

Bladder Cancer 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.

► Intravesical Therapy¹

REGIMEN	DOSING
Immediate Postoperative Intravesical Chemotherapy^a	
Gemcitabine (Category 1) ²⁻⁴	<p>Day 1: Gemcitabine 2,000mg intravesical within 24 hours of TURBT (ideally within 6 hours). Administer for 1 dose after surgery.</p> <p>OR</p> <p>Days 1,8,15,22,29,36: Gemcitabine 2,000mg intravesical or percutaneous. Repeat cycle every 6 weeks beginning 3-4 weeks after surgery for a maximum of 2 cycles, conditionally followed by:</p> <p>Day 1: Gemcitabine 2,000mg intravesical. Administer every 4 weeks for 12 cycles.</p>
Mitomycin (Category 1) ⁵⁻⁷	<p>Day 1: Mitomycin 40mg intravesical within 24 hours of TURBT (ideally within 6 hours). Administer for 1 dose after surgery.</p> <p>OR</p> <p>Days 1,8,15,22,29,36: Mitomycin 40mg intravesical or percutaneous. Repeat cycle every 6 weeks beginning 3-4 weeks after surgery for a maximum of 2 cycles, conditionally followed by:</p> <p>Day 1: Mitomycin 40mg intravesical. Repeat cycle every 4 weeks for 5-11 cycles based on risk group (5 for intermediate risk; 11 for high risk).</p>
Induction (Adjuvant) Intravesicular Chemotherapy or BCG^b	
BCG (Bacillus Calmette-Guérin) ⁸⁻¹¹	<p>If TheraCys product is used:</p> <p>Days 1,8,15,22,29,36: BCG 81mg intravesical or percutaneous. Administer every 6 weeks beginning 3-4 weeks after surgery for a maximum of 2 cycles, followed by maintenance therapy (see below).</p> <p>OR</p> <p>If TICE product is used:</p> <p>Days 1,8,15,22,29,36: BCG 50mg intravesical or percutaneous. Administer every 6 weeks beginning 3-4 weeks after surgery for a maximum of 2 cycles, followed by maintenance therapy (see below).</p>
Docetaxel ^{12,13}	<p>Days 1,8,15,22,29,36: Docetaxel 75mg intravesical. Repeat cycle every 6 weeks beginning 3-4 weeks following surgery for a maximum of 2 cycles, conditionally followed by maintenance therapy with:</p> <p>Day 1: Docetaxel 75mg intravesical. Repeat cycle every 4 weeks for 9 cycles starting 3 months after adjuvant therapy.</p>
Epirubicin ^{14,15}	<p>Days 1,8,15,22,29,36: Epirubicin 50mg intravesical. Repeat cycle every 6 weeks beginning 3-4 weeks after surgery for a maximum of 2 cycles, conditionally followed by maintenance therapy with:</p> <p>Days 1,8,15 of months 3,6,12,18,24,30, and 36 from initiation of adjuvant therapy: Epirubicin 50mg intravesical.</p>
Gemcitabine ²⁻⁴	<p>Day 1: Gemcitabine 2,000mg intravesical within 24 hours of TURBT (ideally within 6 hours). Administer for 1 dose after surgery.</p> <p>OR</p> <p>Days 1,8,15,22,29,36: Gemcitabine 2,000mg intravesical or percutaneous. Repeat cycle every 6 weeks beginning 3-4 weeks after surgery for a maximum of 2 cycles, conditionally followed by:</p> <p>Day 1: Gemcitabine 2,000mg intravesical. Administer every 4 weeks for 12 cycles.</p>
Gemcitabine + Docetaxel ¹⁶	<p>Days 1,8,15,22,29,36: Gemcitabine 1,000mg intravesical, followed by:</p> <p>Days 1,8,15,22,29,36: Docetaxel 37.5mg intravesical. Repeat cycle every 6 weeks beginning 3-4 weeks after surgery for a maximum of 2 cycles.</p>

continued

Bladder Cancer Treatment Regimens

► Intravesical Therapy¹ (continued)

REGIMEN	DOSING
Induction (Adjuvant) Intravesicular Chemotherapy or BCG^b (continued)	
Gemcitabine + Mitomycin ¹⁷	<p>Days 1,8,15,22,29,36: Gemcitabine 1,000mg intravesical, followed by: Days 1,8,15,22,29,36: Mitomycin 40mg intravesical, conditionally followed by maintenance therapy with: Day 1: Gemcitabine 1,000mg intravesical, followed by: Day 1: Mitomycin 40mg intravesical. Repeat cycle every 4 weeks for 12 cycles.</p>
Mitomycin ⁵⁻⁷	<p>Day 1: Mitomycin 40mg intravesical within 24 hours of TURBT (ideally within 6 hours). Administer for 1 dose after surgery. OR Days 1,8,15,22,29,36: Mitomycin 40mg intravesical or percutaneous. Repeat cycle every 6 weeks beginning 3-4 weeks after surgery for a maximum of 2 cycles, conditionally followed by: Day 1: Mitomycin 40mg intravesical. Repeat cycle every 4 weeks for 5-11 cycles based on risk group (5 for intermediate risk; 11 for high risk).</p>
Valrubicin ¹⁸	<p>Days 1,8,15,22,29,36: Valrubicin 800mg intravesical. Repeat every 6 weeks beginning 3-4 weeks after surgery for 2 cycles, conditionally followed by: Day 1: Valrubicin 800mg intravesical. Repeat cycle every 4 weeks for 10 cycles.</p>
Maintenance Intravesical BCG^c	
BCG ⁹⁻¹¹	<p>If TherCys product is used: Days 1,8,15 of months 3,6,12,18,24,30, and 36 from initiation of BCG adjuvant therapy: BCG 81mg intravesical. Begin maintenance therapy after completion of adjuvant BCG therapy, and ideally continue for 1 year for intermediate-risk and 3 years for high-risk disease.</p> <p>If TICE product is used: Day 1: BCG 50mg intravesical. Begin maintenance therapy after completion of adjuvant therapy and repeat cycle monthly for at least 6-12 months; ideally maintenance therapy should continue for 1 year for intermediate-risk and 3 years for high-risk disease.</p>

