Not appropriate for regulatory submission. Please visit www.spectrumchemical.com or contact Tech Services for the most up-to-date information contained in this information package.
# LE117, Leucovorin Calcium, USP

## Table of Contents

- Product Specification
- Certificate of Analysis Sample(s)
- Safety Data Sheet (SDS)
- Certification of Current Good Manufacturing Practices (cGMP)
- Manufacturing Process Flowchart
- Source Statement
- BSE/TSE Statement
- Allergen Statement
- EU Fragrance Allergen Statement
- GMO Statement
  - Melamine Statement
  - Nitrosamine Statement
- Animal Testing Statement
- Organic Compliance Statement
- Shelf Life Statement
- Other Chemicals Statement
- Elemental Impurities Statement
- Residual Solvents Statement
- General Label Information – Sample Label
• General Lot Numbering System Guidance
<table>
<thead>
<tr>
<th>Item Number</th>
<th>LE117</th>
</tr>
</thead>
<tbody>
<tr>
<td>Item</td>
<td>Leucovorin Calcium, USP</td>
</tr>
<tr>
<td>CAS Number</td>
<td>1492-18-8</td>
</tr>
<tr>
<td>Molecular Formula</td>
<td>C\textsubscript{20}H\textsubscript{21}CaN\textsubscript{7}O\textsubscript{7}</td>
</tr>
<tr>
<td>Molecular Weight</td>
<td>511.50</td>
</tr>
<tr>
<td>MDL Number</td>
<td></td>
</tr>
<tr>
<td>Synonyms</td>
<td>Folinic Acid Calcium Salt</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Test</th>
<th>Specification</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Min</strong></td>
<td><strong>Max</strong></td>
</tr>
<tr>
<td>ASSAY (ANHYDROUS BASIS)</td>
<td>95.0 105.0 %</td>
</tr>
<tr>
<td>WATER DETERMINATION</td>
<td>17.0 %</td>
</tr>
<tr>
<td>ORGANIC IMPURITIES:</td>
<td></td>
</tr>
<tr>
<td>5-FORMYL-5,6,7,8-TETRAHYDROPTEROIC ACID</td>
<td>0.5 %</td>
</tr>
<tr>
<td>4-AMINOBENZOYLGLUTAMIC ACID</td>
<td>1.5 %</td>
</tr>
<tr>
<td>10-FORMYLDIHYDROFOLIC ACID</td>
<td>1.0 %</td>
</tr>
<tr>
<td>5,10-DIFORMYLTETRAHYDROFOLIC ACID</td>
<td>1.5 %</td>
</tr>
<tr>
<td>7,8-DIHYROFOLIC ACID</td>
<td>0.5 %</td>
</tr>
<tr>
<td>10-FORMYLFOLIC ACID</td>
<td>0.5 %</td>
</tr>
<tr>
<td>FOLIC ACID</td>
<td>1.5 %</td>
</tr>
<tr>
<td>INDIVIDUAL UNSPECIFIED IMPURITY</td>
<td>0.3 %</td>
</tr>
<tr>
<td>TOTAL IMPURITIES</td>
<td>2.5 %</td>
</tr>
<tr>
<td>5-(y-FOLINOYL)TETRAHYDROFOLATE</td>
<td>0.3 %</td>
</tr>
<tr>
<td>ELEMENTAL IMPURITIES</td>
<td>AS REPORTED</td>
</tr>
<tr>
<td>IDENTIFICATION</td>
<td>TO PASS TEST</td>
</tr>
<tr>
<td>RETEST DATE</td>
<td></td>
</tr>
<tr>
<td>DATE OF MANUFACTURE</td>
<td></td>
</tr>
<tr>
<td>APPEARANCE</td>
<td></td>
</tr>
<tr>
<td>RESIDUAL SOLVENTS</td>
<td>AS REPORTED</td>
</tr>
</tbody>
</table>

**Spectrum Chemical Mfg Corp**

**Corporate Headquarters:**  West Coast Facility:
769 Jersey Ave.  14422 S. San Pedro St.
New Brunswick, NJ 08901  Gardena, CA 90248
732.214.1300  310.516.8000
## Certificate Of Analysis

<table>
<thead>
<tr>
<th>Item Number</th>
<th>LE117</th>
<th>Lot Number</th>
<th>2KJ0335</th>
</tr>
</thead>
<tbody>
<tr>
<td>Item</td>
<td>Leucovorin Calcium, USP</td>
<td>Manufacturer Lot</td>
<td>100-21-4</td>
</tr>
<tr>
<td>CAS Number</td>
<td>1492-18-8</td>
<td>Manufacturer Code</td>
<td>15093</td>
</tr>
<tr>
<td>Molecular Formula</td>
<td>$C_{20}H_{21}CaN_7O_7$</td>
<td>Molecular Weight</td>
<td>511.50</td>
</tr>
</tbody>
</table>

