



Nonprofit corporations and independent licensees
of the Blue Cross and Blue Shield Association

Medical benefit drug policies are a source for BCBSM and BCN medical policy information only. These documents are not to be used to determine benefits or reimbursement. Please reference the appropriate certificate or contract for benefit information. This policy may be updated and therefore subject to change.

RETIRED
Effective Date: 04/16/2021

Fusilev® (levoleucovorin)

FDA approval: 1952 (d, l-leucovorin), 2008 (levoleucovorin)

HCPCS: J0641

Benefit: Medical

Policy:

Requests must be supported by submission of chart notes and patient specific documentation.

- A. Coverage of the requested drug is provided when all the following are met:
 - a. Patient must meet one of the following criteria:
 - i. Using for rescue after high-dose methotrexate therapy in osteosarcoma
 - ii. Using to diminish the toxicity and counteract the effects of impaired methotrexate elimination and inadvertent overdosage of folic acid antagonists
 - iii. Using in combination with 5-fluorouracil in the palliative treatment of patients with advanced metastatic colorectal cancer
 - b. Leucovorin is under shortage, which has been identified by the Food and Drug Administration (FDA) and no other alternative therapies are appropriate
 - c. Prescribed by or in consultation with an oncologist
 - d. Trial and failure of a generic levoleucovorin product
- B. Quantity Limitations, Authorization Period and Renewal Criteria
 - a. Quantity Limits: Align with FDA recommended dosing
 - b. Authorization Period: 6 months at a time
 - c. Renewal Criteria:
 - i. Member must fit one of these criteria:
 - 1. Receiving high dose methotrexate therapy
 - 2. Experiencing toxic serum levels of methotrexate
 - 3. Receiving combination chemotherapy with 5-fluorouracilAND
 - ii. For high dose methotrexate therapy or toxic serum levels of methotrexate, physician must include documentation of:
 - 1. Patients serum creatinine levels
 - 2. Daily methotrexate levels greater than 0.05 micromolar
 - 3. Urinary pH of 7 or higherAND

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iii. Continued leucovorin shortage

***Note: Coverage may differ for Medicare Part B members based on any applicable criteria outlined in Local Coverage Determinations (LCD) or National Coverage Determinations (NCD) as determined by Center for Medicare and Medicaid Services (CMS). See the CMS website at <http://www.cms.hhs.gov/>. Determination of coverage of Part B drugs is based on medically accepted indications which have supported citations included or approved for inclusion determined by CMS approved compendia.

Therapeutic considerations:

A. FDA approved indication/Diagnosis

**Please refer to most recent prescribing information.*

B. Background Information

- a. Fusilev is a folate analog indicated for:
 - i. Rescue after high-dose methotrexate therapy in osteosarcoma
 - ii. Diminishing the toxicity and counteracting the effects of impaired methotrexate elimination and of inadvertent overdosage of folic acid antagonists
 - iii. Use in combination chemotherapy with 5-fluorouracil in the palliative treatment of patients with advanced metastatic colorectal cancer
- b. Fusilev rescue therapy should begin as soon as possible following inadvertent overdosage and within 24 hours of methotrexate administration when there is delayed excretion. As the time interval between antifolate administration and Fusilev rescue increases, Fusilev's effectiveness in counteracting toxicity may decrease. Fusilev should be administered every 6 hours until the serum methotrexate level is less than 10^{-8} M. Serum creatinine and methotrexate levels should be determined at 24 hour intervals. If the 24 hour serum creatinine has increased 50% over baseline or if the 24 hour methotrexate level is greater than 5×10^{-6} M or the 48 hour level is greater than 9×10^{-7} M, the dose of Fusilev should be increased to 50 mg/m² IV every 3 hours until the methotrexate level is less than 10^{-8} M. Hydration and urinary alkalinization with bicarbonate should be employed concomitantly. The bicarbonate dose should be adjusted to maintain the urine pH at 7.0 or greater.
- c. The 2021 National Comprehensive Cancer Network colon cancer guidelines recommend the use of levoleucovorin only at times of a leucovorin shortage. Neither product has been shown to be superior to one another and, as noted in the guidelines, leucovorin provides better value than levoleucovorin. A dose of 200 mg/m² levoleucovorin is equivalent to 400 mg/m² leucovorin.
- d. There are many generically available levoleucovorin medications for use as rescue after high-dose methotrexate therapy, to decrease toxicity and counteract the effects of impaired methotrexate elimination and inadvertent overdosage of folic acid antagonists, and in combination with 5-fluorouracil in patients with colorectal cancer. These treatments options provide the best value.

C. Efficacy

**Please refer to most recent prescribing information.*

D. Medication Safety Considerations

**Please refer to most recent prescribing information.*

E. Dosing and administration

**Please refer to most recent prescribing information.*

F. How supplied

**Please refer to most recent prescribing information.*

References:

1. Fusilev [prescribing information]. Irvine, CA: Spectrum Pharmaceuticals, Inc.; April 2011.
2. National Comprehensive Cancer Network. Colon cancer (Version 2.2021). 2021 Jan 21. Available at: https://www.nccn.org/professionals/physician_gls/pdf/colon.pdf. Accessed on February 1, 2021.
3. Chuang VT & Suno M. Levoleucovorin as replacement for leucovorin in cancer treatment. Ann Pharmacoth. 2012; 46: 1349 - 57.