► Systemic Therapy for Urothelial Bladder Cancer¹

Perioperative Chemotherapy (Neoadjuvant or Adjuvant)^{d,e}	
Preferred	
DDMVAC (Dose-dense Methotrexate, Vinblastine, Doxorubicin, and Cisplatin) [with growth factor support] ^{19-21,f}	<p>Day 1: Methotrexate 30mg/m² IV push Day 1 or on Day 2: Vinblastine 3mg/m² IV over 5-10 minutes Day 1 or on Day 2: Doxorubicin 30mg/m² IV push Day 1 or on Day 2: Cisplatin 70mg/m² IV over 60 minutes. Repeat cycle every 2 weeks for 3-4 cycles.</p>
Gemcitabine + Cisplatin ^{22,23,f}	<p>Days 1,8,15: Gemcitabine 1,000mg/m² IV over 30 minutes, followed by: Day 1 or on Day 2: Cisplatin 70mg/m² IV over 60 minutes. Repeat cycle every 4 weeks for 4 cycles. OR Days 1,8: Gemcitabine 1,000mg/m² IV over 30 minutes, followed by: Day 1 or on Day 2: Cisplatin 70mg/m² IV over 60 minutes. Repeat cycle every 3 weeks for 4 cycles.</p>
Other Recommended Regimens	
CMV (Cisplatin, Methotrexate, Vinblastine) ^{24,f}	<p>Days 1,8: Methotrexate 30mg/m² IV push Days 1,8: Vinblastine 4mg/m² IV over 5-10 minutes Day 2: Cisplatin 100mg/m² IV over 60 minutes. Repeat cycle every 3 weeks for 3 cycles.</p>

continued

Bladder Cancer Treatment Regimens

► Systemic Therapy for Urothelial Bladder Cancer¹ (continued)

REGIMEN	DOSING
First-Line Systemic Therapy for Locally Advanced or Metastatic Disease (Stage IV)	
Cisplatin Eligible Patients	
Preferred	
Gemcitabine + Cisplatin (Category 1) Followed By Avelumab Maintenance Therapy ^{22,23,25,26,f}	<p>Days 1,8,15: Gemcitabine 1,000mg/m² IV over 30 minutes, followed by: Day 1 or on Day 2: Cisplatin 70mg/m² IV over 60 minutes. Repeat cycle every 4 weeks for 4-6 cycles, conditionally followed by maintenance therapy with: Day 1: Avelumab 800mg IV over 60 minutes. Repeat cycle every 2 weeks.</p> <p>OR</p> <p>Days 1,8: Gemcitabine 1,000mg/m² IV over 30 minutes, followed by: Day 1 or on Day 2: Cisplatin 70mg/m² IV over 60 minutes. Repeat cycle every 3 weeks for 4-6 cycles, conditionally followed by maintenance therapy with: Day 1: Avelumab 800mg IV over 60 minutes. Repeat cycle every 2 weeks.</p>
DDMVAC (Category 1) Followed By Avelumab Maintenance Therapy ^{19-21,25,26,f}	<p>Day 1: Methotrexate 30mg/m² IV push Day 1 or on Day 2: Vinblastine 3mg/m² IV over 5-10 minutes Day 1 or on Day 2: Doxorubicin 30mg/m² IV push Day 1 or on Day 2: Cisplatin 70mg/m² IV over 60 minutes. Repeat cycle every 2 weeks for 4-6 cycles, conditionally followed by maintenance therapy with: Day 1: Avelumab 800mg IV over 60 minutes. Repeat cycle every 2 weeks.</p>
Cisplatin Ineligible Patients	
Preferred	
Gemcitabine + Carboplatin Followed By Avelumab Maintenance Therapy ²⁵⁻²⁹	<p>Days 1,8: Gemcitabine 1,000-1,250mg/m² IV over 30 minutes Day 1: Carboplatin AUC 5-6 IV over 30 minutes. Repeat cycle every for 4-6 cycles, conditionally followed by maintenance therapy with: Day 1: Avelumab 800mg IV over 60 minutes. Repeat cycle every 2 weeks.</p>
Atezolizumab (Only for Patients Whose Tumors Express PD-L1 or Who Are Not Eligible For Any Platinum-Containing Chemotherapy Regardless of PD-L1 Expression) ³⁰⁻³³	<p>Day 1: Atezolizumab 840mg IV. Repeat cycle every 2 weeks.</p> <p>OR</p> <p>Day 1: Atezolizumab 1,200mg IV. Repeat cycle every 3 weeks.</p> <p>OR</p> <p>Day 1: Atezolizumab 1,680mg IV. Repeat cycle every 4 weeks.</p>
Pembrolizumab (Only for Patients Whose Tumors Express PD-L1 or Who Are Not Eligible For Any Platinum-Containing Chemotherapy Regardless of PD-L1 Expression) ³⁴⁻³⁸	<p>Day 1: Pembrolizumab 200mg IV over 30 minutes. Repeat cycle every 3 weeks up to 2 years of therapy.</p> <p>OR</p> <p>Day 1: Pembrolizumab 400mg IV over 30 minutes. Repeat cycle every 42 days up to 2 years of therapy.</p>
Other Recommended Regimens	
Gemcitabine ^{39,40}	<p>Days 1,8,15: Gemcitabine 1,000-1,250mg/m² IV over 30 minutes. Repeat cycle every 4 weeks.</p> <p>OR</p> <p>Days 1, 8: Gemcitabine 1,000-1,250mg/m² IV over 30 minutes. Repeat cycle every 3 weeks.</p>
Gemcitabine + Paclitaxel ⁴¹	<p>Day 1: Paclitaxel 175mg/m² IV over 3 hours, followed by: Days 1,8: Gemcitabine 1,000mg/m² IV over 30 minutes. Repeat cycle every 3 weeks.</p>
Useful Under Certain Circumstances	
Ifosfamide + Doxorubicin + Gemcitabine (For Patients With Good Kidney Function and Good PS) ^{42,g}	<p>Days 1-4: Ifosfamide 1,500mg/m² IV over 3 hours daily Days 1-4: Mesna 300mg/m² IV over 15 minutes 3 times daily (one dose before ifosfamide, then at 4 and 8 hours from the start of the ifosfamide dose) Day 3: Doxorubicin 45mg/m² IV push Days 2,4: Gemcitabine 150mg/m² IV over 30 minutes. Repeat cycle every 3 weeks for 3 cycles.</p>

