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Wolters Kluwer

# Chemotherapy of ovarian cancer in pregnancy

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## INTRODUCTION

A gynecologic malignancy is estimated to complicate four to eight of every 100,000 pregnancies [1-4]. Unfortunately, the data on the effects of antineoplastic drugs administered during pregnancy have largely been derived from case reports, small case series, and collected reviews of pregnant women treated for a variety of cancers. There are even less data on long-term outcomes in offspring.

This topic will address the administration of chemotherapy for women diagnosed with ovarian cancer in pregnancy. In order to optimize treatment outcomes, a pregnant woman with a diagnosis of ovarian cancer should be managed by a multidisciplinary team that includes experts in the fields of maternal-fetal medicine, gynecologic oncology, pediatrics, and pathology.

The clinical manifestations and diagnosis of ovarian cancer in pregnancy and surgical management of this disease are reviewed separately. (See "[Adnexal mass in pregnancy](#)".)

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## GENERAL PRINCIPLES

Concerns about the administration of cytotoxic chemotherapy during pregnancy arise because chemotherapy preferentially kills rapidly proliferating cells, and the fetus represents a rapidly proliferating cell mass. All chemotherapy agents used in the treatment of epithelial and nonepithelial ovarian cancers are pregnancy category D, meaning that fetal exposure to individual chemotherapeutic agents have resulted in adverse effects including intrauterine growth restriction, prematurity, and low birth weight in the infants [5]. Chemotherapy may also cause fetal toxicities similar to those observed in the mother (eg, bone marrow suppression).

The risks of spontaneous abortion, fetal death, and major malformations vary depending on the agent used and the trimester of pregnancy. These risks must be weighed against the benefits of immediate versus delayed (ie, postdelivery) chemotherapy for the mother. Ethical considerations of treatment during pregnancy have emphasized the role of patient autonomy and the concept of beneficence and nonmaleficence for both the mother and fetus [6].

Although previous data suggested that the administration of chemotherapy increased the risk of fetal malformations, most data suggest this is not the case. It is now believed that the impact of chemotherapy during pregnancy is predominantly dependent on when treatment is administered:

- During the first four weeks of gestation (first two weeks post conception) the embryo is undifferentiated. Fetal exposure to cytotoxic agents at this point results in "all or none" phenomena: either the pregnancy is lost or it continues with no apparent adverse effect [5,7].
- Organogenesis occurs during weeks 5 to 10 weeks of gestation. The administration of cytotoxic drugs, particularly antimetabolites (eg, [fluorouracil](#) and [methotrexate](#)) and alkylating agents (eg, [busulfan](#), [chlorambucil](#), [cyclophosphamide](#)), during this period carries an increased risk of fetal malformations. In a review of the literature, rates of adverse pregnancy outcomes (APOs) for anti-neoplastic agents in single and combination therapy were 33, 27, and 25 percent for the first, second, and third trimesters. Rates of congenital malformations (included in the APOs) were 16, 8, and 6 percent for the first, second, and third trimesters [8]. The majority of stillborn infants and infants with chromosomal or congenital abnormalities occur when chemotherapy is administered in the first trimester.
- When chemotherapy is delivered to the mother during the second and third trimesters of pregnancy, the risk of fetal malformation is lower. First trimester exposure poses a larger and more permanent risk to the fetus. Administration of chemotherapy within three weeks of anticipated delivery or beyond 35 weeks of gestation may induce neonatal myelosuppression and complicate delivery due to adverse effects of treatment on bone marrow reserves. This includes potential complications such as bleeding, sepsis, and death. Additionally, neonatal toxicity may be higher if chemotherapy is administered peripartum because placental drug clearance is generally more effective than either hepatic and/or renal drug clearance in the neonate [9].