### TEST

<table>
<thead>
<tr>
<th>TEST</th>
<th>SPECIFICATION</th>
<th>RESULT</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ASSAY (ANHYDROUS BASIS)</strong></td>
<td><strong>MIN</strong> 95.0</td>
<td>100.6%</td>
</tr>
<tr>
<td><strong>WATER DETERMINATION</strong></td>
<td>17.0 %</td>
<td>12.3%</td>
</tr>
<tr>
<td><strong>ORGANIC IMPURITIES:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5-FORMYL-5,6,7,8-TETRAHYDROPTEROIC ACID</td>
<td>0.5 %</td>
<td>0.0%</td>
</tr>
<tr>
<td>4-AMINOBENZOYLGlutamic ACID</td>
<td>1.5 %</td>
<td>0.0%</td>
</tr>
<tr>
<td>10-FORMYLDIHYDROFOLIC ACID</td>
<td>1.0 %</td>
<td>0.0%</td>
</tr>
<tr>
<td>5,10-DIFORMYLTETRAHYDROFOLIC ACID</td>
<td>1.5 %</td>
<td>0.0%</td>
</tr>
<tr>
<td>7,8-DIHYROFOLIC ACID</td>
<td>0.5 %</td>
<td>0.0%</td>
</tr>
<tr>
<td>10-FORMYLFOLIC ACID</td>
<td>0.5 %</td>
<td>0.0%</td>
</tr>
<tr>
<td>FOLIC ACID</td>
<td>1.5 %</td>
<td>0.0%</td>
</tr>
<tr>
<td>INDIVIDUAL UNSPECIFIED IMPURITY</td>
<td>0.3 %</td>
<td>0.0%</td>
</tr>
<tr>
<td>TOTAL IMPURITIES</td>
<td>2.5 %</td>
<td>0.0%</td>
</tr>
<tr>
<td>5-(y-FOLINOYL)TETRAHYDROFOLATE</td>
<td>0.3 %</td>
<td>0.0%</td>
</tr>
<tr>
<td>ELEMENTAL IMPURITIES</td>
<td>AS REPORTED</td>
<td>COMPLIES WITH STANDARD</td>
</tr>
<tr>
<td>IDENTIFICATION</td>
<td>TO PASS TEST</td>
<td>PASSES TEST</td>
</tr>
<tr>
<td>RETEST DATE</td>
<td>06-SEP-2023</td>
<td></td>
</tr>
<tr>
<td>DATE OF MANUFACTURE</td>
<td>06-SEP-2021</td>
<td></td>
</tr>
<tr>
<td>APPEARANCE</td>
<td>YELLOWISH -WHITE POWDER</td>
<td></td>
</tr>
<tr>
<td>RESIDUAL SOLVENTS</td>
<td>AS REPORTED</td>
<td></td>
</tr>
<tr>
<td>CLASS 3 (solvent) / ETHANOL</td>
<td>≤5000 PPM</td>
<td></td>
</tr>
</tbody>
</table>

Spectrum Chemical Mfg Corp  
755 Jersey Avenue  
New Brunswick 08901 NJ
All pharmaceutical ingredients are tested using current edition of applicable pharmacopeia.

Read and understand label and SDS before handling any chemicals. All Spectrum’s chemicals are for manufacturing, processing, repacking or research purposes by experienced personnel only. It is the customer’s responsibility to provide adequate hazardous material training and ensure that appropriate Personal Protective Equipment (PPE) is used before handling any chemical.

The Elemental Impurities standards implemented by USP and other Pharmaceutical Compendia reflect a growing understanding of the toxicology of trace levels of elemental impurities that can remain in drug substances originating from either raw materials or manufacturing processes. Identifying and quantifying impurities can be critical to predicting the best possible patient outcomes. Elemental Impurities has been a requirement of all products meeting USP/NF, EP and BP monographs since January 1, 2018. More information can be found in USP sections <232> Elemental Impurities – Limits and <233> Elemental Impurities – Procedures. Data for drug substances furnished by Spectrum Chemical Mfg. Corp can be used to ensure that patient daily exposures by oral administration to the selected elements are not exceeded in the formulation of pharmaceutical products.

Spectrum Chemical Mfg. Corp. repackages Active Pharmaceutical Ingredient chemicals provided by other manufacturers and suppliers. For traceability purposes, Spectrum’s Certificate of Analysis contains an identifier code unique to each manufacturer or supplier, as well as the chemical’s lot number provided on the original manufacturer Certificate of Analysis. This material is manufactured by GMT Fine Chemicals SA at Rue des îles 6, Couvet, 2108, Switzerland (CHE). Copies of the original Certificate of Analysis are available upon request from your Spectrum Sales Representative or by calling Spectrum’s Quality Department at 1-800-772-8786.
1. IDENTIFICATION

