

# 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<sup>®</sup> 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<sup>®</sup> 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 Carcinoma<sup>1</sup>

REGIMEN	DOSING
<b>Adjuvant Therapy When Used for Uterine-Confined Disease</b>	
<b>Chemotherapy<sup>a</sup></b>	
<b>Preferred Regimens</b>	
Carboplatin + Paclitaxel <sup>2-4b</sup>	<b>Day 1:</b> Paclitaxel 175mg/m <sup>2</sup> IV over 3 hours, <b>followed by:</b> <b>Day 1:</b> Carboplatin AUC 6-7.5 IV over 30 minutes. Repeat cycle every 3 weeks for 6 cycles.
<b>Adjuvant Therapy for High-Risk Disease or Primary Therapy for Initially Unresectable Disease</b>	
<b>Chemotherapy<sup>a</sup></b>	
<b>Preferred Regimens</b>	
Carboplatin + Paclitaxel <sup>2-4b</sup>	<b>Day 1:</b> Paclitaxel 175mg/m <sup>2</sup> IV over 3 hours, <b>followed by:</b> Day 1: Carboplatin AUC 6-7.5 IV over 30 minutes. Repeat cycle every 3 weeks for 6 cycles.
<b>Other Recommended Regimens</b>	
Carboplatin <sup>5b</sup>	<b>Day 1:</b> Carboplatin AUC 5-7 IV over 30 minutes. Repeat cycle every 3 weeks for 6 cycles.
Carboplatin + Docetaxel <sup>6,7b,d</sup>	<b>Day 1:</b> Docetaxel 75mg/m <sup>2</sup> IV over 60 minutes, <b>followed by:</b> <b>Day 1:</b> Carboplatin AUC 6 IV over 30 minutes. Repeat cycle every 3 weeks for 6 cycles.
Cisplatin <sup>8,b,c</sup>	<b>Day 1:</b> Cisplatin 50mg/m <sup>2</sup> IV over 60 minutes. Repeat cycle every 3 weeks for 6 cycles.
Cisplatin + Doxorubicin <sup>9,10,b,c</sup>	<b>Day 1:</b> Doxorubicin 60mg/m <sup>2</sup> IV push <b>Day 1:</b> Cisplatin 50mg/m <sup>2</sup> IV over 60 minutes. Repeat cycle every 3 weeks for 6 cycles. <b>OR</b> <b>Day 1:</b> Doxorubicin 45mg/m <sup>2</sup> (if prior pelvic radiation) IV push <b>Day 1:</b> Cisplatin 50mg/m <sup>2</sup> IV over 60 minutes. Repeat cycle every 3 weeks for 6 cycles.
Cisplatin + Doxorubicin + Paclitaxel <sup>10,b,c,f</sup>	<b>Day 1:</b> Doxorubicin 45mg/m <sup>2</sup> IV push <b>Day 1:</b> Cisplatin 50mg/m <sup>2</sup> IV over 60 minutes <b>Day 2:</b> Paclitaxel 160mg/m <sup>2</sup> IV over 3 hours. Repeat cycle every 3 weeks for 6 cycles.
Cisplatin + Ifosfamide (for carcinosarcoma) <sup>11,b,c,e</sup>	<b>Days 1-4:</b> Ifosfamide 1,500mg/m <sup>2</sup> IV over 3 hours <b>Days 1-4:</b> Mesna 300mg/m <sup>2</sup> IV over 15 minutes three times daily, one dose before Ifosfamide, then at 4 and 8 hours from the start of each Ifosfamide dose <b>Days 1-4:</b> Cisplatin 20mg/m <sup>2</sup> IV over 60 minutes. Repeat cycle every 3 weekfor 6 cycles. <b>OR</b> <b>Days 1-4:</b> Ifosfamide 1,200mg/m <sup>2</sup> (if prior pelvic radiation) IV over 3 hours <b>Days 1-4:</b> Mesna 240mg/m <sup>2</sup> IV over 15 minutes three times daily, one dose before Ifosfamide, then at 4 and 8 hours from the start of each Ifosfamide dose <b>Days 1-4:</b> Cisplatin 20mg/m <sup>2</sup> IV over 60 minutes. Repeat cycle every 3 weeks for 6 cycles.
Docetaxel (Category 2B) <sup>12,b,d</sup>	<b>Day 1:</b> Docetaxel 70mg/m <sup>2</sup> IV over 60 minutes. Repeat cycle every 3 weeks for 6 cycles.

