

COLON CANCER TREATMENT REGIMENS (Part 1 of 4)

Clinical Trials: The NCCN recommends cancer patient participation in clinical trials as the gold standard for treatment.

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 National Comprehensive Cancer Network 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.

Advanced or Metastatic Disease¹

NOTE: All recommendations are category 2A unless otherwise indicated.

REGIMEN	DOSING
mFOLFOX6	<ul style="list-style-type: none"> • Oxaliplatin 85mg/m² IV over 2 hours, day 1 • Leucovorin 400mg/m²* IV over 2 hours, day 1 • 5-FU 400mg/m² IV bolus on day 1, then 1,200mg/m²/day × 2 days (total 2,400mg/m² over 46–48 hours)[†] IV continuous infusion Repeat every 2 weeks. ²⁻⁴
mFOLFOX6 + Bevacizumab^{3,5}	<ul style="list-style-type: none"> • Oxaliplatin 85mg/m² IV over 2 hours, day 1 • Leucovorin 400mg/m²* IV over 2 hours, day 1 • 5-FU 400mg/m² IV bolus on day 1, then 1,200mg/m²/day × 2 days (total 2,400mg/m² over 46–48 hours)[†] IV continuous infusion • Bevacizumab 5mg/kg IV, day 1 Repeat every 2 weeks.
mFOLFOX6 + Panitumumab^{3,6}	<ul style="list-style-type: none"> • Oxaliplatin 85mg/m² IV over 2 hours, day 1 • Leucovorin 400mg/m²* IV over 2 hours, day 1 • 5-FU 400mg/m² IV bolus on day 1, then 1,200mg/m²/day × 2 days (total 2,400mg/m² over 46–48 hours)[†] IV continuous infusion • Panitumumab 6mg/kg IV over 60 minutes, day 1 Repeat every 2 weeks.
CapeOX²	<ul style="list-style-type: none"> • Oxaliplatin 130mg/m² IV over 2 hours, day 1 • Capecitabine 850–1,000mg/m² twice daily PO for 14 days Repeat every 3 weeks.
CapeOX + Bevacizumab^{2,7}	<ul style="list-style-type: none"> • Oxaliplatin 130mg/m² IV over 2 hours, day 1 • Capecitabine 850–1,000mg/m² PO twice daily for 14 days • Bevacizumab 7.5mg/kg IV, day 1 Repeat every 3 weeks.
FOLFIRI⁸	<ul style="list-style-type: none"> • Irinotecan 180mg/m² IV over 30–90 minutes, day 1 • Leucovorin 400mg/m²* IV infusion to match duration of irinotecan infusion, day 1 • 5-FU 400mg/m² IV bolus day 1, then 1,200mg/m²/day × 2 days (total 2,400mg/m² over 46–48 hours)[†] continuous infusion Repeat every 2 weeks.
FOLFIRI⁸ + Bevacizumab⁹	<ul style="list-style-type: none"> • Irinotecan 180mg/m² IV over 30–90 minutes, day 1 • Leucovorin 400mg/m²* IV infusion to match duration of irinotecan infusion, day 1 • 5-FU 400mg/m² IV bolus day 1, then 1,200mg/m²/day × 2 days (total 2,400mg/m² over 46–48 hours)[†] IV continuous infusion • Bevacizumab 5mg/kg IV, day 1 Repeat every 2 weeks.
FOLFIRI⁸ + Cetuximab	<ul style="list-style-type: none"> • Irinotecan 180mg/m² IV over 30–90 minutes, day 1 • Leucovorin 400mg/m²* IV infusion to match duration of irinotecan infusion, day 1 • 5-FU 400mg/m² IV bolus day 1, then 1,200mg/m²/day × 2 days (total 2,400mg/m² over 46–48 hours)[†] IV continuous infusion Repeat every 2 weeks <ul style="list-style-type: none"> • Cetuximab 400mg/m² IV over 2 hours first infusion, then 250mg/m² IV over 60 minutes weekly¹⁰ OR <ul style="list-style-type: none"> • Cetuximab 500mg/m² IV over 2 hours, day 1, every 2 weeks.¹¹

continued

COLON CANCER TREATMENT REGIMENS (Part 2 of 4)

Advanced or Metastatic Disease (continued)

