

Endometrial Carcinoma Treatment Regimens

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 National Comprehensive Cancer Network 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.

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

► Systemic Therapy for Endometrial Carcinoma¹

REGIMEN	DOSING
Primary or Adjuvant Treatment When Used for Uterine-Confined High-Risk Disease	
Preferred Regimens	
Carboplatin/Paclitaxel ^{2-6,b} <i>Premedication is required for Paclitaxel</i>	Day 1: Paclitaxel 175mg/m ² IV over 3 hours, followed by: Day 1: Carboplatin AUC 6-7.5 IV over 30 minutes. Repeat cycle every 3 weeks for 6 cycles.
Recurrent or Metastatic Disease^c	
Systemic Therapies	
Preferred Regimens	
Carboplatin/Paclitaxel (Category 1 for carcinosarcoma) ^{2-6,b} <i>Premedication is required for Paclitaxel</i>	Day 1: Paclitaxel 175mg/m ² IV over 3 hours, followed by: Day 1: Carboplatin AUC 6 IV over 30 minutes. Repeat cycle every 3 weeks for a maximum of 7 cycles.
Carboplatin/Paclitaxel/Trastuzumab (Stage III/IV recurrent HER2-positive uterine serious carcinoma) ^{2,3,7,8,b,d} <i>Premedication is required for Paclitaxel</i>	Day 1: Paclitaxel 175mg/m ² IV over 3 hours, followed by: Day 1: Carboplatin AUC 5 IV over 30 minutes Day 1 (Cycle 1): Trastuzumab 8mg/kg IV over 90 minutes, followed by: Day 2 (Beginning with Cycle 2): Trastuzumab 6mg/kg IV over 30 minutes. Repeat cycle every 3 weeks for a maximum of 6 cycles. Followed by: Day 1 (Beginning with Cycle 7): Trastuzumab 6mg/kg IV over 30 minutes. Repeat cycle every 3 weeks.
Other Recommended Regimens	
Albumin-Bound Paclitaxel ^{9-11,e}	Day 1: Albumin-bound paclitaxel 260mg/m ² IV over 30 minutes. Repeat cycle every 3 weeks. OR Day 1,8,15: Albumin-bound paclitaxel 100-125mg/m ² IV over 30 minutes. Repeat cycle every 4 weeks.
Bevacizumab ^{12,13,d,f}	Day 1: Bevacizumab 15mg/kg IV. Repeat cycle every 3 weeks.
Carboplatin ^{3,14}	Day 1: Carboplatin AUC 5-7 IV over 30 minutes. Repeat cycle every 3 weeks.
Carboplatin/Docetaxel ^{3,15-17,f,g,h,i} <i>Premedication is required for Docetaxel</i>	Day 1: Docetaxel 60mg/m ² IV over 1 hour, followed by: Day 1: Carboplatin AUC 6 IV over 30 minutes. Repeat cycle every 3 weeks.
Carboplatin/Paclitaxel/Bevacizumab ^{3,12,18,19,b,d,f} <i>Premedication is required for Paclitaxel</i>	Day 1: Paclitaxel 175mg/m ² IV over 3 hours, followed by: Day 1: Carboplatin AUC 5 IV over 30 minutes Day 1: Bevacizumab 15mg/kg IV. Repeat cycle for 3 weeks every 6-8 cycles, followed by: Day 1: Bevacizumab 15mg/kg IV. Repeat cycle every 3 weeks (maintenance therapy).
Cisplatin ^{20,21,j}	Day 1: Cisplatin 50mg/m ² IV over 1 hour. Repeat cycle every 3 weeks.

continued

Endometrial Carcinoma Treatment Regimens

► Systemic Therapy for Endometrial Carcinoma¹ (continued)