continued

Bladder Cancer Treatment Regimens

► Systemic Therapy for Urothelial Bladder Cancer¹ (continued)

REGIMEN	DOSING
Second-Line Systemic Therapy for Locally Advanced or Metastatic Disease (Stage IV) (Post-Platinum)^{h,i}	
Preferred	
Pembrolizumab (Category 1) ³⁴⁻³⁸	<p>Day 1: Pembrolizumab 200mg IV over 30 minutes. Repeat cycle every 3 weeks up to 2 years of therapy.</p> <p>OR</p> <p>Day 1: Pembrolizumab 400mg IV over 30 minutes. Repeat cycle every 42 days up to 2 years of therapy.</p>
Alternative Preferred Regimens	
Atezolizumab ³⁰⁻³³	<p>Day 1: Atezolizumab 840mg IV. Repeat cycle every 2 weeks.</p> <p>OR</p> <p>Day 1: Atezolizumab 1,200mg IV. Repeat cycle every 3 weeks.</p> <p>OR</p> <p>Day 1: Atezolizumab 1,680mg IV. Repeat cycle every 4 weeks.</p>
Avelumab ^{24,43,44}	<p>Day 1: Avelumab 800mg IV over 60 minutes. Repeat cycle every 2 weeks.</p>
Durvalumab ⁴⁵⁻⁴⁶	<p>Day 1: Durvalumab 10mg/kg IV over 60 minutes. Repeat cycle every 2 weeks.</p>
Erdafitinib (For Patients With Susceptible <i>FGFR2/FGFR3</i> Alterations) ^{47,48}	<p>Days 1-14: Erdafitinib 8mg orally once daily cycle 1, followed by:</p> <p>Days 15-18: Erdafitinib 9mg orally once daily cycle 1 (increase dose based on tolerability after 14 to 21 days if serum phosphate is <5.5 mg/dL and no ocular disorders ≥grade 2 toxicity), followed by:</p> <p>Days 1-28: Erdafitinib 9mg (if tolerated) orally once daily beginning with cycle 2. Repeat cycle every 4 weeks.</p>
Nivolumab ⁵⁰⁻⁵²	<p>Day 1: Nivolumab 240mg IV over 30 minutes. Repeat cycle every 2 weeks.</p> <p>OR</p> <p>Day 1: Nivolumab 480mg IV over 30 minutes. Repeat cycle every 4 weeks.</p>
Other Recommended Regimens	
Docetaxel ⁵³	<p>Day 1: Docetaxel 100mg/m² IV over 60 minutes. Repeat cycle every 3 weeks.</p>
Gemcitabine ^{39,40}	<p>Days 1,8,15: Gemcitabine 1,000-1,250mg/m² IV over 30 minutes. Repeat cycle every 4 weeks.</p> <p>OR</p> <p>Days 1, 8: Gemcitabine 1,000-1,250mg/m² IV over 30 minutes. Repeat cycle every 3 weeks.</p>
Paclitaxel ⁵⁴⁻⁵⁶	<p>Days 1,8,15,22: Paclitaxel 80mg/m² IV over 60 minutes. Repeat cycle every 4 weeks.</p> <p>OR</p> <p>Day 1: Paclitaxel 200mg/m² IV over 3 hours. Repeat cycle every 3 weeks.</p>
Useful in Certain Circumstances Based on Prior Medical History	
DDMAC (with growth factor support) ^{19-21,f}	<p>Day 1: Methotrexate 30mg/m² IV push</p> <p>Day 1 or on Day 2: Vinblastine 3mg/m² IV over 5-10 minutes</p> <p>Day 1 or on Day 2: Doxorubicin 30mg/m² IV push</p> <p>Day 1 or on Day 2: Cisplatin 70mg/m² IV over 60 minutes. Repeat cycle every 2 weeks for 4-6 cycles.</p>
Gemcitabine + Cisplatin ^{22,23,f}	<p>Days 1,8,15: Gemcitabine 1,000mg/m² IV over 30 minutes, followed by:</p> <p>Day 1 or on Day 2: Cisplatin 70mg/m² IV over 60 minutes. Repeat cycle every 4 weeks for 4-6 cycles.</p> <p>OR</p> <p>Days 1,8: Gemcitabine 1,000mg/m² IV over 30 minutes, followed by:</p> <p>Day 1 or on Day 2: Cisplatin 70mg/m² IV over 60 minutes. Repeat cycle every 3 weeks for 4-6 cycles.</p>