Policy History												
#	Date	Change Description										
2.0	Effective Date: 04/16/2022	Retiring Fusilev policy.										
1.9	Effective Date: 04/08/2021	Updated to add a quantity limit										
1.8	Effective Date: 12/01/2020	PA added to BCBS <table><tr><th>Line of Business</th><th>PA Required (Yes/No)</th></tr><tr><td>BCBS</td><td>Yes</td></tr><tr><td>BCN</td><td>Yes</td></tr><tr><td>MAPPO</td><td>Yes</td></tr><tr><td>BCNA</td><td>Yes</td></tr></table>	Line of Business	PA Required (Yes/No)	BCBS	Yes	BCN	Yes	MAPPO	Yes	BCNA	Yes
Line of Business	PA Required (Yes/No)											
BCBS	Yes											
BCN	Yes											
MAPPO	Yes											
BCNA	Yes											
1.7	Effective Date: 4/16/2020	Annual Review										
1.6	Effective Date: 01/01/2020	PA added to MAPPO and BCNA <table><tr><th>Line of Business</th><th>PA Required (Yes/No)</th></tr><tr><td>BCBS</td><td>No</td></tr><tr><td>BCN</td><td>Yes</td></tr><tr><td>MAPPO</td><td>Yes</td></tr><tr><td>BCNA</td><td>Yes</td></tr></table>	Line of Business	PA Required (Yes/No)	BCBS	No	BCN	Yes	MAPPO	Yes	BCNA	Yes
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BCNA	Yes											
1.5	Effective Date: 05/09/2019	Add trial and failure of generic levoleucovorin										
1.4	Effective Date: 11/01/2018	Updated criteria per oncology vendor										
1.3	Effective Date: 08/09/2018	Annual Review of Medical Policy										

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1.2	Effective Date: 08/10/017	Annual Review of Medical Policy										
1.1	Effective Date: 08/11/2016	Annual Review of Medical Policy										
1.0	Effective Date: 05/02/2013	New Criteria Document - Custom/Clinical Formulary: N/A; Reviewed at April 2008 P&T - Custom formulary chapter: N/A - Part D: Specialty, Medicare Part B vs. D - Part D formulary chapter: Antineoplastics and Immunosuppressants: Adjuvant Therapy - Recommended criteria and QL <table><tr><th>Line of Business</th><th>PA Required (Yes/No)</th></tr><tr><td>BCBS</td><td>No</td></tr><tr><td>BCN</td><td>Yes</td></tr><tr><td>MAPPO</td><td>No</td></tr><tr><td>BCNA</td><td>No</td></tr></table>	Line of Business	PA Required (Yes/No)	BCBS	No	BCN	Yes	MAPPO	No	BCNA	No
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BCN	Yes											
MAPPO	No											
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** The prescribing information for a drug is subject to change. To ensure you are reading the most current information it is advised that you reference the most updated prescribing information by visiting the drug or manufacturer website or <http://dailymed.nlm.nih.gov/dailymed/index.cfm>.*

Blue Cross Blue Shield/Blue Care Network of Michigan
Medication Authorization Request Form
Fusilev® (levoleucovorin) J0641 & Khapzory™ (levoleucovorin) J0642



This form is to be used by participating physicians to obtain coverage for Fusilev, and Khapzory. For commercial members only, please complete this form and submit via fax to 1-877-325-5979. If you have any questions regarding this process, please contact BCBSM Provider Relations and Servicing or the Medical Drug Helpdesk at 1-800-437-3803 for assistance.

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PATIENT INFORMATION	PHYSICIAN INFORMATION
Name	Name
ID Number	Specialty
D.O.B. ☐ Male ☐ Female	Address
Diagnosis	City /State/Zip
Drug Name	Phone/Fax: P: () - F: () -
Dose and Quantity	NPI
Directions	Contact Person
Date of Service(s)	Contact Person Phone / Ext.

STEP 1: DISEASE STATE INFORMATION

- Is this request for: ☐ Initiation ☐ Continuation *Date patient started therapy:* _____
- Please provide the NPI number for the place of administration: _____
- Initiation AND Continuation of therapy:**
 - Which of the following is the drug being used for?
 - ☐ Rescue after high-dose methotrexate therapy in osteosarcoma
 - ☐ Decrease toxicity due to overdosage of folic acid antagonists or impaired methotrexate elimination
 - ☐ Combination chemotherapy with 5-fluorouracil for advanced metastatic colorectal cancer
 - ☐ Other, Please list: _____
 - Is the patient currently on leucovorin therapy?
 - ☐ yes ☐ no (go to c), Comment _____
 - Is leucovorin currently under shortage as identified by the Food and Drug Administration (FDA)?
 - ☐ yes ☐ no ☐ unknown
 - Has the patient experienced treatment failure to generic levoleucovorin?
 - ☐ yes ☐ no ☐ unknown
- Continuation of therapy:**
 - Please explain why continuation is necessary?

 - Patient must fit one of these criteria:
 - ☐ High dose methotrexate therapy
 - ☐ Toxic serum levels of methotrexate
 - ☐ Combination chemotherapy with 5-fluorouracil
 - ☐ Other, Please list: _____
 - Is leucovorin still under shortage as identified by the FDA?
 - ☐ yes ☐ no ☐ unknown

Please add any other supporting medical information necessary for our review

Coverage will not be provided if the prescribing physician's signature and date are not reflected on this document.

☐ Request for expedited review: I certify that applying the standard review time frame may seriously jeopardize the life or health of the member or the member's ability to regain maximum function

Physician's Name	Physician Signature	Date
Step 2: Checklist	☐ Form Completely Filled Out ☐ Provide chart notes	☐ Attach test results
Step 3: Submit	By Fax: BCBSM Specialty Pharmacy Mailbox 1-877-325-5979	By Mail: BCBSM Specialty Pharmacy Program P.O. Box 312320, Detroit, MI 48231-2320

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3/15/2019; 10/14/2019