Dactinomycin: Drug information

(For additional information see "Dactinomycin: Patient drug information" and see "Dactinomycin: Pediatric drug information")

For abbreviations and symbols that may be used in Lexicomp (show table)

ALERT: US Boxed Warning

Experienced physician:

Administer dactinomycin only under the supervision of a health care provider who is experienced in the use of cancer chemotherapeutic agents.

Hazardous agent:

This drug is highly toxic and both powder and solution must be handled and administered with care. Inhalation of dust or vapors and contact with skin or mucous membranes, especially those of the eyes, must be avoided. Because of the toxic properties of dactinomycin (eg, corrosivity, carcinogenicity, mutagenicity, teratogenicity), review special handling procedures prior to handling and follow diligently.

Pregnancy:

Avoid exposure during pregnancy.

Extravasation:

Dactinomycin is extremely corrosive to soft tissue. If extravasation occurs during intravenous (IV) use, severe damage to soft tissues will occur. In at least one instance, this has led to contracture of the arms

Brand Names: US

Cosmegen

Brand Names: Canada

Cosmegen

Pharmacologic Category

Antineoplastic Agent, Antibiotic

Dosing: Adult

Note: Medication orders for dactinomycin are commonly written in MICROgrams (eg, 150 mcg) although many regimens list the dose in MILLIgrams (eg, mg/kg or mg/m^2). The dose intensity per 2-week cycle should not exceed 15 mcg/kg/day for 5 days or 400 to 600 mcg/m^2/day for 5 days. The manufacturer recommends calculation of the dosage for obese or edematous adult patients on the basis of body surface area in an effort to relate dosage to lean body mass. Dactinomycin is associated with a high emetic potential; antiemetics are recommended to prevent nausea and vomiting (Basch, 2011).

Ewing sarcoma: IV: 15 mcg/kg/day for 5 days (in various combination regimens and schedules)

Off-label dosing: VAIA regimen: Adults ≤35 years: IV: 500 mcg/m^2/dose for 3 days (dactinomycin alternates with doxorubicin) every 3 weeks for 14 cycles (in combination with vincristine, ifosfamide, and mesna) (Paulussen 2008)

Gestational trophoblastic neoplasm: IV: 12 mcg/kg/day for 5 days (as a single agent) **or** 500 mcg/dose on days 1 and 2 (in combination with etoposide, methotrexate, leucovorin, vincristine, cyclophosphamide, and cisplatin) **or** (off-label dosing for low-risk disease) 1.25 **mg**/m^2 every 2 weeks as a single agent (Osborne 2011)

Rhabdomyosarcoma: IV: 15 mcg/kg/day for 5 days (in various combination regimens and schedules)

Testicular cancer, metastatic (nonseminomatous): IV: 1,000 mcg/m^2 on day 1 (in combination with cyclophosphamide, bleomycin, cisplatin, and vinblastine)

Wilms tumor: IV: 15 mcg/kg/day for 5 days (in various combination regimens and schedules)

Regional perfusion in solid tumors (dosages and techniques may vary by institution; obese patients and patients with prior chemotherapy or radiation therapy may require lower doses): Lower extremity or pelvis: 50 mcg/kg; Upper extremity: 35 mcg/kg

Osteosarcoma (off-label use): IV: 600 mcg/m^2 on days 1, 2, and 3 of weeks 15, 31, 34, 39, and 42 (as part of a combination chemotherapy regimen including cyclophosphamide, bleomycin, methotrexate [high dose], leucovorin, doxorubicin, and cisplatin; refer to protocol for specific details) (Goorin 2003)

Ovarian germ cell tumors, malignant (off-label use): IV: 500 mcg daily for 5 days every 4 weeks (in combination with vincristine and cyclophosphamide) (Gershenson 1985) **or** 300 mcg/m^2/day for 5 days every 4 weeks (in combination with vincristine and cyclophosphamide) (Slayton 1985)

Soft tissue sarcoma of the extremities, locally advanced/unresectable (off-label use): Isolated limb infusion (ILI) protocol: 50 to 100 mcg/L of tissue in 400 mL warmed, heparinized NS (in combination with melphalan) over 20 to 30 minutes (Moncrieff 2008). Additional data may be necessary to further define the role of dactinomycin in the treatment of this condition.