continued

# Endometrial Carcinoma Treatment Regimens

## ► Systemic Therapy for Endometrial Carcinoma<sup>1</sup> (continued)

REGIMEN	DOSING
<b>Adjuvant Therapy for High-Risk Disease or Primary Therapy for Initially Unresectable Disease</b> (continued)	
<b>Chemotherapy<sup>a</sup></b> (continued)	
<b>Other Recommended Regimens</b> (continued)	
Ifosfamide (for carcinosarcoma) <sup>13,e</sup>	<p><b>Days 1-3:</b> Ifosfamide 2,000mg/m<sup>2</sup> IV over 3 hours  <b>Days 1-3:</b> Mesna 400mg/m<sup>2</sup> IV 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 for 6 cycles.</p> <p><b>OR</b></p> <p><b>Days 1-3:</b> Ifosfamide 1,200mg/m<sup>2</sup> (if prior pelvic radiation) over 3 hours  <b>Days 1-3:</b> Mesna 240mg/m<sup>2</sup> IV 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 for 6 cycles.</p>
Ifosfamide + Paclitaxel (Category 1 for carcinosarcoma) <sup>13,b,e</sup>	<p><b>Days 1-3:</b> Ifosfamide 1,600mg/m<sup>2</sup> IV over 3 hours  <b>Days 1-3:</b> Mesna 320mg/m<sup>2</sup> IV over 15 minutes three times daily, one dose before Ifosfamide, then at 4 and 8 hours from the start of each Ifosfamide dose.  <b>Day 1:</b> Paclitaxel 135mg/m<sup>2</sup> IV over 3 hours.                      Repeat cycle every 3 weeks for 6 cycles.</p> <p><b>OR</b></p> <p><b>Days 1-3:</b> Ifosfamide 1,200mg/m<sup>2</sup> (if prior pelvic radiation) IV over 3 hours  <b>Days 1-3:</b> Mesna 240mg/m<sup>2</sup> IV over 15 minutes three times daily, one dose before Ifosfamide, then at 4 and 8 hours from the start of each Ifosfamide dose.  <b>Day 1:</b> Paclitaxel 135mg/m<sup>2</sup> IV over 3 hours.                      Repeat cycle every 3 weeks for 6 cycles.</p>
Paclitaxel <sup>14,15,b</sup>	<p><b>Day 1:</b> Paclitaxel 175mg/m<sup>2</sup> IV over 3 hours.                      Repeat cycle every 3 weeks for 6 cycles.</p>
<b>Adjuvant Therapy: Subsequent Treatment for High-Risk Disease</b>	
<b>Targeted Therapy</b>	
<b>Other Recommended Regimen</b>	
Bevacizumab <sup>16,17,g,h</sup>	<p><b>Day 1:</b> Bevacizumab 15mg/kg IV.                      Repeat cycle every 3 weeks for 6 cycles.</p>
<b>Systemic Therapy for Recurrent or Metastatic Disease</b>	
<b>Chemotherapy<sup>a</sup></b>	
<b>Preferred Regimens</b>	
Carboplatin + Paclitaxel <sup>2-4,b</sup>	<p><b>Day 1:</b> Paclitaxel 175mg/m<sup>2</sup> IV over 3 hours, <b>followed by:</b>  <b>Day 1:</b> Carboplatin AUC 6 IV over 30 minutes.                      Repeat cycle every 3 weeks.</p>
Carboplatin + Paclitaxel + Trastuzumab (for HER2-positive uterine serous carcinoma) <sup>18,19,b,j</sup>	<p><b>Day 1:</b> Paclitaxel 175mg/m<sup>2</sup> IV over 3 hours, <b>followed by:</b>  <b>Day 1:</b> Carboplatin AUC 5 IV over 30 minutes  <b>Day 1:</b> Trastuzumab 8mg/kg IV over 90 minutes (cycle 1), then 6mg/kg IV (starting with cycle 2).                      Repeat every 3 weeks for 6 cycles, <b>followed by:</b>                      Maintenance therapy with:  <b>Day 1 (starting with cycle 7):</b> Trastuzumab 6mg/kg IV.                      Repeat cycle every 3 weeks.</p>
<b>Other Recommended Regimens</b>	
Albumin-Bound Paclitaxel <sup>20,21,j</sup>	<p><b>Day 1:</b> Albumin-Bound Paclitaxel 260mg/m<sup>2</sup> IV over 30 minutes.                      Repeat cycle every 3 weeks.</p> <p><b>OR</b></p> <p><b>Days 1,8,15:</b> Albumin-Bound Paclitaxel 100-125mg/m<sup>2</sup> IV over 30 minutes.                      Repeat cycle every 4 weeks.</p>
Bevacizumab <sup>16,17,g,h</sup>	<p><b>Day 1:</b> Bevacizumab 15mg/m<sup>2</sup> IV.                      Repeat cycle every 3 weeks</p>
Carboplatin <sup>5,a</sup>	<p><b>Day 1:</b> Carboplatin AUC 5-7 IV over 30 minutes.                      Repeat cycle every 3 weeks.</p>

