

# Malignant Pleural Mesothelioma Cancers 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 health care 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 provided only to supplement the latest treatment strategies.

These Guidelines are a work in progress that may be refined as often as new significant data become 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.

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

## ► Induction Chemotherapy<sup>1</sup>

REGIMEN	DOSING
Pemetrexed/Carboplatin <sup>2,7,a,b,d</sup>	<b>Day 1:</b> Pemetrexed 500mg/m <sup>2</sup> IV over 10 minutes, <b>followed by:</b> <b>Day 1:</b> Carboplatin AUC 5 IV over 30 minutes. Repeat cycle every 3 weeks for 6 cycles.
Pemetrexed/Cisplatin (Category 1) <sup>2,7,10,a,c</sup>	<b>Day 1:</b> Pemetrexed 500mg/m <sup>2</sup> IV over 10 minutes, <b>followed by:</b> <b>Day 1:</b> Cisplatin 75mg/m <sup>2</sup> IV over 2 hours. Repeat cycle every 3 weeks for 4 cycles.

## ► Systemic Therapy Regimens<sup>1</sup>

First-Line Systemic Therapy	
Preferred	
Nivolumab + Ipilimumab (Category 1) <sup>11,16,e,f</sup>	<b>Days 1,22:</b> Nivolumab 360mg IV over 30 minutes, <b>followed by:</b> <b>Day 1:</b> Ipilimumab 1mg/kg IV over 30 minutes. Repeat cycle every 6 weeks or up until 2 years of therapy has been completed.
Pemetrexed/Cisplatin (Category 1) <sup>2,7,10,a,c</sup>	<b>Day 1:</b> Pemetrexed 500mg/m <sup>2</sup> IV over 10 minutes, <b>followed by:</b> <b>Day 1:</b> Cisplatin 75mg/m <sup>2</sup> IV over 2 hours. Repeat cycle every 3 weeks.
Pemetrexed/Cisplatin + Bevacizumab followed by Bevacizumab maintenance (Category 1) <sup>2,8,17,18,a-e,g</sup>	<b>Day 1:</b> Pemetrexed 500mg/m <sup>2</sup> IV over 10 minutes, <b>followed by:</b> <b>Day 1:</b> Cisplatin 75mg/m <sup>2</sup> IV over 2 hours <b>Day 1:</b> Bevacizumab 15mg/kg IV. Repeat cycle every 3 weeks for 6 cycles <b>followed by maintenance therapy with:</b> <b>Day 1:</b> Bevacizumab 15mg/kg IV. Repeat cycle every 3 weeks.
Other Recommended	
Pemetrexed/Carboplatin <sup>2,7,a,b,d</sup>	<b>Day 1:</b> Pemetrexed 500mg/m <sup>2</sup> IV over 10 minutes, <b>followed by:</b> <b>Day 1:</b> Carboplatin AUC 5 IV over 30 minutes. Repeat cycle every 3 weeks.
Pemetrexed/Carboplatin + Bevacizumab followed by Bevacizumab maintenance <sup>2,3,7,17,19,a,b,d,e,g</sup>	<b>Day 1:</b> Pemetrexed 500mg/m <sup>2</sup> IV over 10 minutes, <b>followed by:</b> <b>Day 1:</b> Carboplatin AUC 5 IV over 30 minutes <b>Day 1:</b> Bevacizumab 15mg/kg IV. Repeat cycle every 3 weeks for 6 cycles <b>followed by maintenance therapy with:</b> <b>Day 1:</b> Bevacizumab 15mg/kg IV. Repeat cycle every 3 weeks.
Useful in Certain Circumstances	
Gemcitabine/Cisplatin <sup>8,20-22,c</sup>	<b>Days 1,8,15:</b> Gemcitabine 1,000mg/m <sup>2</sup> over 30 minutes, <b>followed by:</b> <b>Day 1:</b> Cisplatin 100 mg/m <sup>2</sup> IV over 2 hours. Repeat every 4 weeks for a maximum of 6 cycles. <b>OR</b> <b>Days 1,8:</b> Gemcitabine 1,250mg/m <sup>2</sup> over 30 minutes, <b>followed by:</b> <b>Day 1:</b> Cisplatin 80 mg/m <sup>2</sup> IV over 2 hours. Repeat every 3 weeks for a maximum of 6 weeks.
Pemetrexed <sup>2,23-25,a,b</sup>	<b>Day 1:</b> Pemetrexed 500mg/m <sup>2</sup> IV over 10 minutes. Repeat cycle every 3 weeks.

continued

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## ► Systemic Therapy Regimens<sup>1</sup> (continued)