Dosing: Pediatric

(For additional information see "Dactinomycin: Pediatric drug information")

Note: Medication orders for dactinomycin are commonly written in MICROgrams (eg, 150 mcg) although many regimens list the dose in MILLIgrams (eg, mg/kg or mg/m^2). The dose intensity per 2-week cycle should not exceed 15 mcg/kg/day for 5 days or 400 to 600 mcg/m^2/day for 5 days. Dactinomycin is associated with a high emetic potential; antiemetics are recommended to prevent nausea and vomiting (Dupuis 2011).

Ewing sarcoma: Children >6 months: IV: 15 mcg/kg/day for 5 days (in various combination regimens and schedules)

Off-label dosing: VAIA regimen: IV: 500 mcg/m^2/dose for 3 days (dactinomycin alternates with doxorubicin) every 3 weeks for 14 cycles (in combination with vincristine, ifosfamide, and mesna) (Paulussen 2008)

Rhabdomyosarcoma: Children >6 months: IV: 15 mcg/kg/day for 5 days (in various combination regimens and schedules)

Off-label dosing: IV:

VAC regimen:

Children <1 year: 25 mcg/kg every 3 weeks, weeks 0 to 45 (in combination with vincristine and cyclophosphamide, and mesna); dose omission required following radiation therapy (Raney 2011)

Children ≥1 year: 45 mcg/kg (maximum dose: 2,500 mcg) every 3 weeks, weeks 0 to 45 (in combination with vincristine and cyclophosphamide, and mesna); dose omission required following radiation therapy (Raney 2011)

Wilms tumor: Children >6 months: IV: 15 mcg/kg/day for 5 days (in various combination regimens and schedules)

Off-label dosing: IV:

DD-4A regimen: 45 mcg/kg on day 1 every 6 weeks for 54 weeks (in combination with doxorubicin and vincristine) (Green 1998)

EE-4A regimen: 45 mcg/kg on day 1 every 3 weeks for 18 weeks (in combination with vincristine) (Green 1998)

VAD regimen:

Children <1 year: 750 mcg/m^2 every 6 weeks for 1 year (stage III disease) (in combination with vincristine and doxorubicin) (Pritchard 1995)

Children ≥1 year: 1500 mcg/m^2 every 6 weeks for 1 year (stage III disease) (in combination with vincristine and doxorubicin) (Pritchard 1995)

Osteosarcoma (off-label use): IV: 600 mcg/m^2 on days 1, 2, and 3 of weeks 15, 31, 34, 39, and 42 (as part of a combination chemotherapy regimen including cyclophosphamide, bleomycin, methotrexate [high dose], leucovorin, doxorubicin, and cisplatin; refer to protocol for specific details) (Goorin 2003)

Dosing: Geriatric

Refer to adult dosing. Elderly patients are at increased risk of myelosuppression; dosing should begin at the low end of the dosing range.

Dosing: Renal Impairment

There are no dosage adjustments provided in the manufacturer's labeling; however, based on the amount of urinary excretion, dosage adjustments may not be necessary.

Dosing: Hepatic Impairment

There are no dosage adjustments provided in manufacturer's labeling.

The following adjustments have also been recommended: Any transaminase increase: Reduce dose by 50%; may increase by monitoring toxicities (Floyd 2006).

Dosing: Obesity *ASCO Guidelines for appropriate chemotherapy dosing in obese adults with cancer:* Utilize patient's actual body weight (full weight) for calculation of body surface area- or weight-based dosing, particularly when the intent of therapy is curative; manage regimen-related toxicities in the same manner as for nonobese patients; if a dose reduction is utilized due to toxicity, consider resumption of full weight-based dosing with subsequent cycles, especially if cause of toxicity (eg, hepatic or renal impairment) is resolved (Griggs 2012).

Dosing: Adjustment for Toxicity Severe myelosuppression, stomatitis, or diarrhea: Interrupt therapy until toxicity has resolved.