continued

Bladder Cancer Treatment Regimens

► Systemic Therapy for Urothelial Bladder Cancer¹ (continued)

REGIMEN	DOSING
Second-Line Systemic Therapy for Locally Advanced or Metastatic Disease (Stage IV) (Post-Platinum)^{h,i} (continued)	
Useful in Certain Circumstances Based on Prior Medical History (continued)	
Gemcitabine + Paclitaxel ⁴¹	Day 1: Paclitaxel 175mg/m ² IV over 3 hours, followed by: Days 1,8: Gemcitabine 1,000mg/m ² IV over 30 minutes. Repeat cycle every 3 weeks.
Ifosfamide + Doxorubicin + Gemcitabine ^{42,g}	Days 1-4: Ifosfamide 1,500mg/m ² IV over 3 hours daily Days 1-4: Mesna 300mg/m ² IV over 15 minutes 3 times daily (one dose before ifosfamide, then at 4 and 8 hours from the start of the ifosfamide dose) Day 3: Doxorubicin 45mg/m ² IV push Days 2,4: Gemcitabine 150mg/m ² IV over 30 minutes. Repeat cycle every 3 weeks for 3 cycles.
Second-Line Systemic Therapy for Locally Advanced or Metastatic Disease (Stage IV) (Post-Checkpoint Inhibitor)^b	
Preferred Regimen For Cisplatin Ineligible and Chemotherapy Naïve Patients	
Gemcitabine + Carboplatin ^{27,29}	Days 1,8: Gemcitabine 1,000-1,250mg/m ² IV over 30 minutes Day 1: Carboplatin AUC 5-6 IV over 30 minutes. Repeat cycle every 3 weeks for 4-6 cycles.
Preferred Regimens for Cisplatin Eligible and Chemotherapy Naïve Patients	
Gemcitabine + Cisplatin ^{22,23,f}	Days 1,8,15: Gemcitabine 1,000mg/m ² IV over 30 minutes, followed by: Day 1 or on Day 2: Cisplatin 70mg/m ² IV over 60 minutes. Repeat cycle every 4 weeks for 4-6 cycles. OR Days 1,8: Gemcitabine 1,000mg/m ² IV over 30 minutes, followed by: Day 1 or on Day 2: Cisplatin 70mg/m ² IV over 60 minutes. Repeat cycle every 3 weeks for 4-6 cycles.
DDMAC (with growth factor support) ^{19,21,f}	Day 1: Methotrexate 30mg/m ² IV push Day 1 or on Day 2: Vinblastine 3mg/m ² IV over 5-10 minutes Day 1 or on Day 2: Doxorubicin 30mg/m ² IV push Day 1 or on Day 2: Cisplatin 70mg/m ² IV over 60 minutes. Repeat cycle every 2 weeks for 4-6 cycles.
Other Recommended Regimens	
Docetaxel ⁵³	Day 1: Docetaxel 100mg/m ² IV over 60 minutes. Repeat cycle every 3 weeks.
Erdafitinib (For Patients With Susceptible <i>FGFR2/FGFR3</i> Alterations) ^{48,49}	Days 1-14: Erdafitinib 8mg orally once daily cycle 1, followed by: Days 15-18: Erdafitinib 9mg (if tolerated) orally once daily cycle 1 (increase dose based on tolerability after 14 to 21 days if serum phosphate is <5.5 mg/dL and no ocular disorders ≥grade 2 toxicity), followed by: Days 1-28: Erdafitinib 9mg orally once daily beginning with cycle 2. Repeat cycle every 4 weeks.
Gemcitabine ^{39,40}	Days 1,8,15: Gemcitabine 1,000-1,250mg/m ² IV over 30 minutes. Repeat cycle every 4 weeks. OR Days 1,8: Gemcitabine 1,000-1,250mg/m ² IV over 30 minutes. Repeat cycle every 3 weeks.
Paclitaxel ⁵⁴⁻⁵⁶	Days 1,8,15,22: Paclitaxel 80mg/m ² IV over 60 minutes. Repeat cycle every 4 weeks. OR Day 1: Paclitaxel 200mg/m ² IV over 3 hours. Repeat cycle every 3 weeks.
Useful in Certain Circumstances Based on Prior Medical History	
Gemcitabine + Paclitaxel ⁴¹	Day 1: Paclitaxel 175mg/m ² IV over 3 hours, followed by: Days 1,8: Gemcitabine 1,000mg/m ² IV over 30 minutes. Repeat cycle every 3 weeks.
Ifosfamide + Doxorubicin + Gemcitabine ^{42,g}	Days 1-4: Ifosfamide 1,500mg/m ² IV over 3 hours daily Days 1-4: Mesna 300mg/m ² IV over 15 minutes 3 times daily (one dose before ifosfamide, then at 4 and 8 hours from the start of the ifosfamide dose) Day 3: Doxorubicin 45mg/m ² IV push Days 2,4: Gemcitabine 150mg/m ² IV over 30 minutes. Repeat cycle every 3 weeks for 3 cycles.