REGIMEN	DOSING
Recurrent or Metastatic Disease^c (continued)	
Systemic Therapies (continued)	
Other Recommended Regimens (continued)	
Cisplatin/Doxorubicin ^{20,22-24,j,k}	<p>Day 1: Doxorubicin 60mg/m² IV push Day 1: Cisplatin 50mg/m² over 1 hour. Repeat cycle every 3 weeks until reaching a lifetime cumulative anthracycline dose.</p> <p>OR</p> <p>Day 1: Doxorubicin 45mg/m² (if pelvic floor radiation) IV push Day 1: Cisplatin 50mg/m² over 1 hour. Repeat cycle every 3 weeks until reaching a lifetime cumulative anthracycline dose.</p>
Cisplatin/Doxorubicin/ Paclitaxel ^{2,20,22,24,b,j,k,l} <i>Premedication is required for Paclitaxel</i>	<p>Day 1: Doxorubicin 45mg/m² IV push Day 1: Cisplatin 50mg/m² over 1 hour Day 2: Paclitaxel 160mg/m² IV over 3 hours. Repeat cycle every 3 weeks until reaching a lifetime cumulative anthracycline dose.</p>
Cisplatin/Ifosfamide (Carcin sarcoma) ^{20,25-27,j,m}	<p>Days 1-4: Ifosfamide 1,500mg/m² IV over 3 hours daily Days 1-4: Mesna 300mg/m² IV over 15 minutes three times daily (one dose before ifosfamide, then at 4 and 8 hours from the start of each ifosfamide dose) Days 1-4: Cisplatin 20mg/m² IV over 1 hour. Repeat cycle every 3 weeks.</p> <p>OR</p> <p>Days 1-4: Ifosfamide 1,200mg/m² (if prior pelvic radiation) IV over 3 hours daily Days 1-4: Mesna 240mg/m² IV over 15 minutes three times daily (one dose before ifosfamide, then at 4 and 8 hours from the start of each ifosfamide dose) Days 1-4: Cisplatin 20mg/m² IV over 1 hour. Repeat cycle every 3 weeks.</p>
Docetaxel (Category 2B) ^{15,28,g,h} <i>Premedication is required for Paclitaxel</i>	<p>Day 1: Docetaxel 70mg/m² IV over 1 hour. Repeat cycle every 3 weeks.</p>
Doxorubicin ^{22,29-31,k}	<p>Day 1: Doxorubicin 60mg/m² IV push. Repeat cycle every 3 weeks until reaching a lifetime cumulative anthracycline dose.</p>
Ifosfamide (Carcin sarcoma) ^{25,32,m}	<p>Days 1-3: Ifosfamide 2,000mg/m² IV over 3 hours daily Days 1-3: Mesna 400mg/m² IV over 15 minutes three times daily (one dose before ifosfamide, then at 4 and 8 hours from the start of each ifosfamide dose). Repeat cycle every 3 weeks.</p> <p>OR</p> <p>Days 1-3: Ifosfamide 1,200mg/m² (if prior pelvic radiation) IV over 3 hours daily Days 1-3: Mesna 240mg/m² IV over 15 minutes three times daily (one dose before ifosfamide, then at 4 and 8 hours from the start of each ifosfamide dose). Repeat cycle every 3 weeks.</p>
Ifosfamide/Paclitaxel (Carcin sarcoma) ^{2,25,32,b,i,m} <i>Premedication is required for Paclitaxel</i>	<p>Days 1-3: Ifosfamide 1,600mg/m² IV over 3 hours daily Days 1-3: Mesna 320mg/m² IV over 15 minutes three times daily (one dose before ifosfamide, then at 4 and 8 hours from the start of each ifosfamide dose) Day 1: Paclitaxel 135mg/m² IV over 3 hours. Repeat cycle every 3 weeks.</p> <p>OR</p> <p>Days 1-4: Ifosfamide 1,200mg/m² (if prior pelvic radiation) IV over 3 hours daily Days 1-4: Mesna 240mg/m² IV over 15 minutes three times daily (one dose before ifosfamide, then at 4 and 8 hours from the start of each ifosfamide dose) Day 1: Paclitaxel 135mg/m² IV over 3 hours. Repeat cycle every 3 weeks.</p>
Liposomal Doxorubicin ^{33-35,k}	<p>Day 1: Liposomal doxorubicin 40-50mg/m² IV push. Repeat cycle every 4 weeks until reaching a lifetime cumulative anthracycline dose.</p>
Paclitaxel ^{2,31,36,b} <i>Premedication is required for Paclitaxel</i>	<p>Day 1: Paclitaxel 175mg/m² IV over 3 hours. Repeat cycle every 3 weeks.</p>
Temsirolimus ^{37,38,o} <i>Premedication is required for Temsirolimus</i>	<p>Days 1,8,15,22: Temsirolimus 25mg IV over 30 minutes. Repeat cycle every 4 weeks.</p>

