GMT Fine Chemicals SA
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VAT N° CHE-108.682.685 TVA

CERTIFICATE OF ANALYSIS

Product:	**CALCIUM LEVOFOLINATE EP**		
	Calcium (6S)-Folinate		
Batch N°:	101-18-15	Analysis No:	LP-1814
Manufacturing Date:	11 October 2018	Retest date:	11 October 2020

TESTS	ACCEPTANCE CRITERIA (limits)	RESULTS
CHARACTERS		
Appearance	White or light yellow, crystalline powder	Conform
IDENTIFICATION		
IR spectrophotometry	Identical to the reference	Conform
HPLC Retention Time	Identical to the reference	Conform
TLC	Identical to the reference	Conform
Calcium	Positive	Positive
Specific Optical Rotation	Complies with the test for specific optical rotation	Complies
TESTS		
Appearance of solution		
Clarity	Clear	Clear
Absorbance at 420 nm	≤ 0.25	0.01
pH	7.5 to 8.5	8.2
Specific optical rotation		
$[\alpha]_D^{25}$ (anhydrous and solvent-free substance)	- 10° to - 15°	-13.0°
Residual solvents		
Ethanol	≤ 3.0 %	< 0.1 %
Acetone *)	≤ 0.5 %	< 0.1 %
Isopropyl alcohol	≤ 0.1 %	< 0.1 %

*) Not used in the production process

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TESTS	ACCEPTANCE CRITERIA (limits)	RESULTS
Related substances:		
- 5-formyltetrahydropteroic acid (E)	≤ 0.80 % [1]	0.15 %
- p-aminobenzoylglutamic acid (A)	≤ 0.80 % [1]	< 0.05%
- 10-formyldihydrofolic acid (F)	≤ 0.80 % [1]	< 0.05 %
- 5,10-diformyltetrahydrofolic acid (B)	≤ 0.80 % [1]	< 0.05 %
- 10-formylfolic acid (D)	≤ 0.80 % m/m [2]	< 0.05 %
- 7,8-dihydrofolic acid (G)	≤ 0.80 % [1]	< 0.05 %
- Folic acid (C)	≤ 0.80 % [1]	< 0.05 %
- Calcium Levofolinate oxydation product	≤ 0.15 % [1]	< 0.05 %
- Any individual unknown impurity	≤ 0.10 % [1]	0.05 %
- Total related substances	≤ 2.0 % [1]	0.20 %
Diastereoisomeric purity		
Calcium (6R)-Folinate (Ph. Eur. Impurity H)	≤ 0.5 %	< 0.05 %
Chlorides	≤ 0.5 %	< 0.1 %
Lead	≤ 0.5 ppm	0.27 ppm
Water	10.0 to 17.0 %	13.7 %

1) % Area/Area calculated on the basis of folinic acid absorption at 280 nm
2) Calculated against 10-formylfolic acid reference standard

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TESTS	ACCEPTANCE CRITERIA (limits)	RESULTS
ASSAY		
Content:		
Calcium (anhydrous and solvent free substance)	7.54 to 8.14 %	7.79 %
Calcium levofolinate (Calcium folinate on anhydrous and solvent free substance against Calcium (6RS)-Folinate reference standard)	97.0 to 102.0 %	99.4 %
Bacterial endotoxins		
LAL test	< 0.35 EU/mg	0.005 EU/mg
Microbial contamination		
Total viable aerobic count	< 500 cfu/g	1 cfu/g
Total yeasts and moulds count	< 100 cfu/g	< 1 cfu/g

GMP STATEMENT:
This active substance has been produced by GMT according to cGMP rules.

The product meets all requirements of the European Pharmacopoeia compendium.

REQUIRED STORAGE CONDITIONS: STORE UNDER VACUUM BETWEEN 2 °C AND 8 °C.

Couvet, 26 October 2018

B. Develle
Quality Control Director