Dosage Forms Excipient information presented when available (limited, particularly for generics); consult specific product labeling.

Solution Reconstituted, Intravenous:

Cosmegen: 0.5 mg (1 ea)

Generic Equivalent Available (US) No

Administration Dactinomycin is associated with a high emetic potential; antiemetics are recommended to prevent nausea and vomiting (Basch 2011, Dupuis 2011).

For IV administration; do not administer IM or SubQ. Administer by slow IV push or infuse over 10 to 15 minutes. Do not filter with cellulose ester membrane filters.

Regional perfusion: Technique may vary by institution; consult protocol for details. Local reactions including epidermolysis, erythema, and edema have been reported (may be severe).

Vesicant; ensure proper needle or catheter placement prior to and during infusion; avoid extravasation.

Extravasation management: If extravasation occurs, stop infusion immediately and disconnect (leave cannula/needle in place); gently aspirate extravasated solution (do **NOT** flush the line); remove needle/cannula; elevate extremity. Apply dry cold compresses for 20 minutes 4 times a day for 1-2 days (Perez Fildago 2012).

Hazardous Drugs Handling Considerations

Hazardous agent (NIOSH 2016 [group 1]).

Use appropriate precautions for receiving, handling, administration, and disposal. Gloves (single) should be worn during receiving, unpacking, and placing in storage.

NIOSH recommends double gloving, a protective gown, ventilated engineering controls (a class II biological safety cabinet or a compounding aseptic containment isolator), and closed system transfer devices (CSTDs) for preparation. Double gloving, a gown, and (if dosage form allows) CSTDs are required during administration (NIOSH 2016).

Use

Ewing sarcoma: Treatment of Ewing sarcoma (as part of a combination chemotherapy and/or multimodality treatment regimen)

Gestational trophoblastic neoplasia: Treatment of gestational trophoblastic neoplasia (as a single agent or in combination with other chemotherapy agents)

Rhabdosarcoma: Treatment of childhood rhabdosarcoma (as part of a combination chemotherapy and/or multimodality treatment regimen)

Solid tumors: Palliative and/or adjunctive treatment of locally recurrent or locoregional solid malignancies (as a component of regional perfusion)

Testicular cancer, metastatic (nonseminomatous): Treatment of metastatic nonseminomatous testicular cancer

Wilms tumor: Treatment of Wilms tumor (as part of a combination chemotherapy and/or multimodality treatment regimen)

Use: Off-Label

Osteosarcoma; Ovarian germ cell tumors (malignant); Soft tissue sarcoma of the extremities (locally advanced or unresectable)

Medication Safety Issues

Sound-alike/look-alike issues:

DACTINomycin may be confused with Dacogen, DAPTOmycin, DAUNOrubicin

Actinomycin may be confused with achromycin

High alert medication:

This medication is in a class the Institute for Safe Medication Practices (ISMP) includes among its list of drug classes which have a heightened risk of causing significant patient harm when used in error.

Adverse Reactions Frequency not defined.

Cardiovascular: Hepatic veno-occlusive disease (hepatic sinusoidal obstruction syndrome)

Central nervous system: Fatigue, lethargy, malaise

Dermatologic: Acne vulgaris, alopecia (reversible), cheilitis, dermal ulcer (following extravasation),

epidermolysis, erythema (of previously irradiated skin), erythema multiforme, exfoliation of skin, localized erythema, skin pigmentation (of previously irradiated skin), skin rash, Stevens-Johnson syndrome, toxic epidermal necrolysis

Endocrine & metabolic: Growth suppression, hyperuricemia, hypocalcemia

Gastrointestinal: Abdominal pain, anorexia, diarrhea, dysphagia, esophagitis, gastrointestinal ulcer, mucositis, nausea, proctitis, stomatitis, vomiting

Hematologic & oncologic: Agranulocytosis, anemia, aplastic anemia, bone marrow depression (onset: 7 days; nadir: 14 to 21 days; recovery: 21 to 28 days), febrile neutropenia, leukopenia, neutropenia, pancytopenia, reticulocytopenia, thrombocytopenia, thrombocytopenia (immune-mediated)