REGIMEN	DOSING
FOLFIRI⁸ + Panitumumab¹²	<ul style="list-style-type: none"> • Irinotecan 180mg/m² IV over 30–90 minutes, day 1 • Leucovorin 400mg/m²* IV infusion to match duration of irinotecan infusion, day 1 • 5-FU 400mg/m² IV bolus day 1, then 1,200mg/m²/day × 2 days (total 2,400mg/m² over 46–48 hours)[†] IV continuous infusion • Panitumumab 6mg/kg IV over 60 minutes, day 1 Repeat every 2 weeks.
FOLFIRI + ziv-aflibercept¹³	<ul style="list-style-type: none"> • Irinotecan 180mg/m² IV over 30–90 minutes, day 1 • Leucovorin 400mg/m²* IV infusion to match duration of irinotecan infusion, day 1 • 5-FU 400mg/m² IV bolus day 1, then 1,200mg/m²/day × 2 days (total 2,400mg/m² over 46–48 hours)[†] continuous infusion • Ziv-aflibercept 4mg/kg IV Repeat every 2 weeks.
Capecitabine¹⁴	850–1,250mg/m ² PO twice daily, days 1–14 Repeat every 3 weeks.
Capecitabine¹⁴ + Bevacizumab⁷	<ul style="list-style-type: none"> • Capecitabine 850–1,250mg/m² PO twice daily, days 1–14 • Bevacizumab 7.5mg/kg IV, day 1 Repeat every 3 weeks.
Bolus or infusional 5-FU/leucovorin Roswell Park regimen¹⁵	<ul style="list-style-type: none"> • Leucovorin 500mg/m² IV over 2 hours, days 1, 8, 15, 22, 29, and 36 • 5-FU 500mg/m² IV bolus 1 hour after start of leucovorin, days 1, 8, 15, 22, 29, and 36 Repeat every 8 weeks.
Simplified biweekly infusional 5-FU/LV (sLV5FU2)⁸	Leucovorin 400mg/m ² * IV over 2 hours on day 1, followed by 5-FU bolus 400mg/m ² and then 1,200mg/m ² /day × 2 days (total 2,400mg/m ² over 46–48 hours) [†] continuous infusion Repeat every 2 weeks.
Weekly infusional LV5FU2	<ul style="list-style-type: none"> • Leucovorin 20mg/m² IV over 2 hours on day 1 • 5-FU 500mg/m² IV bolus injection 1 hour after the start of leucovorin Repeat every week ¹⁶ • 5-FU 2,600mg/m ² by 24-hour infusion plus leucovorin 500mg/m ² Repeat every week. ¹⁷
IROX¹⁸	Oxaliplatin 85mg/m ² IV over 2 hours, followed by irinotecan 200mg/m ² over 30 or 90 minutes every 3 weeks.
FOLFOXIRI¹⁹	<ul style="list-style-type: none"> • Irinotecan 165mg/m² IV day 1, oxaliplatin 85mg/m² day 1 • Leucovorin 400mg/m²* day 1 • Fluorouracil 1,600mg/m²/day × 2 days (total 3,200mg/m² over 48 hours)[†] continuous infusion starting on day 1 Repeat every 2 weeks ± • Bevacizumab ²⁰ 5mg/kg IV, day 1.
Irinotecan	<ul style="list-style-type: none"> • Irinotecan 125mg/m² IV over 30–90 minutes, days 1 and 8 Repeat every 3 weeks ^{21,22} <ul style="list-style-type: none"> • Irinotecan 300–350mg/m² IV over 30–90 minutes, day 1 Repeat every 3 weeks • Cetuximab (KRAS/NRAS WT gene only) ± irinotecan ^{11,23} • Cetuximab 400mg/m ² first infusion, then 250mg/m ² IV weekly OR cetuximab 500mg/m ² IV every 2 weeks ¹¹ ± • Irinotecan 300–350mg/m ² IV every 3 weeks OR irinotecan 180mg/m ² IV every 2 weeks OR irinotecan 125mg/m ² on days 1 and 8 and repeat every 3 weeks.
Cetuximab (KRAS/NRAS WT gene only)	400mg/m ² first infusion, then 250mg/m ² IV weekly ²³ OR 500mg/m ² IV over 2 hours, day 1, every 2 weeks. ¹¹
Panitumumab²⁴ (KRAS/NRAS WT gene only)	6mg/kg IV over 60 minutes every 2 weeks.
Regorafenib²⁵	160mg PO daily, days 1–21 Repeat every 28 days.