Product identifier

Product code: LE117
Product Name: LEUCOVORIN CALCIUM, USP

Other means of identification

Synonyms:
- Calcium 5-formyltetrahydrofolate
- Calcium leucovorin
- Folinic acid calcium salt
- (+)-L-Folinic acid, calcium salt
- Glutamic acid, N-p-((2-amino-5-formyl-5,6,7,8-tetrahydro-3-hydroxy-6-pteridinyl)methyl)amino)benzoyl)-, calcium salt (1:1), L-

CAS #: 1492-18-8
RTECS #: MA0600500
CI#: Not available

Recommended use of the chemical and restrictions on use

Recommended use: Drug. Medication.
Uses advised against: No information available

Supplier:
Spectrum Chemical Mfg. Corp
14422 South San Pedro St.
Gardena, CA 90248
(310) 516-8000

Order Online At: https://www.spectrumchemical.com
Emergency telephone number: Chemtrec 1-800-424-9300
Contact Person: Tom Tyner (USA - West Coast)
Contact Person: Ibad Tirmiz (USA - East Coast)

2. HAZARDS IDENTIFICATION

Classification

This chemical is considered hazardous by the 2012 OSHA Hazard Communication Standard (29 CFR 1910.1200)

Not a dangerous substance or mixture according to the Globally Harmonized System (GHS)

<table>
<thead>
<tr>
<th>Label elements</th>
<th>Category</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin corrosion/irritation</td>
<td>Category 2</td>
</tr>
<tr>
<td>Serious eye damage/eye irritation</td>
<td>Category 2A</td>
</tr>
<tr>
<td>Specific target organ toxicity (single exposure)</td>
<td>Category 3</td>
</tr>
</tbody>
</table>

Warning

Hazard statements
Hazards not otherwise classified (HNOC)
Not Applicable

Other hazards
Not available

Precautionary Statements - Prevention
Wear protective gloves
Wear eye/face protection
Avoid breathing dust/fume/gas/mist/vapors/spray
Use only outdoors or in a well-ventilated area
Wash face, hands and any exposed skin thoroughly after handling

Precautionary Statements - Response
IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. If eye irritation persists: Get medical advice/attention.
IF ON SKIN: Wash with plenty of water
If skin irritation occurs: Get medical advice/attention
Take off contaminated clothing and wash it before reuse
IF INHALED: Remove person to fresh air and keep comfortable for breathing. Call a POISON CENTER or doctor/physician if you feel unwell.

Precautionary Statements - Storage
Store in a well-ventilated place. Keep container tightly closed
Store locked up

Precautionary Statements - Disposal
Dispose of contents/container to an approved waste disposal plant

3. COMPOSITION/INFORMATION ON INGREDIENTS

<table>
<thead>
<tr>
<th>Component</th>
<th>CAS No</th>
<th>Weight-%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leucovorin Calcium</td>
<td>1492-18-8</td>
<td>100</td>
</tr>
</tbody>
</table>

4. FIRST AID MEASURES

First aid measures

General Advice: National Capital Poison Center in the United States can provide assistance if you have a poison emergency and need to talk to a poison specialist. Call 1-800-222-1222.

Skin Contact: Wash off immediately with soap and plenty of water removing all contaminated clothing and shoes. Get medical attention. If skin irritation persists, call a physician.

Eye Contact: Flush eyes with water for 15 minutes. Get medical attention.

Product code: LE117  Product name: LEUCOVORIN CALCIUM, USP
**Inhalation:**
Move to fresh air. If not breathing, give artificial respiration. If breathing is difficult, give oxygen. Get medical attention.

**Ingestion:**
Do not induce vomiting without medical advice. Never give anything by mouth to an unconscious person. Consult a physician if necessary.

**Most important symptoms and effects, both acute and delayed**

**Symptoms**
- Causes serious eye irritation
- Causes skin irritation
- Irritating to respiratory system
- May cause nausea and vomiting
- May cause diarrhea
- May cause constipation
- May cause flushing of the facial skin
- Lightheadedness
- Dizziness
- Fainting
- Fatigue
- May cause alopecia (hair loss)
- Sores inside mouth or on lips

**Indication of any immediate medical attention and special treatment needed**

**Notes to Physician:**
Treat symptomatically.

**Protection of first-aiders**
First-Aid Providers: Avoid exposure to blood or body fluids. Wear gloves and other necessary protective clothing. Dispose of contaminated clothing and equipment as bio-hazardous waste.

---

### 5. FIRE-FIGHTING MEASURES

**Extinguishing Media**

**Suitable Extinguishing Media:**
Dry chemical. Carbon dioxide (CO2). Water spray, mist, or foam.

**Unsuitable Extinguishing Media:**
No information available.

**Specific hazards arising from the chemical**

**Hazardous combustion products**
carbon oxides. Nitrogen oxides (NOx). Calcium oxides.

**Specific hazards**
May be combustible at high temperatures. Fire may produce irritating and/or toxic gases.

**Special Protective Actions for Firefighters**

**Specific Methods:**
No information available

**Special Protective Equipment for Firefighters:**
As in any fire, wear self-contained breathing apparatus pressure-demand, MSHA/NIOSH (approved or equivalent) and full protective gear.
6. ACCIDENTAL RELEASE MEASURES

Personal precautions, protective equipment and emergency procedures

Personal Precautions: Ensure adequate ventilation. Keep people away from and upwind of spill/leak. Use personal protective equipment. Avoid contact with skin, eyes and clothing. Evacuate personnel to safe areas. Avoid breathing dust. Avoid dust formation. Remove all sources of ignition. All equipment used when handling the product must be grounded.

