
Cancer therapy selection, dosing, administration, and the management of related adverse events can be a complex process that should be handled by an experienced healthcare team. Clinicians must choose and verify treatment options based on the individual patient; drug dose modifications and supportive care interventions should be administered accordingly. The cancer treatment regimens below may include both U.S. Food and Drug Administration-approved and unapproved indications/regimens. These regimens are only provided to supplement the latest treatment strategies.

These Guidelines are a work in progress that may be refined as often as new significant data becomes available. The NCCN Guidelines® are a consensus statement of its authors regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult any NCCN Guidelines® is expected to use independent medical judgment in the context of individual clinical circumstances to determine any patient’s care or treatment. The NCCN makes no warranties of any kind whatsoever regarding their content, use, or application and disclaims any responsibility for their application or use in any way.

General Treatment Notes

• Consists of regimens that include both concurrent chemotherapy and radiotherapy and adjuvant chemotherapy.
• Six months of perioperative therapy is preferred in the adjuvant therapy setting.
• Following a shortage of leucovorin, the FDA approved levoleucovorin in combination with 5-FU for the palliative treatment of patients with advanced metastatic colorectal cancer. Levoleucovorin 200mg/m² is the equivalent of leucovorin 400mg/m².

Postoperative Adjuvant Therapy for Patients Not Receiving Preoperative Therapy

Note: All recommendations are Category 2A unless otherwise indicated.

REGIMEN | DOSES
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mFOLFOX6 (oxaliplatin + leucovorin + 5-fluorouracil [5-FU])²,4,a | Day 1: Oxaliplatin 85mg/m² IV over 2 hours + leucovorin 400mg/m² IV over 2 hours, followed by 5-FU 400mg/m² IV bolus, followed by 5-FU 1,200mg/m²/day IV x 2 days (total 2,400mg/m²) as a 46-48-hour continuous infusion. Repeat cycle every 2 weeks for a total of 6 months perioperative therapy.

Capecitabine⁵,e | Days 1-14: Capecitabine 1,000-1,250mg/m² orally twice daily. Repeat cycle every 3 weeks for 6 months perioperative therapy.

CapeOX (oxaliplatin + capecitabine)⁷,8,a | Day 1: Oxaliplatin 130mg/m² IV. Days 1-14: Capecitabine 1,000mg/m² orally twice daily. Repeat cycle every 3 weeks for 6 months perioperative therapy.

Simplified biweekly infusional 5-FU/LV (sLV5FU2)⁶ | Day 1: Leucovorin 400mg/m² IV, followed by 5-FU 400mg/m² IV bolus, followed by 5-FU 1,200mg/m²/day IV x 2 days (total 2,400mg/m²) as a 46-48 hour continuous infusion. Repeat cycle every 2 weeks for 6 months perioperative therapy.

5-FU + leucovorin² | 5-FU 500mg/m² IV bolus weekly x 6 + leucovorin 500mg/m² IV weekly x 6, each 8-week cycle. Repeat cycle every 8 weeks for 6 months perioperative therapy.

Concurrent Chemotherapy + Radiotherapy

External beam radiotherapy (XRT) + 5-FU¹⁰ | Days 1-5 OR 1-7: 5-FU 225mg/m² IV over 24 hours during XRT.

XRT + 5-FU + leucovorin¹¹,e | Days 1-4: 5-FU 400mg/m² IV bolus + leucovorin 20mg/m² IV bolus. Repeat cycle during weeks 1 and 5 of XRT.

XRT + capecitabine¹²,¹³ | Days 1-5: Capecitabine 825mg/m² twice daily + XRT. Repeat cycle weekly for 5 weeks.

Systemic Therapy for Advanced or Metastatic Disease

mFOLFOX6²,⁴-a | Day 1: Oxaliplatin 85mg/m² IV + leucovorin 400mg/m² IV followed by 5-FU 400mg/m² IV bolus, followed by 5-FU 1,200mg/m²/day IV x 2 days (total 2,400mg/m²) as a 46-48-hour continuous infusion. Repeat cycle every 2 weeks.

mFOLFOX7²,⁷,a | Day 1: Oxaliplatin 85mg/m² IV + leucovorin 400mg/m² IV Days 1-2: 5-FU 1200mg/m²/day IV (total 2400mg/m²) as 46-48 continuous infusion. Repeat cycle every 2 weeks.

mFOLFOX6 + bevacizumab¹³-¹⁴,a | Day 1: Oxaliplatin 85mg/m² IV + leucovorin 400mg/m² IV, followed by 5-FU 400mg/m² IV bolus, followed by 5-FU 1,200mg/m²/day IV x 2 days (total 2,400mg/m²) as a 46-48-hour continuous infusion
Day 1: Bevacizumab 5mg/kg IV. Repeat cycle every 2 weeks.

mFOLFOX6 + panitumumab¹⁵-¹⁶,a (KRAS/NRAS wild-type gene only) | Day 1: Oxaliplatin 85mg/m² IV over 2 hours + leucovorin 400mg/m² IV over 2 hours, followed by 5-FU 400mg/m² IV bolus, followed by 5-FU 1,200mg/m²/day IV x 2 days (total 2,400mg/m²) as a 46-48-hour continuous infusion
Day 1: Panitumumab 6mg/kg IV over 1 hour. Repeat cycle every 2 weeks.