continued

# Endometrial Carcinoma Treatment Regimens

## ► Systemic Therapy for Endometrial Carcinoma<sup>1</sup> (continued)

REGIMEN	DOSING
<b>Systemic Therapy for Recurrent or Metastatic Disease</b> (continued)	
<b>Chemotherapy<sup>a</sup></b> (continued)	
<b>Other Recommended Regimens</b> (continued)	
Carboplatin + Docetaxel <sup>6,7,b</sup>	<p><b>Day 1:</b> Docetaxel 60mg/m<sup>2</sup> IV over 60 minutes, <b>followed by:</b>  <b>Day 1:</b> Carboplatin AUC 6 IV over 30 minutes.            Repeat cycle every 3 weeks.</p> <p><b>OR</b></p> <p><b>Day 1:</b> Docetaxel 60mg/m<sup>2</sup> IV over 60 minutes, <b>followed by:</b>  <b>Day 1:</b> Carboplatin AUC 6 IV over 30 minutes.            Repeat every 3 weeks.</p>
Carboplatin + Paclitaxel + Bevacizumab <sup>17,22,23,b,g</sup>	<p><b>Day 1:</b> Paclitaxel 175mg/m<sup>2</sup> IV over 3 hours, <b>followed by:</b>  <b>Day 1:</b> Carboplatin AUC 5 IV, <b>followed by:</b>  <b>Day 1:</b> Bevacizumab 15mg/kg IV.            Repeat cycle every 3 weeks for 6-8 cycles <b>followed by:</b>            Maintenance therapy with:  <b>Day 1:</b> Bevacizumab 15mg/kg IV.            Repeat cycle every 3 weeks.</p>
Cisplatin <sup>8,a,c</sup>	<p><b>Day 1:</b> Cisplatin 50mg/m<sup>2</sup> IV over 60 minutes.            Repeat cycle every 3 weeks.</p>
Cisplatin + Doxorubicin <sup>9,10,b,c</sup>	<p><b>Day 1:</b> Doxorubicin 60mg/m<sup>2</sup> IV push  <b>Day 1:</b> Cisplatin 50mg/m<sup>2</sup> IV over 60 minutes.            Repeat cycle every 3 weeks until disease progression or unacceptable toxicity reaching a lifetime cumulative anthracycline dose.</p> <p><b>OR</b></p> <p><b>Day 1:</b> Doxorubicin 45mg/m<sup>2</sup> (if prior pelvic radiation) IV push  <b>Day 1:</b> Cisplatin 50mg/m<sup>2</sup> IV over 60 minutes.            Repeat cycle every 3 weeks until disease progression or unacceptable toxicity reaching a lifetime cumulative anthracycline dose.</p>