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## OVARIAN CANCER DURING PREGNANCY

There are several different histologic types of malignancy that can arise within the ovary including epithelial ovarian cancer (EOC), ovarian germ cell tumors, and sex-cord stromal tumors. In some series of women presenting with an ovarian malignancy while pregnant, germ cell tumors predominate, while others report a higher frequency of EOC. The indications and medical

treatment of ovarian cancer during pregnancy by histologic type is discussed below. (See ["Adnexal mass in pregnancy"](#), [section on 'Malignant neoplasms'](#).)

## EPITHELIAL OVARIAN CANCER

**Indications** — Following surgery, the indications for adjuvant treatment of epithelial ovarian cancer (EOC) are similar for pregnant and nonpregnant women. However, administration of chemotherapy during the first trimester **should be avoided**. We recommend chemotherapy for:

- Women with early-stage EOC ([table 1](#)) if any of the following high-risk features is present: stage IA/IB, grade 2/3; stage IC or II (any histology); serous or clear cell carcinoma (stage IA, IB, IC, or II)
- Women with stage III or IV EOC

**Regimen** — As with nonpregnant women, we recommend the use of a platinum drug plus taxane for women with EOC in pregnancy because, in general, this combination results in the best survival outcomes. For women diagnosed during pregnancy, we prefer [carboplatin](#) to [cisplatin](#) because it is a better tolerated agent and reduces the risk of long-term side effects (eg, renal and neurotoxicity). Although there are few data to guide the use of taxanes in pregnancy, it has been used to treat breast cancer in pregnancy without apparent adverse events [[10-12](#)]. We prefer [paclitaxel](#) rather than [docetaxel](#) because it is generally less myelotoxic. In the absence of data on the use of [bevacizumab](#), we recommend not using it in pregnancy.

All women with EOC in pregnancy should be informed of the limited data on maternal and fetal outcomes associated with treatment. In one of the largest cohort studies of pregnant women with all types of cancer treated at multiple institutions, 84 were exposed to taxanes and 74 were exposed to platinum-based chemotherapy [[13](#)]. Both drugs were associated with an increased risk of delivery of a small for gestational age infant: platinum odds ratio (OR) 3.12, 95% CI 1.45-6.70 and taxanes OR 2.07, 95% CI 1.11-3.86. However, it was not possible to determine whether these findings were related to in-utero drug exposure or to other factors, such as effects of other medications, maternal stress, lack of adequate gestational weight gain, and other prenatal factors.

**Administration** — Patients can be treated with single agent [carboplatin](#) or a combination of carboplatin and a taxane. A decision should be made on an individual basis taking into account potential risks and benefits of treatment.

**Intraperitoneal therapy** — In the absence of a larger experience, we do not administer intraperitoneal (IP) chemotherapy in these patients. There is only one case report of a woman with ovarian cancer treated with IP therapy for four cycles during pregnancy. She underwent a cesarean section at 37 weeks; the baby was male and had bilateral congenital talipes equinovarus [[14](#)]. The role of IP therapy for advanced ovarian cancer is discussed separately. (See ["First-line](#)

[chemotherapy for advanced \(stage III or IV\) epithelial ovarian, fallopian tubal, and peritoneal cancer](#), section on 'Women with optimally cytoreduced disease'.)

## Timing of chemotherapy

**Early-stage disease** — For pregnant women with high-risk, early-stage EOC, we suggest initiation of chemotherapy following completion of the first trimester. The approach is similar to the treatment of nonpregnant women with early-stage EOC. (See '[Indications](#)' above and "[Adjuvant therapy of early stage \(stage I and II\) epithelial ovarian, fallopian tubal, or peritoneal cancer](#)", section on 'Choice of adjuvant treatment'.)