Environmental precautions: Prevent further leakage or spillage if safe to do so. Prevent product from entering drains. Prevent entry into waterways, sewers, basements or confined areas.

Methods and material for containment and cleaning up

Methods for containment: Stop leak if you can do it without risk. Cover with plastic sheet to prevent spreading.

Methods for cleaning up: Sweep up and shovel. Use appropriate tools to put the spilled material in a suitable chemical waste disposal container. Clean contaminated surface thoroughly.

7. HANDLING AND STORAGE

Precautions for safe handling

Technical Measures/Precautions: Provide sufficient air exchange and/or exhaust in work rooms. Avoid dust formation. Keep away from incompatible materials.

Safe Handling Advice: Wear personal protective equipment. Avoid contact with skin, eyes and clothing. Avoid dust formation. Do not ingest. Do not breathe dust. Keep away from heat and sources of ignition. Handle in accordance with good industrial hygiene and safety practice.

Conditions for safe storage, including any incompatibilities


Incompatible Materials: Oxidizing agents

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Control parameters

National occupational exposure limits

United States

<table>
<thead>
<tr>
<th>Component</th>
<th>CAS No</th>
<th>OSHA</th>
<th>NIOSH</th>
<th>ACGIH</th>
<th>AIHA WEEL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leucovorin Calcium</td>
<td>1492-18-8</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
</tbody>
</table>

Canada

<table>
<thead>
<tr>
<th>Component</th>
<th>CAS No</th>
<th>Canada - Alberta</th>
<th>Canada - British Columbia</th>
<th>Canada - Ontario</th>
<th>Canada - Quebec</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leucovorin Calcium</td>
<td>1492-18-8</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
</tbody>
</table>
Appropriate engineering controls

Engineering measures to reduce exposure: Ensure adequate ventilation. Use process enclosures, local exhaust ventilation, or other engineering controls to keep airborne levels below recommended exposure limits. If user operations generate dust, fume or mist, use ventilation to keep exposure to airborne contaminants below the exposure limit.

Individual protection measures, such as personal protective equipment

Personal Protective Equipment

Eye protection: Safety glasses with side-shields. or Goggles

Skin and body protection: Chemical resistant apron
Long sleeved clothing
Gloves

Respiratory protection: Effective dust mask. or. Wear respirator with dust filter. Use a dust respirator under conditions where exposure to the substance is apparent (e.g. generation of high concentration of dust (dust clouds), inadequate ventilation, development of respiratory tract irritation), and engineering controls are not feasible. Be sure to use an approved/certified respirator or equivalent.

Hygiene measures: Avoid contact with skin, eyes and clothing. When using, do not eat, drink or smoke. Wash hands before breaks and immediately after handling the product.

9. PHYSICAL AND CHEMICAL PROPERTIES

<table>
<thead>
<tr>
<th>Physical state:</th>
<th>Appearance:</th>
<th>Color:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Solid</td>
<td>Powder</td>
<td>White to yellowish.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Odor:</th>
<th>Taste</th>
<th>Formula</th>
</tr>
</thead>
<tbody>
<tr>
<td>Odorless</td>
<td>No information available</td>
<td>C20H21CaN7O7</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Molecular/Formula weight (g/mole):</th>
<th>Flammability (solid, gas)</th>
<th>Flashpoint (°C/°F):</th>
</tr>
</thead>
<tbody>
<tr>
<td>511.50</td>
<td>no data available</td>
<td>No information available</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Flash Point Tested according to:</th>
<th>Autoignition Temperature (°C/°F):</th>
<th>Lower Explosion Limit (%):</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not available</td>
<td>No information available</td>
<td>No information available</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Upper Explosion Limit (%):</th>
<th>Melting point/range(°C/°F):</th>
<th>Decomposition temperature(°C/°F):</th>
</tr>
</thead>
<tbody>
<tr>
<td>No information available</td>
<td>No information available</td>
<td>240-250°C/464-482°F</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Boiling point/range(°C/°F):</th>
<th>Bulk density:</th>
<th>Density (g/cm3):</th>
</tr>
</thead>
<tbody>
<tr>
<td>No information available</td>
<td>No information available</td>
<td>No information available</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Specific gravity:</th>
<th>pH</th>
<th>Vapor pressure @ 20°C (kPa):</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5</td>
<td>6.8-8.0 (2.5%)</td>
<td>No information available</td>
</tr>
</tbody>
</table>

| Evaporation rate: | |
|------------------| |
| |

Product code: LE117  
Product name: LEUCOVORIN CALCIUM, USP
10. STABILITY AND REACTIVITY

Reactivity
Reactive with oxidizing agents

Chemical stability

Stability: Sensitive to light. Exposure to light accelerates decomposition. Stable under recommended storage conditions.

