pH 6.8 buffer or USP-simulated intestinal fluid without enzymes.

14. Solid pharmaceutical formulation according to any of the claims 8 to 13, wherein said Letermovir in the amorphous state exhibits a chemical stability of at least 36 months during storage at room temperature (25°C) and (60%) relative humidity, when determined by gradient reverse phase HPLC as follows:

HPLC Operating Conditions:

Column:	Intertsil ODS III 5 µm or equivalent
Solvent	Acetonitrile/0.1 N HCl; 3 + 7 (v/v)
Eluent A:	Water, pH 2.40; B: Acetonitrile
Detection wavelength:	235 nm
Column temperature:	40ºC
Injection volume:	15 µL
Flow rate:	1.0 ml/min
Run time:	30 minutes.

15. Solid pharmaceutical formulation according to any of claims 8 to 14 for use in a method for prophylaxis or method of treatment for diseases associated with the group

of *Herpesviridae*, preferably associated with cytomegalovirus (CMV), even more preferably associated with human cytomegalovirus (HCMV).

16. Solid pharmaceutical formulation according to claim 15 for use in a method of prophylaxis or method of treatment for diseases selected from the group comprising HCMV infections in a subject, particularly HCMV infections in a subject having AIDS, HCMV-pneumonitis, HCMV-encephalitis, as well as gastrointestinal and systemic HCMV infection, HCMV infections in newborn and children, acute HCMV infection of pregnant women, HCMV infection in immuno-suppressed cancer patients, HCMV-positive cancer patients to address HCMV-mediated tumor progression.

17. Use of a solid pharmaceutical formulation according to any of claims 8 to 14 in the manufacture of a medicament for prophylaxis or treatment for diseases associated with the group of *Herpesviridae*, preferably associated with cytomegalovirus (CMV), even more preferably associated with human cytomegalovirus (HCMV).

18. The use of claim 17, wherein the diseases are selected from the group comprising HCMV infections in a subject, particularly HCMV infections in a subject having AIDS, HCMV-pneumonitis, HCMV-encephalitis, as well as gastrointestinal and systemic HCMV infection, HCMV infections in newborn and children, acute HCMV infection of pregnant women, HCMV infection in immuno-suppressed cancer patients, HCMV-positive cancer patients to address HCMV-mediated tumor progression.