For women who prefer not to receive treatment during pregnancy due to concerns for fetal safety, it may be reasonable to delay adjuvant chemotherapy until after delivery. The evidence to support this comes from two studies that evaluated the impact of a treatment start delay [15]. In these trials, 271 nonpregnant women with high-risk stage I EOC were randomly assigned treatment with adjuvant [cisplatin](#) versus observation (trial 1) or P-32 (trial 2). In both trials, women who were not treated with cisplatin received cisplatin at the time of relapse. The main results were:

- Administration of [cisplatin](#) reduced the risk of relapse in both trials (compared with observation, hazard ratio [HR] 0.35, 95% CI 0.14-0.89; compared with P-32, HR 0.39, 95% CI 0.19-0.77).
- There was no difference in five year overall survival (88 and 82 percent with [cisplatin](#) or observation; HR 1.15, 95% CI 0.44-2.98; 81 and 79 percent with cisplatin or P-32; HR 0.72, 95% CI 0.72, 95% CI 0.37-1.43).

**Advanced-stage disease** — Women with advanced disease should begin chemotherapy as soon as they are out of the first trimester and have recovered from surgery. We generally prefer to initiate treatment in two to four weeks after surgery for ovarian cancer. The approach to treatment is similar to that for nonpregnant women with advanced EOC. Although dose-dense (weekly) [paclitaxel](#) has been reported to improve progression-free survival, other groups have been unable to duplicate these data [16,17]. (See "[First-line chemotherapy for advanced \(stage III or IV\) epithelial ovarian, fallopian tubal, and peritoneal cancer](#)", section on 'Women with suboptimally cytoreduced disease' and "[First-line chemotherapy for advanced \(stage III or IV\) epithelial ovarian, fallopian tubal, and peritoneal cancer](#)", section on 'Women with optimally cytoreduced disease'.)

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## GERM CELL TUMORS

Most germ cell ovarian malignancies occur in young women and are limited to one ovary [3]. Maximal surgical cytoreduction is usually undertaken initially. (See "[Treatment of malignant germ cell tumors of the ovary](#)" and "[Approach to surgery following chemotherapy for advanced testicular germ cell tumors](#)".)

Despite being diagnosed at a relatively early stage, we recommend adjuvant chemotherapy for most women with completely resected malignant ovarian germ cell tumors **except** those with stage IA dysgerminoma ([table 1](#)) or stage I grade one immature teratoma. When indicated, chemotherapy should be delayed at least until completion of the first trimester of pregnancy [[18-20](#)]. The most commonly used regimen is [bleomycin](#), [etoposide](#), and [cisplatin](#) (BEP, ([table 2](#))). (See "[Ovarian germ cell tumors: Pathology, clinical manifestations, and diagnosis](#)" and "[Treatment of malignant germ cell tumors of the ovary](#)".)

In other series, use of [etoposide](#) during pregnancy has been associated with growth restriction and neonatal bone marrow suppression [[5,7](#)]. Etoposide is teratogenic in mice and rats at doses much lower than the human dose and should not be used in the first trimester. A consensus report suggested paclitaxel-carboplatin or cisplatin-vinblastine-bleomycin as alternatives to BEP in pregnancy [[21](#)].

**Timing of chemotherapy** — Given that germ cell neoplasms are exquisitely sensitive to platinum-based chemotherapy, several investigators have published case reports addressing a treatment delay until after the completion of the pregnancy [[22-24](#)]. A summary of findings is presented below:

- One case report documents a woman with a yolk sac (endodermal sinus) tumor that was surgically resected at 19 weeks of gestation [[22](#)]. The pregnancy was allowed to continue and BEP was not initiated until after the baby was delivered at 36 weeks. At a follow-up of 27 months, there was no evidence of recurrence disease.
- Another report described a patient with a yolk sac tumor resected at 22 weeks of gestation, after which the pregnancy was allowed to continue [[23](#)]. Unfortunately, at 34 weeks she was found to have tumor regrowth. After secondary debulking and delivery of the infant, the mother was successfully treated with BEP and was without evidence of disease 39 months after her last treatment with chemotherapy.

These reports suggest that delaying adjuvant chemotherapy may increase the risk of recurrence, although without an apparent risk to long-term recurrence free survival. Given the low quality of the data, however, a decision on the timing of adjuvant chemotherapy for women with a germ cell tumor should take into account the individual circumstances and preferences of the mother.