Possibility of Hazardous Reactions: Hazardous polymerization does not occur


Incompatible Materials: Oxidizing agents

Hazardous decomposition products:
Carbon oxides. Calcium oxides. Nitrogen oxides (NOx).

Other Information
Corrosivity: Non-corrosive in presence of glass.

Special Remarks on Corrosivity: No information available

11. TOXICOLOGICAL INFORMATION

Information on likely routes of exposure

Principal Routes of Exposure: Ingestion. Inhalation. Skin. Eyes.

Acute Toxicity

Component Information

<table>
<thead>
<tr>
<th>Component</th>
<th>CAS No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leucovorin Calcium</td>
<td>1492-18-8</td>
</tr>
<tr>
<td>LD50/oral/rat</td>
<td>&gt; 8 g/kg Oral LD50 Rat</td>
</tr>
<tr>
<td>LD50/oral/mouse</td>
<td>&gt; 7 g/kg oral LD50 mouse</td>
</tr>
<tr>
<td>LD50/dermal/rabbit</td>
<td>No information available</td>
</tr>
<tr>
<td>LD50/dermal/rat</td>
<td>No information available</td>
</tr>
<tr>
<td>LC50/inhalation/rat</td>
<td>No information available</td>
</tr>
<tr>
<td>LC50/inhalation/mouse</td>
<td>No information available</td>
</tr>
<tr>
<td>Other LD50 or LC50 information</td>
<td>No information available</td>
</tr>
</tbody>
</table>
Product Information

LD50/oral/rat =
Value - Acute Tox = > 8000 mg/kg

LD50/oral/mouse =
Value - Acute Tox Oral = 7000 mg/kg

LD50/dermal/rabbit
Value - Acute Tox = No information available

LD50/dermal/rat
VALUE - Acute Tox Dermal = No information available

LC50/inhalation/rat
VALUE-Vapor = No information available
VALUE-Gas = No information available
VALUE-Dust/Mist = No information available

LC50/Inhalation/mouse
VALUE-Vapor = No information available
VALUE - Gas = No information available
VALUE - Dust/Mist = No information available

Symptoms

Skin Contact:
Causes skin irritation. Moderate skin irritation.

Eye Contact:
Causes serious eye irritation. Moderately irritating to the eyes.

Inhalation
Irritating to respiratory system.

Ingestion
Ingestion may cause nausea, vomiting, diarrhea. May cause facial flushing. May cause weakness. May cause fainting. May cause fatigue.

Aspiration hazard
No information available.

Delayed and immediate effects as well as chronic effects from short and long-term exposure

Chronic Toxicity
No information available.

Sensitization:
No information available.

Mutagenic Effects:
No information available

Carcinogenic effects:
Not considered carcinogenic.

<table>
<thead>
<tr>
<th>Component</th>
<th>CAS No</th>
<th>IARC</th>
<th>ACGIH - Carcinogens</th>
<th>NTP</th>
<th>OSHA HCS - Carcinogens</th>
<th>Australia - Notifiable Carcinogenic Substances</th>
<th>Australia - Prohibited Carcinogenic Substances</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leucovorin Calcium</td>
<td>1492-18-8</td>
<td>Not listed</td>
<td>Not listed</td>
<td>Not listed</td>
<td>Not listed</td>
<td>Not listed</td>
<td>Not listed</td>
</tr>
</tbody>
</table>

ACGIH (American Conference of Governmental Industrial Hygienists)

IARC (International Agency for Research on Cancer)

Product code: LE117
Product name: LEUCOVORIN CALCIUM, USP
Reproductive toxicity: No data is available

Reproductive Effects: No information available
Developmental Effects: No information available
Teratogenic Effects: No information available

Specific Target Organ Toxicity

STOT - single exposure: respiratory system.
STOT - repeated exposure: No information available.
Target Organs: Respiratory system.

12. ECOLOGICAL INFORMATION

Ecotoxicity

Ecotoxicity effects: No data available.

Persistence and degradability: No information available

Bioaccumulative potential: No information available.

Mobility in soil: No information available
Other adverse effects: No information available.

13. DISPOSAL CONSIDERATIONS

Disposal Methods

Waste from residues / unused products:
Waste must be disposed of in accordance with Federal, State and Local regulation.