continued

Bladder Cancer Treatment Regimens

► Systemic Therapy for Urothelial Bladder Cancer¹ (continued)

REGIMEN	DOSING
Subsequent-Line Systemic Therapy for Locally Advanced or Metastatic Disease (Stage IV)^{h,j}	
Preferred	
Enfortumab Vedotin ⁵⁷	Days 1,8,15: Enfortumab Vedotin-ejfv 1.25mg/kg IV (maximum 125mg) over 30 minutes. Repeat cycle every 4 weeks.
Erdafitinib (For Patients With Susceptible <i>FGFR2/FGFR3</i> Alterations) ^{48,49}	Days 1-14: Erdafitinib 8mg orally once daily cycle 1, followed by: Days 15-18: Erdafitinib 9mg orally once daily cycle 1 (increase dose based on tolerability after 14 to 21 days if serum phosphate is <5.5 mg/dL and no ocular disorders ≥grade 2 toxicity), followed by: Days 1-28: Erdafitinib 9mg (if tolerated) orally once daily beginning with cycle 2. Repeat cycle every 4 weeks.
Other Recommended Regimens	
DDMVAC (with growth factor support) ^{19,21,f}	Day 1: Methotrexate 30mg/m ² IV push Day 1 or on Day 2: Vinblastine 3mg/m ² IV over 5-10 minutes Day 1 or on Day 2: Doxorubicin 30mg/m ² IV push Day 1 or on Day 2: Cisplatin 70mg/m ² IV over 60 minutes. Repeat cycle every 2 weeks for 4-6 cycles.
Docetaxel ⁵³	Day 1: Docetaxel 100mg/m ² IV over 60 minutes. Repeat cycle every 3 weeks.
Gemcitabine ^{39,40}	Days 1,8,15: Gemcitabine 1,000-1,250mg/m ² IV over 30 minutes. Repeat cycle every 4 weeks. OR Days 1, 8: Gemcitabine 1,000-1,250mg/m ² IV over 30 minutes. Repeat cycle every 3 weeks.
Gemcitabine + Cisplatin ^{22,23,f}	Days 1,8,15: Gemcitabine 1,000mg/m ² IV over 30 minutes, followed by: Day 1 or on Day 2: Cisplatin 70mg/m ² IV over 60 minutes. Repeat cycle every 4 weeks for 4-6 cycles. OR Days 1,8: Gemcitabine 1,000mg/m ² IV over 30 minutes, followed by: Day 1 or on Day 2: Cisplatin 70mg/m ² IV over 60 minutes. Repeat cycle every 3 weeks for 4-6 cycles.
Gemcitabine + Paclitaxel ⁴¹	Day 1: Paclitaxel 175mg/m ² IV over 3 hours, followed by: Days 1,8: Gemcitabine 1,000mg/m ² IV over 30 minutes. Repeat cycle every 3 weeks.
Ifosfamide + Doxorubicin + Gemcitabine ^{42,g}	Days 1-4: Ifosfamide 1,500mg/m ² IV over 3 hours daily Days 1-4: Mesna 300mg/m ² IV over 15 minutes 3 times daily (one dose before ifosfamide, then at 4 and 8 hours from the start of the ifosfamide dose) Day 3: Doxorubicin 45mg/m ² IV push Days 2,4: Gemcitabine 150mg/m ² IV over 30 minutes. Repeat cycle every 3 weeks for 3 cycles.
Paclitaxel ⁽⁵⁴⁻⁵⁶⁾	Days 1,8,15,22: Paclitaxel 80mg/m ² IV over 60 minutes. Repeat cycle every 4 weeks. OR Day 1: Paclitaxel 200mg/m ² IV over 3 hours. Repeat cycle every 3 weeks.
Radiosensitizing Chemotherapy Regimens for Organ-Preserving Chemoradiation^k	
Preferred Regimens (Doublet Chemotherapy is Preferred When Feasible)	
Cisplatin ^{58-62,f}	Days 1-2,8-9,15-16 of Cycle 1 (Induction): Cisplatin 20mg/m ² IV over 60 minutes, followed by: Days 1-2,8-9 of Cycle 2 (Consolidation): Cisplatin 20mg/m ² IV over 60 minutes. Repeat cycle every 42 days for 1-2 cycles with concurrent RT.
Cisplatin + Fluorouracil ^{61,62,f}	Days 1-3,15-17 of Cycle 1 (Induction): Fluorouracil 400mg/m ² IV continuous infusion over 24 hours, followed by: Days 1-3,8-10 of Cycle 2 (Consolidation): Fluorouracil 400mg/m ² IV continuous infusion over 24 hours. Days 1-3,8-10,15-17 of Cycle 1 (Induction): Cisplatin 15mg/m ² IV over 60 minutes, followed by: Days 1-2,8-9 of Cycle 2 (Consolidation): Cisplatin 15mg/m ² IV over 60 minutes. Repeat cycle every 56 days for 1-2 cycles with concurrent twice daily RT.

