# CERTIFICATE OF ANALYSIS

| | | |
|---|---|---|
| Customer | : | METAPHARMACEUTICAL IND., S.L. |
| Customer PO | : | 2017 - 1 / 386 / 09-OCT-2017 |
| Order Number | : | 81700318 |
| **Product Name** | : | **(6S)-CALCIUM FOLINATE / CALCIUM LEVOFOLINATE EP** |
| Description | : | PA/PE bag in PE/Alu bag, both vacuum sealed, in cardboard box |
| Product Code | : | 610003-03-02 |
| Lot | : | C00272-B00051 |
| Manufacturing Date | : | 25-APR-2017 |
| Release Date | : | 16-OCT-2017 |
| Retest Date | : | 15-APR-2019 |
| Storage Conditions | : | Store at 2-8 °C under vacuum, protected from light. |

| Tests | Specifications | | | Unit of Measure | Results |
|---|---|---|---|---|---|
| | Target | Min | Max | | |
| Packaging | Packaging conform | | | | Conform |
| Labeling | Label conform | | | | Conform |
| Appearance | White to yellowish powder | | | | Conform |
| IR spectrum | Comparable to reference spectrum | | | | Comparable |
| Test for calcium | Positive for calcium | | | | Positive |
| Specific optical rotation (1.0% in THAM buffer, pH 8.1, 25 °C) | | -15 | -10 | - | -13 |
| 10-formylfolic acid | | | 0.8 | % | 0.11 |
| p-aminobenzoylglutamic acid | | | 0.8 | % | < 0.05 |
| 5,10-diformyltetrahydrofolic acid | | | 0.8 | % | 0.06 |
| Folic acid | | | 0.8 | % | < 0.05 |
| 5-formyltetrahydropteroic acid | | | 0.8 | % | < 0.05 |
| 10-formyldihydrofolic acid | | | 0.8 | % | 0.08 |
| 7,8-dihydrofolic acid | | | 0.8 | % | < 0.05 |
| Any unspecified impurity (major) | | | 0.10 | % | 0.08 |
| Sum of related substances (excluding 10-formylfolic acid) | | | 2.0 | % | 0.26 |
| (6R)-folinic acid (impurity H) | | | 0.5 | % | < 0.3 |
| Residual ethanol | | | 3.0 | % | 0.4 |
| Residual acetone | | | 0.5 | % | < 0.10 |
| pH (0.8% in water) | | 7.5 | 8.5 | - | 7.9 |
| Clarity (0.8% in water) | Clear solution | | | | Clear |
| Absorbance (0.8% in water, 420 nm) | | | 0.25 | Au | 0.03 |
| Heavy metals | | | 50 | ppm | 10 |
| Water content (by Karl Fischer) | | 10.0 | 17.0 | % | 12.5 |
| Chlorides | Not more than 0.5% | | | | Conform |



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cerbios

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| Lot | : | C00272-B00051 |

| Tests | Specifications | | | Unit of Measure | Results |
|---|---|---|---|---|---|
| | Target | Min | Max | | |
| Total aerobic microbial count | | | 500 | cfu/g | 0 |
| Escherichia coli | Absent/g | | | | Absent/g |
| Salmonella spp. | Absent/10 g | | | | Absent/10 g |
| Staphylococcus aureus | Absent/g | | | | Absent/g |
| Pseudomonas aeruginosa | Absent/g | | | | Absent/g |
| Total molds and yeasts | | | 100 | cfu/g | 0 |
| Bacterial endotoxins (LAL test) | | | 0.500 | EU/mg | < 0.100 |
| (6S)-calcium folinate (anhydrous and solvent free substance) | | 97.0 | 102.0 | % | 99.6 |
| Calcium | | 7.54 | 8.14 | % | 7.89 |

**Conformity Statement:**

We herewith certify that this lot was manufactured, packaged and analysed by Cerbios-Pharma SA, CH-6917 Barbengo/Lugano, Switzerland, according to cGMP and to the current registration dossier by trained personnel; results were found to comply with the registered specifications.

No quality relevant deviations occurred during the lot manufacturing and quality control.

The manufacturing and analytical records have been reviewed and approved.

Based on the above, this lot is conform and released.

Note: With regard to platinum to be controlled according to the EP monograph for this drug substance, we state that the drug substance is manufactured without using platinum catalyst, and it is not tested for routinely, but that the drug substance would meet specification if it were tested for.

Barbengo, October 16, 2017

Cerbios-Pharma SA
Alessandro Perenna
Quality Assurance
Unit



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