Contaminated packaging:
Empty containers should be taken for local recycling, recovery or waste disposal

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Leucovorin Calcium</td>
<td>1492-18-8</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
</tbody>
</table>

14. TRANSPORT INFORMATION

DOT

UN-No: Not Regulated
Proper Shipping Name: No information available
Hazard Class: No information available
Subsidiary Class: No information available
Packing group: No information available
Emergency Response Guide Number: No information available
Marine Pollutant: No data available
15. REGULATORY INFORMATION

International Inventories

Product code: LE117  Product name: LEUCOVORIN CALCIUM, USP
<table>
<thead>
<tr>
<th>Component</th>
<th>CAS No</th>
<th>U.S. TSCA</th>
<th>KOREA KECL</th>
<th>Philippines (PICCS)</th>
<th>Japan ENCS</th>
<th>China IECSC</th>
<th>Australia AICS</th>
<th>EINECS-No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leucovorin Calcium</td>
<td>1492-18-8</td>
<td>Not Listed</td>
<td>Present KE-17067</td>
<td>Not present</td>
<td>Not present</td>
<td>Not listed</td>
<td>Present</td>
<td>216-082-8</td>
</tr>
</tbody>
</table>

**U.S. Regulations**

**California Prop. 65: Safe Drinking Water and Toxic Enforcement Act of 1986.**

**Chemicals Known to the State of California to Cause Cancer:**
This product does not contain a chemical requiring a warning under California Prop. 65. (See table below)

**Chemicals Known to the State of California to Cause Reproductive Toxicity:**
This product does not contain a chemical requiring a warning under California Prop. 65. (See table below)

<table>
<thead>
<tr>
<th>Component</th>
<th>CAS No</th>
<th>Carcinogen</th>
<th>Developmental Toxicity</th>
<th>Male Reproductive Toxicity</th>
<th>Female Reproductive Toxicity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leucovorin Calcium</td>
<td>1492-18-8</td>
<td>Not Listed</td>
<td>Not Listed</td>
<td>Not Listed</td>
<td>Not Listed</td>
</tr>
</tbody>
</table>

**CERCLA/SARA**

<table>
<thead>
<tr>
<th>Component</th>
<th>CAS No</th>
<th>CERCLA - Hazardous Substances and their Reportable Quantities</th>
<th>Section 302 Extremely Hazardous Substances and TPQs</th>
<th>Section 302 Extremely Hazardous Substances and RQs</th>
<th>Section 313 - Chemical Category</th>
<th>Section 313 - Reporting de minimis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leucovorin Calcium</td>
<td>1492-18-8</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
</tbody>
</table>

**U.S. TSCA**

<table>
<thead>
<tr>
<th>Component</th>
<th>CAS No</th>
<th>TSCA Section 5(a)2 - Chemicals With Significant New Use Rules (SNURS)</th>
<th>TSCA 8(d) - Health and Safety Reporting</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leucovorin Calcium</td>
<td>1492-18-8</td>
<td>Not Applicable</td>
<td>Not Applicable</td>
</tr>
</tbody>
</table>

**Canada**

**WHIMIS 2015 - GHS Classifications**

The WHMIS 2015 classification of this product has not been validated or reviewed yet.

**Canada Hazardous Products Regulation**
This product has been classified according to the hazard criteria of the HPR (Hazardous Products Regulation) and the SDS contains all of the information required by the HPR.

**DSL/NDSL**

<table>
<thead>
<tr>
<th>Component</th>
<th>CAS No</th>
<th>Canada (DSL)</th>
<th>Canada (NDSL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leucovorin Calcium</td>
<td>1492-18-8</td>
<td>Not Listed</td>
<td>Not Listed</td>
</tr>
</tbody>
</table>

**Component**

<table>
<thead>
<tr>
<th>Component</th>
<th>CAS No</th>
<th>CEPA Schedule I - Toxic Substances</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leucovorin Calcium</td>
<td>1492-18-8</td>
<td>Not listed</td>
</tr>
<tr>
<td>Component</td>
<td>CAS No</td>
<td>CEPA - 2010 Greenhouse Gases Subject to Mandatory Reporting</td>
</tr>
<tr>
<td>Leucovorin Calcium</td>
<td>1492-18-8</td>
<td>Not listed</td>
</tr>
</tbody>
</table>

**Product code:** LE117  **Product name:** LEUCOVORIN CALCIUM, USP
### EU Classification

EU GHS - SV - CLP 1272/2008

<table>
<thead>
<tr>
<th>Component</th>
<th>CAS No</th>
<th>EU GHS - SV - CLP (1272/2008)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leucovorin Calcium</td>
<td>1492-18-8</td>
<td></td>
</tr>
</tbody>
</table>

#### R-phrase(s)

R36/37/38 - Irritating to eyes, respiratory system and skin  
R42/43 - May cause sensitization by inhalation and skin contact

#### S-phrase(s)

none

<table>
<thead>
<tr>
<th>Component</th>
<th>CAS No</th>
<th>Classification</th>
<th>Concentration Limits:</th>
<th>Safety Phrases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leucovorin Calcium</td>
<td>1492-18-8</td>
<td></td>
<td></td>
<td>No information</td>
</tr>
</tbody>
</table>

