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Leucovorin Calcium Compounded Oral Suspension

DEFINITION

Leucovorin Calcium Compounded Oral Suspension contains NLT 90.0% and NMT 110.0% of the labeled amount of leucovorin ($C_{20}H_{23}N_7O_7$).

Prepare Leucovorin Calcium Compounded Oral Suspension containing 5 mg/mL of leucovorin as follows (see *Pharmaceutical Compounding—Nonsterile Preparations ⟨795⟩*).

Leucovorin Calcium tablets[a] equivalent to	500 mg of leucovorin
Sodium Hydroxide (1 N)	To adjust pH to 7.1–7.6
Syrup, a sufficient quantity to make	100 mL

[a] Leucovorin calcium 25-mg tablets, Teva Pharmaceuticals, Sellersville, PA.

Place the *Leucovorin Calcium tablets* into a suitable container. Wet the tablets with a small amount of *Syrup* and triturate to make a smooth paste. Add the *Syrup* to make the contents pourable. Transfer contents stepwise and quantitatively to a calibrated container using the *Syrup*. Adjust with *Sodium Hydroxide (1 N)* to a pH of 7.1–7.6. Add sufficient *Syrup* to bring to final volume. Shake to mix well. [NOTE—pH may decrease to 6.1 after bringing to final volume with *Syrup* without affecting the stability of the preparation.]

ASSAY

• **PROCEDURE**

Solution A: Methanol and 5 mM tetrabutylammonium phosphate (20:80). Adjust with tetrabutylammonium hydroxide to a pH of 6.6. [NOTE—Tetrabutylammonium phosphate appearing wet should not be used as it may coelute with leucovorin.]

Mobile phase: See *Table 1*.

Table 1

Time (min)	Methanol (%)	Solution A (%)
0	0	100
20	10	90
20.1	0	100
30	0	100

Diluent: Methanol and water (20:80)

Standard solution: 0.05 mg/mL of leucovorin prepared from USP Leucovorin Calcium RS and *Diluent*. Vortex and sonicate until dissolved.

Sample solution: Transfer 1.0 mL of Oral Suspension to a 100-mL volumetric flask, and rinse the pipette with about 2 mL of *Diluent*. Dilute with *Diluent* to volume.

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 290 nm

Column: 4.6-mm × 15-cm; 2.7-µm packing L7

Column temperature: 55°

Flow rate: 0.75 mL/min

Injection volume: 10 µL

System suitability

Sample: *Standard solution*

[NOTE—The retention time for leucovorin is about 20.3 min.]

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0% for replicate injections

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of leucovorin ($C_{20}H_{23}N_7O_7$) in the portion of Oral Suspension taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

C_S = concentration of leucovorin from USP Leucovorin Calcium RS in the *Standard solution* (mg/mL)

C_U = nominal concentration of leucovorin in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–110.0%

SPECIFIC TESTS

• **pH** ⟨791⟩**:** 6.1–7.1

ADDITIONAL REQUIREMENTS

• **PACKAGING AND STORAGE:** Package in tight, light-resistant plastic containers. Store in a refrigerator or at controlled room temperature.

• **BEYOND-USE DATE:** NMT 90 days after the date on which it was compounded when stored in a refrigerator; NMT 30 days after the date on which it was compounded when stored at controlled room temperature

• **LABELING:** Label it to be well shaken before use, and to state the *Beyond-Use Date*.

• **USP REFERENCE STANDARDS** ⟨11⟩

USP Leucovorin Calcium RS

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
LEUCOVORIN CALCIUM COMPOUNDED ORAL SUSPENSION	Brian Serumaga Science Program Manager	CMP2020 Compounding 2020
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	CMP2020 Compounding 2020

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