

## TESTICULAR CANCER TREATMENT REGIMENS (Part 1 of 2)

The selection, dosing, and administration of anticancer agents and the management of associated toxicities are complex. Drug dose modifications and schedule and initiation of supportive care interventions are often necessary because of expected toxicities and because of individual patient variability, prior treatment, and comorbidities. Thus, the optimal delivery of anticancer agents requires a healthcare delivery team experienced in the use of such agents and the management of associated toxicities in patients with cancer. The cancer treatment regimens below may include both FDA-approved and unapproved uses/regimens and are provided as references only to the latest treatment strategies. Clinicians must choose and verify treatment options based on the individual patient.

NOTE: GREY SHADED BOXES CONTAIN UPDATED REGIMENS.

### General treatment notes:

- Good-risk patients (denoted with an \*) means those patients with cancer at any primary site and with no nonpulmonary visceral metastases and a normal alpha-fetoprotein (AFP) level, any human chorionic gonadotropin (HCG) value, and any lactate dehydrogenase (LDH) value.
- Intermediate-risk patients (denoted with a †) means those patients with cancer at any primary site and nonpulmonary visceral metastases and normal AFP, any HCG value, and any LDH value.

| REGIMEN                                                                                                       | DOSING                                                                                                                                                                                                                                                                                                     |
|---------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Pure Seminoma Germ Cell Tumor</b>                                                                          |                                                                                                                                                                                                                                                                                                            |
| <b>Primary Treatment Stage 1A, 1B</b>                                                                         |                                                                                                                                                                                                                                                                                                            |
| <b>Carboplatin</b> (Paraplatin) <sup>1</sup>                                                                  | Carboplatin AUC=7mg/mL/min IV for 1 or 2 cycles.                                                                                                                                                                                                                                                           |
| <b>Primary Treatment Stage IIB (selected patients) and Stage IIC, III (good-risk patients*)</b>               |                                                                                                                                                                                                                                                                                                            |
| <b>EP</b> (etoposide [Tuposar, VePesid, Etopophos; VP-16] + <b>cisplatin</b> [Platinol; CDDP]) <sup>1,2</sup> | <b>Days 1-5:</b> Etoposide 100mg/m <sup>2</sup> IV + cisplatin 20mg/m <sup>2</sup> IV.<br>Repeat cycle every 3 weeks for 4 cycles.                                                                                                                                                                         |
| <b>BEP</b> (bleomycin [Blenoxane] + etoposide + cisplatin) <sup>1,3</sup>                                     | <b>Days 1-5:</b> Cisplatin 20mg/m <sup>2</sup> IV, <b>plus</b><br><b>Days 1, 8 and 15:</b> Bleomycin 30units IV + etoposide 100mg/m <sup>2</sup> IV.<br>Repeat cycle every 3 weeks for 3 cycles.<br>Some NCCN institutions give bleomycin on Days 2, 9 and 16.                                             |
| <b>Primary Treatment for Stage IIC, III (intermediate risk patients†)</b>                                     |                                                                                                                                                                                                                                                                                                            |
| <b>BEP</b> <sup>1,3</sup>                                                                                     | <b>Days 1-5:</b> Cisplatin 20mg/m <sup>2</sup> IV, <b>plus</b><br><b>Days 1, 8 and 15:</b> Bleomycin 30units IV + etoposide 100mg/m <sup>2</sup> IV.<br>Repeat cycle every 3 weeks for 4 cycles.<br>Some NCCN institutions give bleomycin on Days 2, 9 and 16.                                             |
| <b>Nonseminomatous Germ Cell Tumor</b>                                                                        |                                                                                                                                                                                                                                                                                                            |
| <b>Primary Treatment for Stage 1B</b>                                                                         |                                                                                                                                                                                                                                                                                                            |
| <b>BEP</b> <sup>1,3</sup>                                                                                     | <b>Days 1-5:</b> Cisplatin 20mg/m <sup>2</sup> IV, <b>plus</b><br><b>Days 1, 8 and 15:</b> Bleomycin 30units IV + etoposide 100mg/m <sup>2</sup> IV.<br>Repeat cycle every 3 weeks for 2 cycles.<br>Some NCCN institutions give bleomycin on Days 2, 9 and 16.                                             |
| <b>Primary Treatment for Stage IIA, IIB, IIC, IIIA (good-risk patients*)</b>                                  |                                                                                                                                                                                                                                                                                                            |
| <b>EP</b> <sup>1,2</sup>                                                                                      | <b>Days 1-5:</b> Etoposide 100mg/m <sup>2</sup> IV + cisplatin 20mg/m <sup>2</sup> IV.<br>Repeat cycle every 3 weeks for 4 cycles.                                                                                                                                                                         |
| <b>BEP</b> <sup>1,3</sup>                                                                                     | <b>Days 1-5:</b> Cisplatin 20mg/m <sup>2</sup> IV, <b>plus</b><br><b>Days 1, 8 and 15:</b> Bleomycin 30units IV + etoposide 100mg/m <sup>2</sup> IV.<br>Repeat cycle every 3 weeks for 3 cycles.<br>Some NCCN institutions give bleomycin on Days 2, 9 and 16.                                             |
| <b>Primary Treatment for Stage IIIB (intermediate risk patients†)</b>                                         |                                                                                                                                                                                                                                                                                                            |
| <b>BEP</b> <sup>1,3</sup>                                                                                     | <b>Days 1-5:</b> Cisplatin 20mg/m <sup>2</sup> IV, <b>plus</b><br><b>Days 1, 8 and 15:</b> Bleomycin 30units IV + etoposide 100mg/m <sup>2</sup> IV.<br>Repeat cycle every 3 weeks for 4 cycles.<br>Some NCCN institutions give bleomycin on Days 2, 9 and 16.                                             |
| <b>VIP</b> (etoposide + ifosfamide + cisplatin + mesna [Mesnex]) (for selected patients) <sup>1,4</sup>       | <b>Days 1-5:</b> Etoposide 75mg/m <sup>2</sup> IV + ifosfamide 1,200mg/m <sup>2</sup> IV (give mesna 120mg/m <sup>2</sup> by slow IV push prior to ifosfamide on Day 1) + cisplatin 20mg/m <sup>2</sup> + mesna 1,200mg/m <sup>2</sup> continuous IV infusion.<br>Repeat cycle every 3 weeks for 4 cycles. |
| <b>Second-Line Treatment Conventional Dose Chemotherapy</b>                                                   |                                                                                                                                                                                                                                                                                                            |
| <b>VeIP</b> (vinblastine [Alkaban-AQ, Velban; VLB] + ifosfamide [Ifex] + cisplatin + mesna) <sup>1,5</sup>    | <b>Days 1 and 2:</b> Vinblastine 0.11mg/kg IV push, <b>plus</b><br><b>Days 1-5:</b> Ifosfamide 1,200mg/m <sup>2</sup> IV + cisplatin 20mg/m <sup>2</sup> IV + mesna 1,200mg/m <sup>2</sup> IV (400mg/m <sup>2</sup> every 8 hrs).<br>Repeat cycle every 3 weeks.                                           |

