LEUCOVORIN CALCIUM INJECTION, USP
LEUCOVORIN CALCIUM FOR INJECTION

Leucovorin is a water-soluble vitamin of the folic acid and vitamin B12 family. It is sometimes referred to as calcium levulinate or calcium l-levulinate. Leucovorin is synthesized by bacteria in the intestines. It is also found in foods such as yeast, liver, and spinach. Leucovorin is used in increased amounts when the body's ability to produce folic acid is decreased. This may occur in patients with: poor diets or inadequate intake of folic acid; malabsorption syndromes secondary to the lack of vitamin B12; use of some antibiotics; certain forms of cancer; or having symptoms of gastrointestinal toxicity of any severity, until those symptoms improve.

PHARMACOKINETICS

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INDICATIONS AND USAGE

Leucovorin calcium is indicated for use in combination with fluoropyrimidines, including 5-fluorouracil (5-FU), to reduce the frequency and severity of fluoro-uracil-induced mucositis. Leucovorin calcium is also indicated for use in combination with 5-fluorouracil to prolong survival in the palliative treatment of patients with advanced colorectal cancer. Leucovorin is also indicated for use in combination with 5-fluorouracil to prolong survival in the palliative treatment of patients with advanced colorectal cancer. Leucovorin is also indicated for use in combination with 5-fluorouracil to prolong survival in the palliative treatment of patients with advanced colorectal cancer. Leucovorin is also indicated for use in combination with 5-fluorouracil to prolong survival in the palliative treatment of patients with advanced colorectal cancer.

CONTRAINDICATIONS

Leucovorin calcium is contraindicated in patients who have symptoms of gastrointestinal toxicity of any severity, until those symptoms improve.

WARNINGS

Monitoring of the serum methotrexate concentration is essential in determining the duration of treatment with leucovorin. The concomitant use of leucovorin with trimethoprim-sulfamethoxazole for the acute treatment of Pneumocystis carinii pneumonia in patients with HIV infection has been associated with increased rates of methotrexate toxicity and mortality in patients receiving concurrent methotrexate.
Pregnancy: Leucovorin is not contraindicated in pregnancy. However, because many drugs are excreted in human milk, caution should be exercised when Leucovorin is administered to a nursing mother. Leucovorin may enhance the toxicity of 5-fluorouracil (see Drug Interactions).

The following table summarizes significant adverse events occurring in 316 patients treated with the leucovorin/5-fluorouracil combinations compared against 70 patients treated with 5-fluorouracil alone for advanced colorectal carcinoma.

<table>
<thead>
<tr>
<th>Grade</th>
<th>Leucovorin/5-fluorouracil (%)</th>
<th>5-fluorouracil (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 1</td>
<td>22</td>
<td>22</td>
</tr>
<tr>
<td>Grade 2</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Grade 3</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

An allergic sensitization, including anaphylactoid reactions and urticaria, has been reported with leucovorin. Leucovorin 10 mg/m² should be administered IV, IM, or PO every 15 minutes until the desired serum methotrexate level is achieved. If toxicity occurs, leucovorin should be administered until the serum methotrexate level decreases to below 1 mg/mL. Hydration (3 L/d) and urinary alkalinization with sodium bicarbonate solution should be provided (see Hydration and urinary alkalinization). Leucovorin should not be mixed in the same infusion as 5-fluorouracil to avoid the formation of a precipitate.

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Leucovorin Dosage: Leucovorin is administered at 200 mg/m² by slow intravenous injection over a minimum of 3 minutes, followed by 5-fluorouracil at 370 mg/m² by intravenous injection. Either of the following two regimens is recommended:

1. Leucovorin is administered at 200 mg/m² by slow intravenous injection followed by 5-fluorouracil at 370 mg/m² by intravenous injection. Leucovorin and 5-fluorouracil should be administered separately to avoid the formation of a precipitate.

2. 5-fluorouracil and leucovorin should be administered separately to avoid the formation of a precipitate.

Leucovorin should be given to a pregnant woman only if clearly needed.

WARNINGS

Drug Interactions: Leucovorin and 5-fluorouracil should be administered separately to avoid the formation of a precipitate.