continued

COLON CANCER TREATMENT REGIMENS (Part 3 of 4)

Adjuvant Chemotherapy Regimens

Principals of Adjuvant Therapy[†]

- Capecitabine appears to be equivalent to bolus 5-FU/leucovorin in patients with stage III colon cancer.²⁶
- FOLFOX is superior to fluoropyrimidine therapy alone for patients with stage III colon cancer.^{27,28} FOLFOX is reasonable for high-risk or intermediate-risk stage II patients and is not indicated for good- or average-risk patients with stage II colon cancer. FLOX is an alternative to FOLFOX.²⁹
- A survival benefit has not been demonstrated for the addition of oxaliplatin to 5-FU/leucovorin in stage II colon cancer.³⁰
- A benefit for the addition of oxaliplatin to 5-FU/leucovorin in patients age 70 and older has not been proven.³⁰
- Bolus 5-FU/leucovorin/irinotecan should not be used in adjuvant therapy,³¹ and infusional 5-FU/leucovorin/irinotecan (FOLFIRI) has not been shown to be superior to 5-FU/LV.^{32,33} Capecitabine/oxaliplatin is superior to bolus 5-FU/leucovorin.³⁴
- Bevacizumab, cetuximab, panitumumab, or irinotecan should not be used in the adjuvant setting for patients with stage II or III colon cancer outside the setting of a clinical trial.

REGIMEN	DOSING
mFOLFOX6	<ul style="list-style-type: none"> • Oxaliplatin 85mg/m² IV over 2 hours, day 1 • Leucovorin 400mg/m²* IV over 2 hours, day 1 • 5-FU 400mg/m² IV bolus on day 1, then 1,200mg/m²/day × 2 days (total 2,400mg/m² over 46–48 hours)[†] continuous infusion Repeat every 2 weeks. ^{35–37}
FLOX³⁸	5-FU 500mg/m ² IV bolus weekly × 6 + leucovorin 500mg/m ² IV weekly × 6, each 8-week cycle × 3 with oxaliplatin 85mg/m ² IV administered on weeks 1, 3, and 5 of each 8-week cycle × 3.
Capecitabine³⁹	1,250mg/m ² twice daily PO, days 1–14 every 3 weeks × 24 weeks.
CapeOx⁴⁰	<ul style="list-style-type: none"> • Oxaliplatin 130mg/m² over 2 hours, day 1 • Capecitabine 1,000mg/m² twice daily PO, days 1–14 every 3 weeks × 24 weeks.
5-FU/leucovorin	<ul style="list-style-type: none"> • Leucovorin 500mg/m² given as a 2-hour infusion and repeated weekly × 6 • 5-FU 500mg/m² given IV bolus 1 hour after the start of leucovorin and repeated 6 × weekly. Every 8 weeks for 4 cycles⁴¹ • Simplified biweekly infusional 5-FU/LV (sLV5FU2)⁴² • Leucovorin 400mg/m²* IV over 2 hours on day 1, followed by 5-FU bolus 400mg/m² and then 1,200mg/m²/day × 2 days (total 2,400mg/m² over 46–48 hours)[†] continuous infusion. Repeat every 2 weeks.

* Leucovorin 400mg/m² is the equivalent of levoleucovorin 200mg/m².

† NCCN recommends limiting chemotherapy orders to 24-hour units (i.e., 1,200mg/m²/day NOT 2,400mg/m² over 48 hours) to minimize medication errors.

‡ The majority of safety and efficacy data for this regimen have been developed in Europe, where a capecitabine starting dose of 1,000mg/m² twice daily for 14 days, repeated every 21 days, is standard. Evidence suggests that North American patients may experience greater toxicity with capecitabine (as well as with other fluoropyrimidines) than European patients, and may require a lower dose of capecitabine. The relative efficacy of CapeOx with lower starting doses of capecitabine has not been addressed in large-scale randomized trials.

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COLON CANCER TREATMENT REGIMENS (Part 4 of 4)

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