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## TUMORS OF LOW MALIGNANT POTENTIAL

Tumors of low malignant potential have an excellent prognosis and management is the same as that for nonpregnant patients [[25](#)]. In general, treatment is surgical and most patients do not require adjuvant chemotherapy. (See "[Borderline ovarian tumors](#)".)

## SEX CORD-STROMAL TUMORS

Most of these tumors are limited to one ovary, of low malignant potential and/or slowly progressive. The benefit of postoperative treatment for women with stage 1B to IV disease ([table 1](#)) is unclear and practice is variable. Therefore, we suggest oophorectomy alone for disease diagnosed during pregnancy. The decision for chemotherapy, if any, can be deferred to the postpartum period. (See "[Sex cord-stromal tumors of the ovary: Granulosa-stromal cell tumors](#)".)

## BREASTFEEDING

Cytotoxic agents may reach significant levels in breast milk and thus breastfeeding while on chemotherapy is generally contraindicated [[26](#)]. The United States National Library of Medicine Drugs and Lactation Database ([LactMed](#)) is an excellent resource for information on transfer of specific drugs into human milk and possible effects on the infant or on lactation, if known. Possible adverse effects include immune suppression, impaired growth, or association with carcinogenesis [[27](#)]. We agree with the World Health Organization's recommendation against nursing while receiving chemotherapy [[28](#)].

## SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "[Society guideline links: Ovarian, fallopian tubal, and peritoneal cancer](#)".)

## SUMMARY AND RECOMMENDATIONS

- The development of a gynecologic cancer during pregnancy is a rare event, affecting 4 to 8 pregnancies in 100,000. (See '[Introduction](#)' above.)
- The risks of chemotherapy administration during pregnancy depend on the specific drugs used and the gestational age of the fetus. (See '[General principles](#)' above.)
- Early delivery to avoid fetal exposure to chemotherapy is reasonable provided the fetus is  $\geq 34$  weeks of gestation and/or fetal lung maturity can be documented. In this setting, the risks of prematurity are relatively low. (See "[Adnexal mass in pregnancy](#)".) Prematurity can be associated with impaired cognitive development, and therefore iatrogenic prematurity should be avoided when possible.
- If chemotherapy is indicated, we recommend instituting platinum-based chemotherapy during pregnancy rather than waiting until after delivery ([Grade 1B](#)). We recommend delaying

administration until at least the second trimester in order to minimize the potential for fetal injury ([Grade 1B](#)). (See ['General principles'](#) above.)

- For women with epithelial ovarian cancer in pregnancy, we recommend platinum-based therapy ([Grade 1B](#)). Patients should be informed of the limited data on maternal and fetal outcomes associated with platinum and/or taxane therapy.
- For most women with germ cell tumors, we recommend adjuvant platinum-based combination chemotherapy ([Grade 1B](#)). However, women with stage IA dysgerminomas or stage I grade 1 immature teratomas have a good prognosis. We recommend not treating these patients with chemotherapy ([Grade 1A](#)). (See ["Treatment of malignant germ cell tumors of the ovary"](#).)
- Oophorectomy is the standard treatment for tumors of low malignant potential and sex cord stromal tumors diagnosed during pregnancy. These patients should not receive chemotherapy in pregnancy. (See ['Sex cord-stromal tumors'](#) above.)