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Endometrial Carcinoma Treatment Regimens

► Systemic Therapy for Endometrial Carcinoma¹ (continued)

REGIMEN	DOSING
Recurrent or Metastatic Disease ^c (continued)	
Systemic Therapies (continued)	
Other Recommended Regimens (continued)	
Topotecan ^{39,40}	Days 1-5: Topotecan 1mg/m ² IV over 30 minutes daily. Repeat cycle every 3 weeks. OR Days 1-5: Topotecan 0.8mg/m ² (if prior pelvic radiation) IV over 30 minutes daily. Repeat cycle every 3 weeks.
Biomarker-Directed Systemic Therapy for Second-Line Treatment	
Preferred Regimens	
Lenvatinib/Pembrolizumab (Category 1) (Non-MSI-H/non-dMMR tumors) ^{41-43,a,n}	Days 1-21: Lenvatinib 20mg orally daily. Day 1: Pembrolizumab 200mg IV. Repeat cycle every 3 weeks.
Pembrolizumab (TMB-H or non-MSI-H/non-dMMR tumors) ^{41,44,45,a,n}	Days 1: Pembrolizumab 200mg IV over 30 minutes. Repeat cycle every 3 weeks until up to 24 months of therapy has been completed. OR Day 1: Pembrolizumab 400mg IV over 30 minutes. Repeat cycle every 6 weeks until up to 24 months of therapy has been completed.
Other Recommended Regimens	
Avelumab (MSI-H/dMMR tumors) ^{46,a,n}	See NCCN Uterine Neoplasms Guidelines ¹
Cabozantinib ⁴⁷	See NCCN Uterine Neoplasms Guidelines ¹
Dostarlimab-gxly (MSI-H/dMMR tumors) ^{48,49,a,n}	Day 1 (Cycles 1-4): Dostarlimab-gxly 500 mg IV. Repeat every 3 weeks, followed by: Day 1 (Beginning with Cycle 5): Dostarlimab-gxly 1000 mg IV. Repeat cycle every 6 weeks.
Entrectinib (Category 2B) (<i>NTRK</i> gene fusion-positive tumors) ⁵⁰	See NCCN Uterine Neoplasms Guidelines ¹
Larotrectinib (Category 2B) (<i>NTRK</i> gene fusion-positive tumors) ⁵¹	See NCCN Uterine Neoplasms Guidelines ¹
Nivolumab (MSI-H/dMMR tumors) ^{52,53,a,n}	See NCCN Uterine Neoplasms Guidelines ¹
Hormone Therapy ^p	
Preferred Regimens	
Anastrozole ⁵⁴	See NCCN Uterine Neoplasms Guidelines ¹
Exemestane ⁵⁵	See NCCN Uterine Neoplasms Guidelines ¹
Fulvestrant ⁵⁶	See NCCN Uterine Neoplasms Guidelines ¹
Letrozole ⁵⁷	See NCCN Uterine Neoplasms Guidelines ¹
Levonorgesterol IUD (Select fertility-sparing cases)	See NCCN Uterine Neoplasms Guidelines ¹
Megestrol Acetate	See NCCN Uterine Neoplasms Guidelines ¹
Megestrol Acetate/Tamoxifen (Alternating)	See NCCN Uterine Neoplasms Guidelines ¹
Medroxyprogesterone Acetate	See NCCN Uterine Neoplasms Guidelines ¹
Medroxyprogesterone Acetate/Tamoxifen (Alternating)	See NCCN Uterine Neoplasms Guidelines ¹
Tamoxifen ⁵⁸	See NCCN Uterine Neoplasms Guidelines ¹