REGIMEN	DOSING
<b>First-Line Systemic Therapy</b> (continued)	
<b>Useful in Certain Circumstances</b> (continued)	
Vinorelbine <sup>26-29</sup>	<p><b>Day 1:</b> Vinorelbine 25-30mg/m<sup>2</sup> IV over 5-10 minutes. Repeat cycle every week.</p> <p><b>OR</b></p> <p><b>Days 1,8,15,22,29,36:</b> Vinorelbine 25-30mg/m<sup>2</sup> IV over 5-10 minutes Repeat cycle every 8 weeks (6 weeks on followed by 2 weeks off treatment).</p> <p><b>OR</b></p> <p><b>Days 1,8:</b> Vinorelbine 25-30mg/m<sup>2</sup> IV over 5-10 minutes. Repeat cycle every 3 weeks.</p>
<b>Subsequent Systemic Therapy</b>	
<b>Preferred</b>	
Nivolumab <sup>11-13,30</sup>	<p><b>Day 1:</b> Nivolumab 240mg IV over 30 minutes. Repeat cycle every 2 weeks.</p> <p><b>OR</b></p> <p><b>Day 1:</b> Nivolumab 480mg IV over 30 minutes. Repeat cycle every 4 weeks.</p>
Nivolumab + Ipilimumab (if not administered first-line) <sup>11-16,e,f</sup>	<p><b>Day 1:</b> Nivolumab 240mg IV over 30 minutes, <b>with:</b> <b>Day 1:</b> Ipilimumab 1mg/kg IV over 30 minutes. Repeat cycle every 6 weeks for 4 cycles.</p> <p><b>OR</b></p> <p><b>Days 1,15,29:</b> Nivolumab 3mg/kg IV over 30 minutes, <b>followed by:</b> <b>Day 1:</b> Ipilimumab 1mg/kg IV over 30 minutes. Repeat cycle every 6 weeks or until up to 2 years of therapy has been completed.</p>
Pembrolizumab <sup>31-34</sup>	<p><b>Day 1:</b> Pembrolizumab 200mg IV over 30 minutes. Repeat cycle every 3 weeks or until up to 2 years of therapy has been completed.</p> <p><b>OR</b></p> <p><b>Day 1:</b> Pembrolizumab 400mg IV over 30 minutes. Repeat cycle every 6 weeks or until up to 2 years of therapy has been completed.</p>
Pemetrexed (if not administered first-line; consider rechallenge if good sustained response at the time initial chemotherapy was interrupted) (Category 1) <sup>2,23-25,a,b</sup>	<p><b>Day 1:</b> Pemetrexed 500mg/m<sup>2</sup> IV over 10 minutes. Repeat cycle every 3 weeks.</p>
<b>Useful in Certain Circumstances</b>	
Gemcitabine <sup>20,22,29</sup>	<p><b>Days 1,8,15:</b> Gemcitabine 1,000-1250mg/m<sup>2</sup> IV over 30 minutes. Repeat cycle every 4 weeks.</p> <p><b>OR</b></p> <p><b>Days 1,8:</b> Gemcitabine 1,000mg/m<sup>2</sup> IV over 30 minutes. Repeat cycle every 3 weeks.</p>
Vinorelbine <sup>26-29</sup>	<p><b>Day 1:</b> Vinorelbine 25-30mg/m<sup>2</sup> IV over 5-10 minutes. Repeat cycle every week.</p> <p><b>OR</b></p> <p><b>Days 1,8,15,22,29,36:</b> Vinorelbine 25-30mg/m<sup>2</sup> IV over 5-10 minutes. Repeat cycle every 8 weeks (6 weeks on followed by 2 weeks off treatment).</p> <p><b>OR</b></p> <p><b>Days 1,8:</b> Vinorelbine 25-30mg/m<sup>2</sup> IV over 5-10 minutes. Repeat cycle every 3 weeks.</p>

<sup>a</sup> Premedication and supplemental medications to reduce the incidence and severity of hematologic, gastrointestinal, and cutaneous toxicities are required for Pemetrexed. The recommended dosing is: vitamin B12 (cyanocobalamin) 1,000mcg IM during the week preceding the first cycle of pemetrexed and every 3 cycles thereafter, and folic acid 400-1,000mcg oral once daily starting 1 week before the first cycle and continuing for 3 weeks after the last dose of pemetrexed, and dexamethasone 4 mg orally twice daily for 3 days starting the day prior to pemetrexed.

<sup>b</sup> Pemetrexed-based chemotherapy may also be used for malignant peritoneal mesothelioma, pericardial mesothelioma, and tunica vaginalis testis mesothelioma.

<sup>c</sup> Hydration is required with supplemental electrolytes pre- and post-administration of cisplatin.

<sup>d</sup> Appropriate for patients not eligible for cisplatin

<sup>e</sup> The combination regimens pemetrexed/cisplatin/bevacizumab, pemetrexed/carboplatin/bevacizumab, and nivolumab/ipilimumab are only for unresectable disease.

<sup>f</sup> Nivolumab/ipilimumab is preferred for patients with biphasic or sarcomatoid histology and is also an option with epithelioid histology

<sup>g</sup> An FDA-approved biosimilar is an appropriate substitute for bevacizumab.

continued

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