FOLFOX + cetuximab¹⁷-¹⁶,a (KRAS/NRAS wild-type gene only) | Day 1: Oxaliplatin 85mg/m² IV over 2 hours + leucovorin 400mg/m² IV over 2 hours, followed by 5-FU 400mg/m² IV bolus, followed by 5-FU 1,200mg/m²/day IV x 2 days (total 2,400mg/m²) as a 46-48-hour continuous infusion
PLUS Day 1: Cetuximab 400mg/m² IV over 2 hours first infusion, then 250mg/m² IV over 60 minutes weekly.
OR Day 1: Cetuximab 500mg/m² IV over 2 hours every 2 weeks.
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| **CapeOX**<sup>17,1.e,d</sup> | **Day 1:** Oxaliplatin 130mg/m² IV  
**Days 1–14:** Capecitabine 1,000mg/m² orally twice daily. Repeat cycle every 3 weeks. |
| **CapeOX + bevacizumab**<sup>2,7,17,a,d</sup> | **Day 1:** Oxaliplatin 130mg/m² IV  
**Days 1–14:** Capecitabine 1,000mg/m² orally twice daily  
**Day 1:** Bevacizumab 7.5mg/kg IV. Repeat cycle every 3 weeks. |
| **FOLFIRI**<sup>18,19</sup> | **Day 1:** Irinotecan 180mg/m² IV over 30–90 minutes + leucovorin 400mg/m² IV, to match duration of irinotecan infusion, **followed by** 5-FU 400mg/m² IV bolus, **followed by** 5-FU 1,200mg/m²/day IV x 2 days (total 2,400mg/m²) as a 46–48-hour continuous infusion. Repeat cycle every 2 weeks. |
| **FOLFIRI + bevacizumab**<sup>18,19,38</sup> | **Day 1:** Irinotecan 180mg/m² IV over 30–90 minutes + leucovorin 400mg/m² IV, to match duration of irinotecan infusion, **followed by** 5-FU 400mg/m² IV bolus, **followed by** 5-FU 1,200mg/m²/day IV x 2 days (total 2,400mg/m²) as a 46–48-hour continuous infusion  
**Day 1:** Bevacizumab 5mg/kg IV. Repeat cycle every 2 weeks. |
| **FOLFIRI + cetuximab**<sup>19,20,21</sup> (KRAS/NRAS wild-type gene only) | **Day 1:** Irinotecan 180mg/m² IV + leucovorin 400mg/m² IV, to match duration of irinotecan infusion, **followed by** 5-FU 400mg/m² IV bolus, **followed by** 5-FU 1,200mg/m²/day IV x 2 days (total 2,400mg/m²) as a 46–48-hour continuous infusion. Repeat cycle every 2 weeks.  
**PLUS**  
**Day 1:** Cetuximab 400mg/m² IV over 2 hours first infusion, then 250mg/m² IV over 60 minutes weekly.  
**OR**  
**Day 1:** Cetuximab 500mg/m² IV over 2 hours every 2 weeks. |
| **FOLFIRI + panitumumab**<sup>17,22</sup> (KRAS/NRAS wild-type gene only) | **Day 1:** Irinotecan 180mg/m² IV over 30–90 minutes + leucovorin 400mg/m² IV, to match duration of irinotecan infusion, **followed by** 5-FU 400mg/m² IV bolus, **followed by** 5-FU 1,200mg/m²/day IV x 2 days (total 2,400mg/m²) as a 46–48-hour continuous infusion  
**Day 1:** Panitumumab 6mg/kg IV over 1 hour. Repeat cycle every 2 weeks. |
| **FOLFIRI + ziv-aflibercept**<sup>13</sup> | **Day 1:** Irinotecan 180mg/m² IV + leucovorin 400mg/m² IV, **followed by** 5-FU 400mg/m² IV bolus, **followed by** 5-FU 1,200mg/m²/day IV x 2 days (total 2,400mg/m²) as a 46–48-hour continuous infusion  
**Day 1:** Ziv-aflibercept 4mg/kg IV. Repeat cycle every 2 weeks. |
| **FOLFIRI + ramucirumab**<sup>19</sup> | **Day 1:** Irinotecan 180mg/m² IV over 30–90 minutes + leucovorin 400mg/m² IV, to match duration of irinotecan infusion, **followed by** 5-FU 400mg/m² IV bolus, **followed by** 5-FU 1,200mg/m²/day IV x 2 days (total 2,400mg/m²) as a 46–48-hour continuous infusion  
**Day 1:** Ramucirumab 8mg/kg over 1 hour. Repeat cycle every 2 weeks. |
| **Capecitabine**<sup>17</sup> | **Days 1–14:** Capecitabine 850–1,250mg/m² orally twice daily. Repeat cycle every 3 weeks. |
| **Capecitabine + bevacizumab**<sup>40,4</sup> | **Days 1–14:** Capecitabine 850–1,250mg/m² orally twice daily  
**Day 1:** Bevacizumab 7.5mg/kg IV. Repeat cycle every 3 weeks. |
| **Bolus or Infusional 5-FU/Leucovorin (Roswell-Park Regimen)**<sup>25</sup> | **Days 1, 8, 15, 22, 29, and 36:** Leucovorin 500mg/m² IV over 2 hours, **followed by** 5-FU 500mg/m² IV bolus 1 hour after start of leucovorin. Repeat cycle every 8 weeks. |
| **Simplified Biweekly Infusional 5-FU/LV (sLV5FU2)**<sup>18</sup> | **Day 1:** Leucovorin 400mg/m² IV over 2 hours, **followed by** 5-FU 400mg/m² IV bolus, **followed by** 5-FU 1,200mg/m²/day IV x 2 days (total 2,400mg/m²) as a 46–48-hour continuous infusion. Repeat cycle every 2 weeks. |
| **Weekly 5-FU + Leucovorin**<sup>76</sup> | **Day 1:** Leucovorin 20mg/m² IV over 2 hours, **followed by** 5-FU 500mg/m² IV bolus 1 hour after start of leucovorin. Repeat cycle weekly.  
**OR**  
**Day 1:** Leucovorin 500mg/m² IV, **followed by** 5-FU 2,600mg/m² continuous infusion. Repeat cycle weekly. |
| **IROX**<sup>35,a</sup> | **Day 1:** Oxaliplatin 85mg/m² IV + irinotecan 200mg/m² IV over 30–90 minutes. Repeat cycle every 3 weeks. |
## Systemic Therapy for Advanced or Metastatic Disease