Cisplatin + Doxorubicin + Paclitaxel <sup>10,b,c,f</sup>	<p><b>Day 1:</b> Doxorubicin 45mg/m<sup>2</sup> IV push  <b>Day 1:</b> Cisplatin 50mg/m<sup>2</sup> IV over 60 minutes  <b>Day 2:</b> Paclitaxel 160mg/m<sup>2</sup> IV over 3 hours.            Repeat cycle every 3 weeks until disease progression or unacceptable toxicity reaching a lifetime cumulative anthracycline dose.</p>
Cisplatin + Ifosfamide (for carcinosarcoma) <sup>11,b,c,e</sup>	<p><b>Days 1-4:</b> Ifosfamide 1,500mg/m<sup>2</sup> IV over 3 hours  <b>Days 1-4:</b> Mesna 300mg/m<sup>2</sup> IV over 15 minutes before Ifosfamide, then at 4 and 8 hours from the start of each Ifosfamide dose  <b>Days 1-4:</b> Cisplatin 20mg/m<sup>2</sup> IV over 60 minutes.            Repeat cycle every 3 weeks.</p> <p><b>OR</b></p> <p><b>Days 1-4:</b> Ifosfamide 1,200mg/m<sup>2</sup> (if prior pelvic radiation) IV over 3 hours daily  <b>Days 1-4:</b> Mesna 240mg/m<sup>2</sup> IV over 15 minutes before Ifosfamide, then at 4 and 8 hours from the start of each Ifosfamide dose  <b>Days 1-4:</b> Cisplatin 20mg/m<sup>2</sup> IV over 60 minutes.            Repeat cycle every 3 weeks.</p>
Docetaxel (Category 2B) <sup>12,b,d</sup>	<p><b>Day 1:</b> Docetaxel 70mg/m<sup>2</sup> IV over 60 minutes.            Repeat cycle every 3 weeks.</p>
Doxorubicin <sup>24-26</sup>	<p><b>Day 1:</b> Doxorubicin 80mg/m<sup>2</sup> IV push.            Repeat cycle every 3 weeks until disease progression or unacceptable toxicity including reaching a lifetime cumulative anthracycline dose.</p>
Ifosfamide (for carcinosarcoma) <sup>13,e</sup>	<p><b>Days 1-3:</b> Ifosfamide 2,000mg/m<sup>2</sup> IV over 3 hours daily  <b>Days 1-3:</b> Mesna 400mg/m<sup>2</sup> IV over 15 minutes before Ifosfamide, then at 4 and 8 hours from the start of each Ifosfamide dose.            Repeat cycle every 3 weeks.</p> <p><b>OR</b></p> <p><b>Days 1-3:</b> Ifosfamide 1,200mg/m<sup>2</sup> (if prior pelvic radiation) IV over 3 hours daily  <b>Days 1-3:</b> Mesna 240mg/m<sup>2</sup> IV over 15 minutes before Ifosfamide, then at 4 and 8 hours from the start of each Ifosfamide dose.            Repeat cycle every 3 weeks.</p>