The product is classified in accordance with Annex VI to Directive 67/548/EEC

### Indication of danger:

Xi - Irritant

![Xi](image)

### 16. OTHER INFORMATION

**Preparation Date:** 8/12/2015  
**Revision date:** 3/15/2019  
**Prepared by:** Sonia Owen

**Disclaimer:**  
All chemicals may pose unknown hazards and should be used with caution. This Safety Data Sheet (SDS) applies only to the material as packaged. If this product is combined with other materials, deteriorates, or becomes contaminated, it may pose hazards not mentioned in this SDS. The physical properties reported in this SDS are obtained from the literature and do not constitute product specifications. Information contained herein does not constitute a warranty, whether expressed or implied, as to the safety, merchantability or fitness of the goods for a particular purpose. Spectrum Chemicals & Laboratory Products, Inc. assumes no responsibility for results obtained or for incidental or consequential damages, including lost profits, arising from the use of these data. No warranty against infringement of any patent, copyright or trademark is made or implied. It shall be the user's responsibility to develop proper methods of handling and personal protection based on the actual conditions of use. While this SDS is based on technical data judged to be reliable, Spectrum assumes no responsibility for the completeness or accuracy of the information contained herein.

End of Safety Data Sheet

**Product code:** LE117  
**Product name:** LEUCOVORIN CALCIUM, USP

---

**Page**
Certification of Compliance with current Good Manufacturing Practices

Dear Valued Customer:

Spectrum Chemical Mfg Corp certifies that the following product(s) is produced, processed, packaged and held in compliance with current Good Manufacturing Practices (cGMP) in accordance with the applicable parts of 21 CFR, parts 210 and 211 of the Code of Federal Regulations.

<table>
<thead>
<tr>
<th>Catalog Number</th>
<th>Product Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>LE117</td>
<td>Leucovorin Calcium, USP</td>
</tr>
</tbody>
</table>

Spectrum is an FDA registered and inspected Drug Establishment. Our United States Food and Drug Administration (USFDA) Registration numbers are as follows:

Spectrum-Gardena, CA: 2020632
Spectrum-New Brunswick, NJ: 2246824

Thank you for your interest in Spectrum products. If we may be of further assistance, please feel free to contact the Quality Assurance department at 310-516-8000 or via email at qualityassurance@spectrumchemical.com

Sincerely,

Oralia Chavez
Quality Assurance Specialist
Manufacturing Process Flowchart
Leucovorin Calcium, USP (Cat# LE117)

Folic Acid

Reduction

Tetrahydrofolate Acid

Formulation Salification

Raw Leucovorin Calcium

Crystallization

Leucovorin Calcium
LE117, Leucovorin Calcium, USP

Source Statement
The above mentioned catalog item is manufactured by chemical synthesis. No animal or plant derived products are used in the manufacturing process.

BSE/TSE Statement
The above mentioned catalog item does not contain nor is manufactured using any animal derived products and is therefore, BSE/TSE free.

Allergen Statement
The above mentioned catalog item does not contain any of the following:

- Milk
- Egg
- Fish
- Shellfish
- Tree Nuts
- Wheat
- Peanuts
- Soy
- Cereals containing Gluten
- Celery
- Mustard
- Sesame Seed
- Corn
- Latex
- Sulfites > 10 ppm

EU Fragrance Allergen Statement
The above mentioned catalog item does not contain any of the 26 EU fragrance allergens listed in Annex III lines 67-92. These substances are not intentionally added to the above mentioned catalog item and therefore are not expected to be present.

GMO Statement
The above mentioned catalog item is manufactured without the use of genetically modified organisms and is therefore GMO free.

Melamine Statement
The above mentioned catalog does not use or add melamine to the manufacturing process and is considered melamine-free.
Nitrosamine Statement

Based on knowledge of the manufacturing process, nitrosamine impurities are not known or suspected to be present in this material.

Animal Testing Statement

The above mentioned catalog item has not been tested on animals.

Organic Compliance Statement

The above mentioned catalog item has not been produced using GMOs, irradiation, ethylene oxide (EtO) or sewage sludge.

Shelf Life Statement

The above mentioned catalog item is typically assigned a shelf life of 24 months from the date of manufacture. The actual assigned shelf life for any specific lot should be referenced on the Certificate of Analysis.

Other Chemicals Statement

Spectrum does not have any reason to suspect the above mentioned catalog item contains any of the following chemicals. This product does not come into contact with these chemicals during packaging or storage:

- Aflatoxins
- Antibiotics
- Bisphenol A (BPA)
- CMR Substances
- Parabens
- Pesticides
- Phthalates
- Preservatives
RE: Elemental Impurities - Leucovorin Calcium, USP (Cat# LE117)

To Whom It May Concern:

Thank you for your interest in Spectrum high quality chemicals.