continued

## TESTICULAR CANCER TREATMENT REGIMENS (Part 2 of 2)

| REGIMEN                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | DOSING                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
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| <b>Second-Line Treatment Conventional Dose Chemotherapy (continued)</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
| <b>TIP</b> (paclitaxel [Taxol] + ifosfamide + mesna + cisplatin) <sup>1,6</sup>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | <b>Day 1:</b> Paclitaxel 250mg/m <sup>2</sup> IV, <b>followed by</b><br><b>Days 2-5:</b> Ifosfamide 1,500mg/m <sup>2</sup> + cisplatin 25mg/m <sup>2</sup> IV daily + mesna 500mg/m <sup>2</sup> IV before ifosfamide and then 4 hrs and 8 hrs after each dose of ifosfamide.<br>Repeat cycle every 3 weeks.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
| <b>Second-Line Treatment High-Dose Chemotherapy</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
| <b>Carboplatin + etoposide</b> <sup>1,7</sup>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | <b>Days -5, -4 and -3:</b> Carboplatin 700mg/m <sup>2</sup> IV + etoposide 750mg/m <sup>2</sup> IV administered 3 consecutive days 3 days prior to peripheral blood stem cell infusion for 2 cycles.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
| <b>Paclitaxel + ifosfamide + carboplatin + etoposide + mesna</b> <sup>1,8</sup>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | <b>Day 1:</b> Paclitaxel 200mg/m <sup>2</sup> IV as a 24-hr continuous infusion with peripheral stem cell infusion, <b>plus</b><br><b>Days 1-3:</b> Carboplatin AUC=7-8mg/mL/min IV + etoposide 400mg/m <sup>2</sup> IV over 60 min, <b>plus</b><br><b>Days 2-4:</b> Ifosfamide 2,000mg/m <sup>2</sup> IV over 4 hrs (with mesna 2,000mg/m <sup>2</sup> ).<br>Repeat cycle every 2 or 3 weeks for 3 cycles.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
| <b>Palliative Chemotherapy Regimen</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
| <b>GEMOX</b> (gemcitabine [Gemzar] + oxaliplatin [Eloxatin]) <sup>1,9-11</sup>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | <b>Days 1 and 8:</b> Gemcitabine 1,000mg/m <sup>2</sup> IV, <b>plus</b><br><b>Day 1:</b> Oxaliplatin 130mg/m <sup>2</sup> IV.<br>Repeat cycle every 3 weeks.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
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| <b>Gemcitabine + paclitaxel</b> <sup>1,12</sup>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | <b>Days 1, 8 and 15:</b> Gemcitabine 1,000mg/m <sup>2</sup> IV over 30 min + paclitaxel 100mg/m <sup>2</sup> IV over 1 hr.<br>Repeat every 4 weeks for a max 6 cycles.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
| <b>Gemcitabine + paclitaxel + oxaliplatin</b> <sup>1,13</sup>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | <b>Days 1 and 8:</b> Gemcitabine 800mg/m <sup>2</sup> IV + paclitaxel 80mg/m <sup>2</sup> IV.<br><b>Day 1:</b> Oxaliplatin 130mg/m <sup>2</sup> IV.<br>Repeat every 3 weeks for at least 2 cycles.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| <b>References</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