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## GRAPHICS

### Ovary, fallopian tube, and primary peritoneal carcinoma TNM staging AJCC UICC 8th edition

Primary tumor (T)		
T category	FIGO stage	T criteria
TX		Primary tumor cannot be assessed
T0		No evidence of primary tumor
T1	I	Tumor limited to ovaries (one or both) or fallopian tube(s)
T1a	IA	Tumor limited to one ovary (capsule intact) or fallopian tube, no tumor on ovarian or fallopian tube surface; no malignant cells in ascites or peritoneal washings
T1b	IB	Tumor limited to both ovaries (capsules intact) or fallopian tubes; no tumor on ovarian or fallopian tube surface; no malignant cells in ascites or peritoneal washings
T1c	IC	Tumor limited to one or both ovaries or fallopian tubes, with any of the following:
T1c1	IC1	<ul style="list-style-type: none"> <li>Surgical spill</li> </ul>
T1c2	IC2	<ul style="list-style-type: none"> <li>Capsule ruptured before surgery or tumor on ovarian or fallopian tube surface</li> </ul>
T1c3	IC3	<ul style="list-style-type: none"> <li>Malignant cells in ascites or peritoneal washings</li> </ul>
T2	II	Tumor involves one or both ovaries or fallopian tubes with pelvic extension below pelvic brim or primary peritoneal cancer
T2a	IIA	Extension and/or implants on the uterus and/or fallopian tube(s) and/or ovaries
T2b	IIB	Extension to and/or implants on other pelvic tissues
T3	III	Tumor involves one or both ovaries or fallopian tubes, or primary peritoneal cancer, with microscopically confirmed peritoneal metastasis outside the pelvis and/or metastasis to the retroperitoneal (pelvic and/or para-aortic) lymph nodes
T3a	IIIA2	Microscopic extrapelvic (above the pelvic brim) peritoneal involvement with or without positive retroperitoneal lymph nodes
T3b	IIIB	Macroscopic peritoneal metastasis beyond pelvis 2 cm or less in greatest dimension with or without metastasis to the retroperitoneal lymph nodes
T3c	IIIC	Macroscopic peritoneal metastasis beyond the pelvis more than 2 cm in greatest dimension with or without metastasis to the retroperitoneal lymph nodes (includes extension of tumor to capsule of

		liver and spleen without parenchymal involvement of either organ)	
<b>Regional lymph nodes (N)</b>			
<b>N category</b>	<b>FIGO stage</b>	<b>N criteria</b>	
NX		Regional lymph nodes cannot be assessed	
N0		No regional lymph node metastasis	
N0(i+)		Isolated tumor cells in regional lymph node(s) no greater than 0.2 mm	
N1	IIIA1	Positive retroperitoneal lymph nodes only (histologically confirmed)	
N1a	IIIA1i	Metastasis up to and including 10 mm in greatest dimension	
N1b	IIIA1ii	Metastasis more than 10 mm in greatest dimension	
<b>Distant metastasis (M)</b>			
<b>M category</b>	<b>FIGO stage</b>	<b>M criteria</b>	
M0		No distant metastasis	
M1	IV	Distant metastasis, including pleural effusion with positive cytology; liver or splenic parenchymal metastasis; metastasis to extra-abdominal organs (including inguinal lymph nodes and lymph nodes outside the abdominal cavity); and transmural involvement of intestine	
M1a	IVA	Pleural effusion with positive cytology	
M1b	IVB	Liver or splenic parenchymal metastases; metastases to extra-abdominal organs (including inguinal lymph nodes and lymph nodes outside the abdominal cavity); transmural involvement of intestine	
<b>Prognostic stage groups</b>			
<b>When T is...</b>	<b>And N is...</b>	<b>And M is...</b>	<b>Then the stage group is...</b>
T1	N0	M0	I
T1a	N0	M0	IA
T1b	N0	M0	IB
T1c	N0	M0	IC
T2	N0	M0	II
T2a	N0	M0	IIA
T2b	N0	M0	IIB
T1/T2	N1	M0	IIIA1
T3a	NX, N0, N1	M0	IIIA2
T3b	NX, N0, N1	M0	IIIB
T3c	NX, N0, N1	M0	IIIC
Any T	Any N	M1	IV
Any T	Any N	M1a	IVA

Any T

Any N

M1b

IVB

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TNM: tumor, node, metastasis; AJCC: American Joint Committee on Cancer; UICC: Union for International Cancer Control.