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Endometrial Carcinoma Treatment Regimens

► Systemic Therapy for Endometrial Carcinoma¹ (continued)

REGIMEN	DOSING
Recurrent or Metastatic Disease^e (continued)	
Hormone Therapy^p (continued)	
Other Recommended Regimens	
Everolimus/Letrozole (Endometrioid histology)^{57,59,60}	Days 1-28: Everolimus 10mg orally daily Days 1-28: Letrozole 2.5 mg orally daily. Repeat cycle every 4 weeks.

^a CSFs = colony-stimulating factors; dMMR = deficient mismatch repair; IUD = intrauterine device; MSI-H = high levels of microsatellite instability; TMB-H = tumor mutational burden-high

^b For Paclitaxel: Premedication for hypersensitivity is required. The recommended dosing is:

- H2 antagonist
—Famotidine 20mg IV or orally (or equivalent H2 blocker) 30-60 minutes pre-Paclitaxel AND
- H1 antagonist
—Diphenhydramine 12.5-50mg IV or orally 30-60 minutes pre-Paclitaxel AND
- Dexamethasone (for 21-day regimen):
—Dexamethasone 20mg orally approximately 12 and 6 hours pre-Paclitaxel OR
—Dexamethasone 20mg IV 30 minutes pre-Paclitaxel
- Dexamethasone (for weekly regimens):
—Dexamethasone 10mg IV 30 minutes pre-Paclitaxel

^c Chemotherapy regimens can be used for all carcinoma histologies. Carcinosarcomas are now considered and treated as high-grade carcinomas.

^d An FDA-approved biosimilar is an appropriate substitute for Trastuzumab and Bevacizumab.

^e Albumin-bound Paclitaxel is a reasonable substitute for patients with a hypersensitivity to Paclitaxel if the skin testing to Paclitaxel is negative. If the patient has a positive skin test to Paclitaxel then the patient requires desensitization to paclitaxel. Albumin-bound Paclitaxel is not a reasonable substitute for the patient skin test is positive.

^f Bevacizumab may be considered for use in patients who have progressed on prior cytotoxic chemotherapy.

^g For Docetaxel: Premedication with Dexamethasone for fluid retention is required. One recommended dosing strategy is: Dexamethasone 8mg orally the night before, the morning of, and the night of Docetaxel administration.

^h Docetaxel may be considered for patients in whom Paclitaxel is contraindicated.

ⁱ CSFs may be considered for primary prophylaxis based on the febrile neutropenia risk of the chemotherapy regimen.

^j Hydration is required with supplemental electrolytes pre- and post-administration of Cisplatin.

^k Doxorubicin is an anthracycline. Cumulative anthracycline dosage should be monitored.

^l The Cisplatin/Doxorubicin/Paclitaxel regimen is not widely used because of concerns related to toxicity.

^m Hydration is required pre- and post-administration of Ifosfamide.

ⁿ Early- and late-onset immune-related adverse events affecting multiple organ systems can occur in patients receiving immune checkpoint inhibitors. Patients with neurologic or life-threatening autoimmune disorders as well as receiving high levels of immunosuppression for their underlying disease should be approached with caution when considering immunotherapy. All patients will require extensive resources including ongoing intensive monitoring and supportive care.

^o For Temezilimus: premedication for hypersensitivity and/or infusion reactions is required. The recommended dosing is diphenhydramine 12.5-50mg IV or orally 30 minutes pre-Temezilimus.

^p Hormonal therapy is typically used for lower-grade endometrioid histologies, preferable in patients with small tumor volume or an indolent growth pace.

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