Hepatic: Abnormal hepatic function tests, ascites, hepatic failure, hepatitis, hepatomegaly, hepatopathy thrombocytopenia syndrome, hepatotoxicity, increased serum bilirubin

Hypersensitivity: Anaphylactoid reaction

Infection: Infection, sepsis (including neutropenic sepsis)

Local: Localized edema, local pain

Neuromuscular & skeletal: Myalgia

Renal: Renal function abnormality

Respiratory: Pharyngitis, pneumonitis

Miscellaneous: Fever, tissue necrosis

Contraindications

Hypersensitivity to dactinomycin or any component of the formulation; patients with concurrent or recent infection with chickenpox or herpes zoster

Warnings/Precautions

Concerns related to adverse effects:

• Bone marrow suppression: Leukopenia, thrombocytopenia, and anemia may occur. Onset may occur at 2 to 4 days following treatment course and may require 1 to 2 weeks to reach maximum severity. Discontinue treatment with severe myelosuppression.

• Extravasation: Vesicant; ensure proper needle or catheter placement prior to and during infusion. Avoid extravasation. **[US Boxed Warning]: Extremely corrosive to soft tissues; if extravasation occurs during IV use, severe damage to soft tissues will occur; has led to contracture of the arms (rare). Recommended for IV administration only.**

• Gastrointestinal toxicity: Dactinomycin is associated with a high emetic potential; antiemetics are recommended to prevent nausea and vomiting (Basch 2011, Dupuis 2011). Discontinue treatment if diarrhea or stomatitis occur.

• Hepatotoxicity: May cause hepatic sinusoidal obstruction syndrome (SOS; formerly called veno-occlusive liver disease [VOD]), increased risk in children <4 years of age; use with caution in hepatobiliary dysfunction. Monitor for signs or symptoms of hepatic SOS, including bilirubin >1.4 mg/dL, unexplained weight gain, ascites, hepatomegaly, or unexplained right upper quadrant pain

(Arndt 2004).

• Secondary malignancies: Long-term observation of cancer survivors is recommended due to the increased risk of second primary tumors following treatment with radiation and antineoplastic agents.

Concurrent drug therapy issues:

• Drug-drug interactions: Potentially significant interactions may exist, requiring dose or frequency adjustment, additional monitoring, and/or selection of alternative therapy. Consult drug interactions database for more detailed information.

Special populations:

• Elderly: Use with caution; may be associated with an increased risk of myelosuppression.

• Pediatric: Avoid use in infants <6 months of age (toxic effects may occur more frequently). The risk of fatal hepatic SOS is increased in children <4 years of age.

• Pregnancy: **[US Boxed Warning]: Avoid exposure during pregnancy.**

• Radiation therapy recipients: Potentiates the effects of radiation therapy; use with caution in patients who have received radiation therapy; reduce dosages in patients who are receiving dactinomycin and radiation therapy simultaneously; combination with radiation therapy may result in increased toxicity (eg, GI toxicity, myelosuppression, severe oropharyngeal mucositis). Erythema from prior radiation therapy may be reactivated by dactinomycin. Avoid dactinomycin use within 2 months of radiation treatment for right-sided Wilms tumor, may increase the risk of hepatotoxicity.

Special handling:

• **[US Boxed Warning]: Avoid inhalation of vapors or contact with skin, mucous membrane, or eyes; use caution for handling and administration.** If accidental exposure occurs, immediately irrigate copiously for at least 15 minutes with water, saline, or balanced ophthalmic irrigation solution (eye exposure) and at least 15 minutes with water (skin exposure); prompt ophthalmic or medical consultation is also recommended. Contaminated clothing should be destroyed and shoes thoroughly cleaned prior to reuse.

Other warnings/precautions:

• Dosage expression: Dosage is usually expressed in **MICRO**grams and should be calculated on the basis of body surface area (BSA) in obese or edematous adult patients (to relate dose to lean body mass).