continued

Bladder Cancer Treatment Regimens

► Systemic Therapy for Urothelial Bladder Cancer¹ (continued)

REGIMEN	DOSING
Radiosensitizing Chemotherapy Regimens for Organ-Preserving Chemoradiation^k (continued)	
Preferred Regimens (Doublet Chemotherapy is Preferred When Feasible) (continued)	
Cisplatin + Paclitaxel ^{62,63,f}	Days 1,8,15 of Cycle 1 (Induction): Paclitaxel 50mg/m ² IV over 60 minutes, followed by: Days 1,8 of Cycle 2 (Consolidation): Paclitaxel 50mg/m ² IV over 60 minutes. Days 1-3,8-10,15-17 of Cycle 1 (Induction): Cisplatin 15mg/m ² IV over 60 minutes, followed by: Days 1-2,8-9 of Cycle 2 (Consolidation): Cisplatin 15mg/m ² IV over 60 minutes. Repeat cycle every 56 days for 1-2 cycles with concurrent twice daily RT.
Fluorouracil + Mitomycin ⁶⁴	Day 1: Mitomycin 12mg/m ² IV push. Days 1-8,22-26: Fluorouracil 500mg/m ² IV continuous infusion over 24 hours daily. Administer for one 28- to 45-day cycle with concurrent RT.
Other Recommended Regimens	
Low-Dose Gemcitabine (Category 2B) ⁶¹	Days 1,4,8,11,15,18,22,25 (induction): Gemcitabine 27mg/m ² IV over 30 minutes. Administer for one 4-week cycle with concurrent RT, followed by: Days 1,4,8,11,15 (Consolidation): Gemcitabine 27mg/m ² over 30 minutes. Administer for one 3-week cycle with concurrent RT.
Radiosensitizing Chemotherapy Given Concurrently With Conventionally Fractionated Radiation With Palliative Intent for Regional Disease^{k,i}	
Preferred	
Cisplatin ^{58-62,f}	Days 1-2,8-9,15-16 of Cycle 1 (Induction): Cisplatin 20mg/m ² IV over 60 minutes Days 1-2,8-9 of Cycle 2 (Consolidation): Cisplatin 20mg/m ² IV over 60 minutes. Repeat cycle every 42 days for 1-2 cycles with concurrent RT.
Other Recommended Regimens	
Capecitabine (Category 3) ⁶⁵	Days 1-5: Capecitabine 1,200-1,500mg/m ² /day divided into 2 daily doses orally and administered on days of RT. Repeat cycle every 7 days with concurrent RT.
Fluorouracil (Category 2B) ⁶⁴	Days 1-5; 22-26: Fluorouracil 500mg/m ² IV continuous infusion over 24 hours daily. Administer for one 28- to 45-day cycle with concurrent RT.
Fluorouracil + Mitomycin (Category 2B) ⁶⁴	Day 1: Mitomycin 12mg/m ² IV push. Days 1-8,22-26: Fluorouracil 500mg/m ² IV continuous infusion over 24 hours daily. Administer for one 28- to 45-day cycle with concurrent RT.
Low-Dose Gemcitabine (Category 2B) ⁶¹	Days 1,4,8,11,15,18,22,25 (induction): Gemcitabine 27mg/m ² IV over 30 minutes. Administer for one 4-week cycle with concurrent RT, followed by: Days 1,4,8,11,15 (Consolidation): Gemcitabine 27mg/m ² over 30 minutes. Administer for one 3-week cycle with concurrent RT.
Paclitaxel (Category 2B) ⁶⁶	Days 1,8,15,22,29,36,43: Paclitaxel 50mg/m ² IV over 60 minutes. Administer for one 49-day cycle with concurrent RT/

► Systemic Therapy for Bladder Cancer Characterized by Non-Urothelial and Urothelial With Variant Histology¹

Mixed Histology

Usually treated in a similar manner to pure urothelial carcinoma of the bladder. See NCCN Bladder Cancer Guidelines.¹