| <ol style="list-style-type: none"> <li>1. NCCN Clinical Practice Guidelines in Oncology™. Testicular Cancer. v 1.2012. Available at: <a href="http://www.nccn.org/professionals/physician_gls/pdf/testicular.pdf">http://www.nccn.org/professionals/physician_gls/pdf/testicular.pdf</a>. Accessed April 20, 2012.</li> <li>2. Xiao H, Mazumdar M, Bajorin DF, et al. Long-term follow-up of patients with good-risk germ cell tumors treated with etoposide and cisplatin. <i>J Clin Oncol.</i> 1997;15:2553-2558.</li> <li>3. Saxman SB, Finch D, Gonin R, Einhorn LH, et al. Long-term follow-up of a phase III study of three versus four cycles of bleomycin, etoposide, and cisplatin in favorable-prognosis germ-cell tumors: the Indiana University experience. <i>J Clin Oncol.</i> 1998;16:702-706.</li> <li>4. Nichols CR, Catalano PJ, Crawford ED, et al. Randomized comparison of cisplatin and etoposide and either bleomycin or ifosfamide in treatment of advanced disseminated germ cell tumors: an Eastern Cooperative Oncology Group, Southwest Oncology Group, and Cancer and Leukemia Group B Study. <i>J Clin Oncol.</i> 1998;16:1287-1293.</li> <li>5. Loehrer PJ Sr, Lauer R, Roth BJ, et al. Salvage therapy in recurrent germ cell cancer: ifosfamide and cisplatin plus either vinblastine or etoposide. <i>Ann Intern Med.</i> 1988;109:540-546.</li> <li>6. Kondagunta GV, Bacik J, Donadio A, et al. Combination of paclitaxel, ifosfamide, and cisplatin is an effective second-line therapy for patients with relapsed testicular germ cell tumors. <i>J Clin Oncol.</i> 2005;23:6549-6555.</li> <li>7. Einhorn LH, Williams SD, Chammess A, et al. High-dose chemotherapy and stem-cell rescue for metastatic germ-cell tumors. <i>N Engl J Med.</i> 2007;357:340-348.</li> </ol> | <ol style="list-style-type: none"> <li>8. Kondagunta GV, Bacik J, Sheinfeld J, et al. Paclitaxel plus ifosfamide followed by high-dose carboplatin plus etoposide in previously treated germ cell tumors. <i>J Clin Oncol.</i> 2007;25:85-90.</li> <li>9. Pectasides D, Pectasides M, Farmakis D, et al. Gemcitabine and oxaliplatin (GEMOX) in patients with cisplatin-refractory germ cell tumors: a phase II study. <i>Ann Oncol.</i> 2004;15:493-497.</li> <li>10. Kollmannsberger C, Beyer J, Liersch R, et al. Combination chemotherapy with gemcitabine plus oxaliplatin in patients with intensively pretreated or refractory germ cell cancer: a study of the German Testicular Cancer Study Group. <i>J Clin Oncol.</i> 2004;22:108-114.</li> <li>11. De Giorgi U, Rosti G, Aieta M, et al. Phase II study of oxaliplatin and gemcitabine salvage chemotherapy in patients with cisplatin-refractory nonseminomatous germ cell tumor. <i>Eur Urol.</i> 2006;50:1032-1038.</li> <li>12. Einhorn LH, Brames MJ, Juliar B, et al. Phase II study of paclitaxel plus gemcitabine salvage chemotherapy for germ cell tumors after progression following high-dose chemotherapy with tandem transplant. <i>J Clin Oncol.</i> 2007;25:513-516.</li> <li>13. Bokemeyer C, Oechsle K, Honecker F, et al. Combination chemotherapy with gemcitabine, oxaliplatin, and paclitaxel in patients with cisplatin-refractory or multiply relapsed germ-cell tumors: a study of the German Testicular Cancer Study Group. <i>Ann Oncol.</i> 2008;19:448-453.</li> </ol> |
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