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**Bleomycin, etoposide, and cisplatin (BEP) chemotherapy for germ cell tumors<sup>[1]</sup>**

<b>Cycle length:</b> 21 days. <b>Total cycles:</b> 3 to 4.*			
<b>Drug</b>	<b>Dose and route</b>	<b>Administration</b>	<b>Given on days</b>
Bleomycin <sup>¶</sup>	30 units <sup>Δ</sup> IV per dose	Dilute in 50 mL normal saline (NS) and administer over 10 minutes.	Days 1, 8, and 15
Etoposide	100 mg/m <sup>2</sup> IV per day	Dilute in 500 mL NS (concentration less than 0.4 mg/mL) and administer over one hour.	Days 1 through 5
Cisplatin	20 mg/m <sup>2</sup> IV per day	Dilute in 250 mL NS and administer over two hours. Do not administer with aluminum needles or intravenous sets.	Days 1 through 5
<b>Pretreatment considerations:</b>			
<b>Hydration</b>	<ul style="list-style-type: none"> <li>Induction of diuresis using at least 2000 mL of NS minimizes the risk of cisplatin nephrotoxicity. Fluid administration should be adequate to establish a urine flow of at least 100 mL/hour for two hours prior to and two hours after cisplatin administration.</li> <li>Refer to UpToDate topic on "Cisplatin nephrotoxicity."</li> </ul>		
<b>Emesis risk</b>	<ul style="list-style-type: none"> <li>HIGH (&gt;90% frequency of emesis).</li> <li>Refer to UpToDate topic on "Prevention and treatment of chemotherapy-induced nausea and vomiting in adults."</li> </ul>		
<b>Vesicant/irritant properties</b>	<ul style="list-style-type: none"> <li>Bleomycin, etoposide, and cisplatin are classified as irritants. Cisplatin can cause significant tissue damage; avoid extravasation.<sup>[2]</sup></li> <li>Refer to UpToDate topic on "Extravasation injury from chemotherapy and other non-antineoplastic vesicants."</li> </ul>		
<b>Infection prophylaxis</b>	<ul style="list-style-type: none"> <li>Primary prophylaxis with granulocyte colony stimulating factors (G-CSF) is not indicated.</li> <li>Refer to UpToDate topic on "Use of granulocyte colony stimulating factors in adult patients with chemotherapy-induced neutropenia and conditions other than acute leukemia, myelodysplastic syndrome, and hematopoietic cell transplantation."</li> </ul>		
<b>Dose adjustment for baseline liver or renal dysfunction</b>	<ul style="list-style-type: none"> <li>Bleomycin should not be administered in patients with a baseline creatinine &gt;2.0 mg/dL. A lower initial dose of cisplatin or etoposide may be needed for patients with renal or hepatic dysfunction.<sup>[2,3]</sup></li> <li>Refer to UpToDate topics on "Chemotherapy hepatotoxicity and dose modification in patients with liver disease" and "Chemotherapy nephrotoxicity and dose modification in patients with renal insufficiency: Conventional cytotoxic agents."</li> </ul>		
<b>Monitoring parameters:</b>			
<ul style="list-style-type: none"> <li>CBC with differential and platelet count weekly during treatment.</li> </ul>			
<ul style="list-style-type: none"> <li>Basic metabolic panel (creatinine and electrolytes) prior to each treatment cycle.</li> </ul>			
<ul style="list-style-type: none"> <li>Liver function tests prior to each treatment cycle.</li> </ul>			
<ul style="list-style-type: none"> <li>Assessment of baseline pulmonary function tests (PFTs), including a diffusing capacity for carbon monoxide (DLCO), should be performed prior to bleomycin treatment and repeated at intervals during therapy.</li> </ul>			