Pure Squamous Histology

- No proven role for neoadjuvant/adjuvant chemotherapy for pure squamous cell carcinoma of the bladder.
- For advanced disease, clinical trial preferred.
- See NCCN Bladder Cancer Guidelines.¹

ITP (Paclitaxel, Ifosfamide, and Cisplatin) (for selected patients) ^{67,g}	Days 1-3: Ifosfamide 1,500mg/m ² IV over 3 hours Days 1-3: Mesna 300mg/m ² IV over 15 minutes 3x daily (one dose before Ifosfamide dose) Day 1: Cisplatin 70mg/m ² IV over 2 hours. Day 1: Paclitaxel 200mg/m ² IV over 3 hours. Repeat cycle every 3 or 4 weeks for a maximum of 6 cycles.
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Bladder Cancer Treatment Regimens

► Systemic Therapy for Bladder Cancer Characterized by Non-Urothelial and Urothelial With Variant Histology¹ (continued)

REGIMEN	DOSING
Pure Adenocarcinoma Including Urachal	
<ul style="list-style-type: none"> No proven role for neoadjuvant/adjuvant chemotherapy for pure adenocarcinoma of the bladder including urachal carcinoma. See NCCN Bladder Cancer Guidelines.¹ 	
Node-Positive Disease	
GemFLP (Fluorouracil + Leucovorin + Gemcitabine + Cisplatin) ^{68,f}	<p>Days 1-5: Fluorouracil 200mg/m² IV continuous infusion over multiple days within this regimen. (The defined dose is a 24-hour daily dose.)</p> <p>Days 1-5: Leucovorin 10mg/m² IV daily</p> <p>Days 1-5: Cisplatin 20mg/m² IV over 60 minutes daily</p> <p>Day 1: Gemcitabine 200mg/m² IV over 30 minutes, followed by:</p> <p>Day 5: Gemcitabine 200mg/m² IV over 30 minutes.</p> <p>Repeat cycle every 3 weeks.</p>
mFOLFOX6 ⁶⁹⁻⁷⁰	<p>Day 1: Oxaliplatin 85mg/m² IV over 2 hours, with:</p> <p>Day 1: Leucovorin 400mg/m² IV over 2 hours, followed by:</p> <p>Day 1: Fluorouracil 400mg/m² IV push, followed by:</p> <p>Days 1-2: Fluorouracil 1,200mg/m² IV continuous infusion over 24 hours daily (2,400mg/m² IV over 46-48 hours).</p> <p>Repeat cycle every 2 weeks.</p>
Advanced Disease^x	
Carboplatin + Paclitaxel ⁷¹⁻⁷²	<p>Day 1: Paclitaxel 200mg/m² IV, followed by:</p> <p>Day 1: Carboplatin AUC 6 IV over 30 minutes.</p> <p>Repeat cycle every 3 weeks.</p>
Cisplatin + Paclitaxel ^{71,73-75,f}	<p>Day 1: Paclitaxel 135mg/m² IV over 3 hours, followed by:</p> <p>Day 1: Cisplatin 75mg/m² IV over 2 hours.</p> <p>Repeat cycle every 3 weeks.</p>
GemFLP (Fluorouracil + Leucovorin + Gemcitabine + Cisplatin) ^{68,f}	<p>Days 1-5: Fluorouracil 200mg/m² IV continuous infusion over multiple days within this regimen. (The defined dose is a 24-hour daily dose.)</p> <p>Days 1-5: Leucovorin 10mg/m² IV daily</p> <p>Days 1-5: Cisplatin 20mg/m² IV over 60 minutes daily</p> <p>Day 1: Gemcitabine 200mg/m² IV over 30 minutes, followed by:</p> <p>Day 5: Gemcitabine 200mg/m² IV over 30 minutes.</p> <p>Repeat cycle every 3 weeks.</p>
ITP (Paclitaxel + Ifosfamide + Cisplatin) ^{67,f,g}	<p>Days 1-3: Ifosfamide 1,500mg/m² IV over 3 hours</p> <p>Days 1-3: Mesna 300mg/m² IV over 15 minutes 3x daily (one dose before Ifosfamide, then at 4 and 8 hours from the start of each Ifosfamide dose)</p> <p>Day 1: Cisplatin 70mg/m² IV over 2 hours.</p> <p>Day 1: Paclitaxel 200mg/m² IV over 3 hours.</p> <p>Repeat cycle every 3 or 4 weeks for a maximum of 6 cycles.</p>
mFOLFOX6 ^{69,70}	<p>Day 1: Oxaliplatin 85mg/m² IV over 2 hours, with:</p> <p>Day 1: Leucovorin 400mg/m² IV over 2 hours, followed by:</p> <p>Day 1: Fluorouracil 400mg/m² IV push, followed by:</p> <p>Days 1-2: Fluorouracil 1,200mg/m² IV continuous infusion over 24 hours daily (2,400mg/m² IV over 46-48 hours).</p> <p>Repeat cycle every 2 weeks.</p>
Any Small-Cell Component (or Neuroendocrine Features)	
<ul style="list-style-type: none"> Concurrent Chemoradiotherapy for Neoadjuvant Chemotherapy Followed By Local Treatment is Recommended for Any Patients With Small-Cell Component Histology With Localized Disease Regardless of Stage. See NCCN Bladder Cancer Guidelines.¹ 	
Neoadjuvant Chemotherapy	
Standard Cisplatin Eligible Patients	
Etoposide + Cisplatin ^{76,77f}	<p>Days 1-5: Cisplatin 20mg/m² IV over 60 minutes</p> <p>Days 1-5: Etoposide 80mg/m² IV over 2 hours.</p> <p>Repeat cycle every 3 weeks for 4 cycles.</p>

continued

Bladder Cancer Treatment Regimens

► Systemic Therapy for Bladder Cancer Characterized by Non-Urothelial and Urothelial With Variant Histology¹ (continued)