The above material complies with the USP<232>, <233> Elemental Impurities and the ICH Q3D Elemental Impurities Guideline. The following elemental impurities are likely to be present:

<table>
<thead>
<tr>
<th>Elemental Impurity</th>
<th>Class</th>
<th>Expected Concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tin</td>
<td>Sn</td>
<td>&lt; 2 ppm</td>
</tr>
</tbody>
</table>

Other elemental impurities considered by USP <232>, <233> and ICH Q3D which are not addressed in the above mentioned table are not likely to be present. These substances are not used in the production process, are not intentionally added or known to be present in the above mentioned material.

This information is subject to change and is intended for risk assessment only. It is responsibility of the end user to evaluate suitability of any chemical for the intended use as well as to assess compound-specific limits of daily intake of metal impurities. For lot-specific information, please refer to the respective Certificate of Analysis.

If you have any further questions, please contact us by telephone at 1(800)772-8786 Option 2, or by email at TechServices@spectrumchemical.com.

Sincerely,

Technical Services
Spectrum Chemical Mfg. Corp.

This document has been produced electronically and is valid without a signature.
To Whom It May Concern:

Thank you for your interest in Spectrum high quality chemicals.

The above mentioned catalog item complies with the requirements of USP <467> Residual Solvents and ICH Q3C Residual Solvents Guideline. The following solvents are likely to be present:

<table>
<thead>
<tr>
<th>Residual Solvent</th>
<th>Class</th>
<th>Expected Concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ethanol</td>
<td>3</td>
<td>&lt; 5000 pmm</td>
</tr>
</tbody>
</table>

No Class 1, Class 2 or other solvents are used or produced in the manufacturing process of this material.

For lot-specific information, please refer to the respective Certificate of Analysis.

If you have any further questions, please contact us by telephone at 1(800)772-8786 Option 2, or by email at TechServices@spectrumchemical.com.

Sincerely,

Technical Services
Spectrum Chemical Mfg. Corp.

This document has been produced electronically and is valid without a signature.
Leucovorin Calcium
(Folinic Acid Calcium Salt)
USP
CAS 1492-18-8

C₂₀H₂₁CaN₇O₇  F.W. 511.50

Assay (Anhydrous Basis) ........................................................95.0-105.0%
Water Determination ..........................................................................17.0%
Organic Impurities:
5-Formyl-5,6,7,8-tetrahydropteroic Acid ...........................................0.5%
4-Aminobenzoylglutamic Acid ...........................................................1.5%
5,10-Diformyltetrahydrofolic Acid  ....................................................1.5%
5-Formylfolic Acid ...........................................................................0.5%
Folic Acid ...........................................................................................1.5%
Individual Unspecified Impurity ...........................................................0.3%
Total Impurities .................................................................................2.5%
5-(y-Folinoyl)tetrahydrofolate...............................................................0.3%
Elemental Impurities ................................................................ As reported
Residual Solvents .....................................................................To pass test

WARNING: Cancer and Reproductive Harm- www.P65Warnings.ca.gov

KEEP FROM CHILDREN

G 16/J8GHS-A          G 16/J8GHS-A
Lot No. XQ####

The Spectrum label presents technical and safety information in an easily understood format. Our technical specialists stay abreast of the latest requirements of the Globally Harmonized System for Classification and Labelling of Chemicals (GHS), as well as the Occupational Safety and Health Administration (OSHA), the Food and Drug Administration (FDA) and other government regulatory agencies in order to ensure compliance, accuracy and concise hazard communication. Below you will find a typical label example for this catalog item.
RE: Lot Numbering System

Dear Valued Customer:

This letter is to inform you of Spectrum Chemicals and Laboratory Products’ Lot Numbering System. The system is based on an alpha-numerical sequence which provides the month, year and location of production.

The lot numbering system utilized until 2010 is a sequence of six characters, two letters followed by four numbers. The first letter represents the year, for example, Y denotes 2009 and Z denotes 2010. The second letter represents the month and site, for example, A-L denotes January through December at Spectrum’s Gardena, CA facility, while M-X denotes January through December at the New Brunswick, NJ facility. The following four numbers are sequentially assigned.

Example: ZI0928 = The 928th material produced in California in September 2010

The lot numbering system utilized for 2011 and forward, is a sequence of seven characters. The first character, a number, represents the production facility:

1 = Gardena, CA Facility
2 = New Brunswick, NJ Facility
3 = China Facility
4 = Pharmacy, NJ Facility

The second character, a letter, represents the year. For example, A denotes 2011 and B denotes 2012. The third character, a letter, represents the month, with A denoting January and L denoting December. The following four numbers are sequentially assigned.

Example: 2AA0706 = The 706th material produced in New Jersey in January 2011

Thank you for your interest with Spectrum products. Please feel free to contact us at 310-516-8000 or via email at quality_assurance@spectrumchemical.com if we may be of further assistance.

Sincerely,

Oralia Chavez,
Quality Assurance Specialist