<b>Suggested dose modifications for toxicity:</b>	
<b>Myelotoxicity</b>	<ul style="list-style-type: none"> <li>Each cycle should begin on schedule regardless of the degree of myelosuppression.<sup>[1]</sup> If febrile neutropenia or thrombocytopenic bleeding occurs, a dose reduction of 25% for etoposide should be used for subsequent cycles. If neutrophil count remains <math>\leq 2500</math> cells/microL or platelets remain <math>\leq 100,000</math>/microL, G-CSF should be administered.</li> <li>Refer to UpToDate topic on "Use of granulocyte colony stimulating factors in adult patients with chemotherapy-induced neutropenia and conditions other than acute leukemia, myelodysplastic syndrome, and hematopoietic cell transplantation."</li> </ul>
<b>Pulmonary toxicity</b>	<ul style="list-style-type: none"> <li>Bleomycin can be associated with the development of life-threatening pulmonary toxicity. Maximum lifetime bleomycin dose should not exceed 400 mg. Discontinue bleomycin in patients with clinical or radiographic evidence of pulmonary injury, or decline in the DLCO of 25% or more, even if asymptomatic. Do not reintroduce bleomycin to patients with any bleomycin-induced lung injury.</li> </ul>
<b>Neurologic toxicity</b>	<ul style="list-style-type: none"> <li>Neuropathy usually is seen after cumulative doses of cisplatin beyond 400 mg/m<sup>2</sup>, although there is marked interindividual variation. Patients with mild neuropathy can continue to receive full cisplatin doses. However, if the neuropathy interferes with function, the risk of potentially disabling neurotoxicity must be weighed against the benefit of continued treatment. Peripheral neuropathies can occur with prolonged courses (four to seven months) of cisplatin. Cisplatin treatment should be discontinued with the first signs and symptoms of the development of neurotoxicity.<sup>[2,5]</sup></li> <li>Refer to UpToDate topic on "Overview of neurologic complications of platinum-based chemotherapy."</li> </ul>
<b>Renal toxicity</b>	<ul style="list-style-type: none"> <li>Treatment in the setting of renal impairment (ie, creatinine &gt;2.0 mg/dL or GFR &lt;50 mL/min) requires a balanced discussion of the goals of treatment and the risks of cisplatin nephrotoxicity in the face of impaired renal function.</li> </ul>
<b>If there is a change in body weight of at least 10%, doses should be recalculated.</b>	

**This table is provided as an example of how to administer this regimen; there may be other acceptable methods. This regimen must be administered by a clinician trained in the use of chemotherapy, who should use independent medical judgment in the context of individual circumstances to make adjustments, as necessary.**

IV: intravenous; CBC: complete blood count; GFR: glomerular filtration rate.

\* The precise number of cycles depends on the stage of the germ cell tumor.

¶ Cumulative lifetime dose of bleomycin should be limited to 400 units because of the increased rates of pulmonary toxicity. Refer to UpToDate topic on "Bleomycin-induced lung injury."

Δ 1 unit = 1 mg.

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## Contributor Disclosures

**Carolyn D Runowicz, MD** Nothing to disclose **Molly Brewer, DVM, MD, MS** Nothing to disclose **Barbara Goff, MD** Employment (Spouse): Lilly [General oncology (Gemcitabine, pemetrexed)] - No relevant conflict on topics. **Don S Dizon, MD, FACP** Grant/Research/Clinical Trial Support: Bristol-Myers Squibb [Ovarian cancer, cervical cancer (Nivolumab, ipilimumab)]; Kazia [Ovarian cancer (Cantrixil)]. Consultant/Advisory Boards: AstraZeneca [Ovarian cancer (Olaparib, durvalumab)]; Clovis Oncology [Ovarian cancer (Rucaparib)]; Regeneron Pharmaceuticals [Squamous cell carcinoma (Cemiplimab)]. **Sadhna R Vora, MD** Nothing to disclose **Vanessa A Barss, MD, FACOG** Nothing to disclose

Contributor disclosures are reviewed for conflicts of interest by the editorial group. When found, these are addressed by vetting through a multi-level review process, and through requirements for references to be provided to support the content. Appropriately referenced content is required of all authors and must conform to UpToDate standards of evidence.

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