continued

# Endometrial Carcinoma Treatment Regimens

## ► Systemic Therapy for Endometrial Carcinoma<sup>1</sup> (continued)

REGIMEN	DOSING
<b>Systemic Therapy for Recurrent or Metastatic Disease</b> (continued)	
<b>Chemotherapy<sup>a</sup></b> (continued)	
<b>Other Recommended Regimens</b> (continued)	
Ifosfamide + Paclitaxel (Category 1 for carcinosarcoma) <sup>13,b,e</sup>	<b>Days 1-3:</b> Ifosfamide 1,600mg/m <sup>2</sup> IV over 3 hours daily <b>Days 1-3:</b> Mesna 320mg/m <sup>2</sup> IV over 15 minutes before Ifosfamide, then at 4 and 8 hours from the start of Ifosfamide dose. <b>Day 1:</b> Paclitaxel 135mg/m <sup>2</sup> IV over 3 hours. Repeat cycle every 3 weeks.
Liposomal Doxorubicin <sup>27,28,b</sup>	<b>Day 1:</b> Liposomal Doxorubicin 40-50mg/m <sup>2</sup> IV Repeat cycle every 4 weeks until disease progression or unacceptable toxicity including reaching a lifetime cumulative anthracycline dose.
Paclitaxel <sup>14,15,b</sup>	<b>Day 1:</b> Paclitaxel 175mg/m <sup>2</sup> IV over 3 hours. Repeat cycle every 3 weeks.
Temsirolimus <sup>29,30</sup>	<b>Days 1,8,15,22:</b> Temsirolimus 25mg IV over 30 minutes. Repeat cycle every 4 weeks.
Topotecan <sup>31</sup>	<b>Days 1-5:</b> Topotecan 1mg/m <sup>2</sup> IV over 30 minutes. Repeat cycle every 3 weeks. <b>OR</b> <b>Days 1-5:</b> Topotecan 0.8mg/m <sup>2</sup> (if prior pelvic radiation) IV over 30 minutes. Repeat cycle every 3 weeks.
<b>Chemotherapy + Hormonal Therapy</b>	
<b>Other Recommended Regimens</b>	
Everolimus + Letrozole (for endometrioid histology) <sup>32-34</sup>	<b>Days 1-28:</b> Everolimus 10mg orally daily <b>Days 1-28:</b> Letrozole 2.5mg orally daily. Repeat cycle every 4 weeks.
<b>Targeted Therapy + Immunotherapy</b>	
<b>Other Recommended Regimens</b>	
Lenvatinib + Pembrolizumab <sup>35-37,k</sup>	<b>Days 1-21:</b> Lenvatinib 20mg orally <b>Day 1:</b> Pembrolizumab 200mg IV. Repeat cycle every 3 weeks.
<b>Subsequent Systemic Therapy for Recurrent Disease</b>	
<b>Immunotherapy</b>	
<b>Useful in Certain Circumstances</b>	
Pembrolizumab (for MSI-H/dMMR tumors) <sup>36,38,l</sup>	<b>Day 1:</b> Pembrolizumab 200mg IV over 30 minutes. Repeat cycle every 3 weeks.
<b>Systemic Therapy for Lower-Grade Endometrioid Histologies, Preferably in Patients With Small Tumor Volume or an Indolent Growth Pace</b>	
<b>Hormone Therapy<sup>m</sup></b>	
<b>Preferred Regimens</b>	
Anastrozole <sup>39</sup>	See NCCN Uterine Neoplasms Guidelines <sup>1</sup>
Exemestane <sup>40</sup>	
Fulvestrant <sup>41</sup>	
Letrozole	
Levonorgestrel intrauterine device (IUD) (for select fertility-sparing cases)	
Megestrol Acetate	
Megestrol Acetate, Tamoxifen (alternating)	
Medroxyprogesterone Acetate	
Tamoxifen	

continued

# Endometrial Carcinoma Treatment Regimens

## ► Systemic Therapy for Endometrial Carcinoma<sup>1</sup> (continued)

- a. Chemotherapy regimens can be used for all carcinoma histologies. Carcinosarcomas are now considered and treated as high-grade carcinomas. However, ifosfamide-based regimens were previously used for carcinosarcomas.
- b. Cisplatin, carboplatin, liposomal doxorubicin, paclitaxel, and docetaxel may cause drug reactions. (See NCCN Ovarian Cancer Guidelines – Management of Drug Reactions.)
- c. Hydration is required with supplemental electrolytes pre- and post-administration of Cisplatin.
- d. Docetaxel may be considered for patients in whom paclitaxel is contraindicated.
- e. Hydration is required pre- and postadministration of Ifosfamide.
- f. The cisplatin/doxorubicin/paclitaxel regimen is not widely used because of concerns about toxicity.
- g. An FDA-approved biosimilar is an appropriate substitute for bevacizumab.
- h. Bevacizumab may be considered for use in patients who have progressed on prior cytotoxic chemotherapy.
- i. Only for advanced (stage III/IV) and recurrent uterine serous carcinomas that are HER2-positive.
- j. 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 required desensitization to paclitaxel. Albumin-bound paclitaxel is not a reasonable substitute for paclitaxel if the patient's skin test is positive.
- k. For advanced and recurrent disease only.
- l. For recurrent endometrial cancer, NCCN recommends MSI-H or dMMR testing if not previously done. Pembrolizumab is indicated for patients with MSI-H or dMMR tumors that have progressed following prior cytotoxic chemotherapy.
- m. Hormonal therapy is typically used for lower-grade endometrioid histologies, preferably in patients with small tumor volume or an indolent growth pace.

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