REGIMEN	DOSING
Any Small-Cell Component (or Neuroendocrine Features) (continued)	
Neoadjuvant Chemotherapy (continued)	
Standard Cisplatin Eligible Patients (continued)	
Alternating Ifosfamide + Doxorubicin With Etoposide + Cisplatin ^{76,78,f,g}	<p>Days 1-4: Ifosfamide 2000mg/m² IV over 3 hours.</p> <p>Days 1-4: Mesna 300mg/m² IV over 15 minutes 3x daily (one dose before Ifosfamide, then at 4 and 8 hours from the start of each Ifosfamide dose)</p> <p>Days 1-3: Doxorubicin 25mg/m² IV push.</p> <p>Repeat cycle every 3 weeks for 2 cycles, alternating with:</p> <p>Days 1-5: Etoposide 80mg/m² IV over 2 hours</p> <p>Days 1-5: Cisplatin 20mg/m² IV push.</p> <p>Repeat cycle every 3 weeks for 2 cycles.</p>
Standard Cisplatin Ineligible Patients	
Etoposide + Carboplatin ⁷⁹	<p>Day 1: Carboplatin AUC 5 IV over 30 minutes.</p> <p>Days 1-3: Etoposide 100mg/m² IV over 60 minutes.</p> <p>Repeat cycle every 3 weeks for 4-6 cycles.</p>
Metastatic Chemotherapy	
Standard Cisplatin Eligible Patients	
Etoposide + Cisplatin ^{76,77f}	<p>Days 1-5: Cisplatin 20mg/m² IV over 60 minutes</p> <p>Days 1-5: Etoposide 80mg/m² IV over 2 hours.</p> <p>Repeat cycle every 3 weeks.</p>
Standard Cisplatin Ineligible Patients	
Etoposide + Carboplatin ⁷⁹	<p>Day 1: Carboplatin AUC 5 IV over 30 minutes.</p> <p>Days 1-3: Etoposide 100mg/m² IV over 60 minutes.</p> <p>Repeat cycle every 3 weeks.</p>
Alternative Regimen for Selected Patients	
Alternating Ifosfamide + Doxorubicin With Etoposide + Cisplatin ^{76,78,f,g}	<p>Days 1-4: Ifosfamide 2000mg/m² IV over 3 hours.</p> <p>Days 1-4: Mesna 300mg/m² IV over 15 minutes 3x daily (one dose before Ifosfamide, then at 4 and 8 hours from the start of each Ifosfamide dose)</p> <p>Days 1-3: Doxorubicin 25mg/m² IV push.</p> <p>Repeat cycle every 3 weeks for 2 cycles beyond maximal response, alternating with:</p> <p>Days 1-5: Etoposide 80mg/m² IV over 2 hours</p> <p>Days 1-5: Cisplatin 20mg/m² IV push.</p> <p>Repeat cycle every 3 weeks for 2 cycles beyond maximal response.</p>
Primary Bladder Sarcoma	
<ul style="list-style-type: none"> • See NCCN Soft Tissue Sarcoma Guidelines.⁸⁰ 	

^a A single instillation of chemotherapy is administered within 24 hours of surgery (ideally within 6 hours).

^b The most commonly used agents are BCG, Mitomycin, and Gemcitabine.

^c Ideally, maintenance should be given for 1 year for intermediate-risk and 3 years for high-risk non-muscle-invasive bladder cancer.

^d For patients who are not candidates for cisplatin, there are no data to support a recommendation for perioperative chemotherapy.

^e Carboplatin should not be substituted for cisplatin in the perioperative setting. For patients with borderline renal function or minimal dysfunction, a split-dose administration of cisplatin may be considered (such as 35mg/m² on days 1 and 2 or days 1 and 8) (Category 2B). While safer, the relative efficacy of the cisplatin-containing combination administered with such modifications remains undefined.

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

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

^h Participation in clinical trials of new agents is recommended.

ⁱ If PFS >12 months after platinum (eg, cisplatin or carboplatin), consider re-treatment with platinum if the patients is still platinum eligible.

^j Patients should have already received platinum and a checkpoint inhibitor, if eligible.

^k Carboplatin is not an effective radiation sensitizer and should not be substituted for cisplatin with radiation therapy (Rodel C, Grabenbauer GG, Kuhn R, et al. Combined modality treatment and selective organ preservation in invasive bladder cancer: long-term results. *J Clin Oncol.* 2002;20:3061.)

continued

Bladder Cancer Treatment Regimens

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