### REGIMEN

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| FOLFOXIRI ± bevacizumab²⁹,³⁰,a  | Day 1: Oxaliplatin 165mg/m² IV + oxaliplatin 85mg/m² IV + leucovorin 400mg/m² IV  
Days 1 and 2: 5-FU, 1,600mg/m²/day continuous infusion IV over 48 hours  
 OR  
Day 1: Bevacizumab 5mg/kg IV.  
Repeat cycle every 2 weeks. |
| Irinotecan²¹,³²                | Days 1 and 8: Irinotecan 125mg/m² IV over 30–90 minutes.  
 OR  
Day 1: Irinotecan 180mg/m² IV over 30–90 minutes.  
 Repeat cycle every 2 weeks.  
 OR  
Day 1: Irinotecan 300–350mg/m² IV over 30–90 minutes.  
 Repeat cycle every 3 weeks. |
| Cetuximab + irinotecan²¹,²³    | Day 1: Cetuximab 400mg/m² IV first infusion, then 250mg/m² IV every 7 days  
 OR  
Day 1: Cetuximab 500mg/m² IV every 2 weeks  
 OR  
Day 1: Irinotecan 300–350mg/m² IV over 30–90 minutes every 3 weeks.  
 OR  
Day 1: Irinotecan 180mg/m² IV over 30–90 minutes every 2 weeks.  
 OR  
Day 1 and 8: Irinotecan 125mg/m² IV over 30–90 minutes every 3 weeks. |
| Cetuximab²¹,²³ (KRAS/NRAS wild-type gene only) | Cetuximab 400mg/m² first infusion, then 250mg/m² IV weekly.  
 OR  
Cetuximab 500mg/m² IV over 2 hours every 2 weeks. |
| Panitumumab³⁴                  | Day 1: Panitumumab 6mg/kg IV over 60 minutes.  
 Repeat cycle every 2 weeks. |
| Regorafenib³⁵,a,f               | Days 1–21: Regorafenib 160mg orally once daily.  
 Repeat cycle every 28 days. |
| Trifluridine/tipiracil³⁸       | Days 1–5 and 8–12: Trifluridine/tipiracil 35mg/m² up to a maximum of 80mg/m² per dose (based on the trifluridine component) orally twice daily.  
 Repeat every 28 days. |
| Pembrolizumab³¹               | Day 1: Pembrolizumab 2mg/kg.  
 Repeat cycle every 3 weeks. |
| Nivolumab³²                   | Day 1: Nivolumab 3mg/kg.  
 Repeat cycle every 2 weeks.  
 OR  
Day 1: Nivolumab 240mg/kg.  
 Repeat cycle every 2 weeks. |

### References