• Experienced physician: **[US Boxed Warning]: Should be administered under the supervision of an experienced cancer chemotherapy physician.**

• Regional perfusion therapy: May result in local limb edema, soft tissue damage, and possible venous thrombosis. Dactinomycin leakage into systemic circulation may result in hematologic toxicity, infection, impaired wound healing, and mucositis.

• Vaccines: Avoid administration of live vaccines during dactinomycin treatment.

Metabolism/Transport Effects

None known.

Drug Interactions

(For additional information: Launch drug interactions program) Lexicomp®

BCG (Intravesical): Immunosuppressants may diminish the therapeutic effect of BCG (Intravesical). *Risk X: Avoid combination*

BCG (Intravesical): Myelosuppressive Agents may diminish the therapeutic effect of BCG (Intravesical). *Risk X: Avoid combination*

CloZAPine: Myelosuppressive Agents may enhance the adverse/toxic effect of CloZAPine. Specifically, the risk for neutropenia may be increased. *Risk C: Monitor therapy*

Coccidioides immitis Skin Test: Immunosuppressants may diminish the diagnostic effect of Coccidioides immitis Skin Test. *Risk C: Monitor therapy*

Deferiprone: Myelosuppressive Agents may enhance the neutropenic effect of Deferiprone. *Risk X: Avoid combination*

Denosumab: May enhance the adverse/toxic effect of Immunosuppressants. Specifically, the risk for serious infections may be increased. *Risk C: Monitor therapy*

Dipyrone: May enhance the adverse/toxic effect of Myelosuppressive Agents. Specifically, the risk for agranulocytosis and pancytopenia may be increased *Risk X: Avoid combination*

Echinacea: May diminish the therapeutic effect of Immunosuppressants. *Risk D: Consider therapy modification*

Fingolimod: Immunosuppressants may enhance the immunosuppressive effect of Fingolimod. Management: Avoid the concomitant use of fingolimod and other immunosuppressants when possible. If combined, monitor patients closely for additive immunosuppressant effects (eg, infections). *Risk D: Consider therapy modification*

Leflunomide: Immunosuppressants may enhance the adverse/toxic effect of Leflunomide. Specifically, the risk for hematologic toxicity such as pancytopenia, agranulocytosis, and/or thrombocytopenia may be increased. Management: Consider not using a leflunomide loading dose in patients receiving other immunosuppressants. Patients receiving both leflunomide and another immunosuppressant should be monitored for bone marrow suppression at least monthly. *Risk D: Consider therapy modification*

Lenograstim: Antineoplastic Agents may diminish the therapeutic effect of Lenograstim. *Risk D: Consider therapy modification*

Natalizumab: Immunosuppressants may enhance the adverse/toxic effect of Natalizumab. Specifically, the risk of concurrent infection may be increased. *Risk X: Avoid combination*

Nivolumab: Immunosuppressants may diminish the therapeutic effect of Nivolumab. *Risk D: Consider therapy modification*

Ocrelizumab: May enhance the immunosuppressive effect of Immunosuppressants. *Risk C: Monitor therapy*

Palifermin: May enhance the adverse/toxic effect of Antineoplastic Agents. Specifically, the duration and severity of oral mucositis may be increased. Management: Do not administer palifermin within 24 hours

before, during infusion of, or within 24 hours after administration of myelotoxic chemotherapy. *Risk D: Consider therapy modification*

Pimecrolimus: May enhance the adverse/toxic effect of Immunosuppressants. *Risk X: Avoid combination*

Promazine: May enhance the myelosuppressive effect of Myelosuppressive Agents. *Risk C: Monitor therapy*

Roflumilast: May enhance the immunosuppressive effect of Immunosuppressants. *Risk D: Consider therapy modification*

Sipuleucel-T: Immunosuppressants may diminish the therapeutic effect of Sipuleucel-T. *Risk C: Monitor therapy*

Tacrolimus (Topical): May enhance the adverse/toxic effect of Immunosuppressants. *Risk X: Avoid combination*

Tertomotide: Immunosuppressants may diminish the therapeutic effect of Tertomotide. *Risk C: Monitor therapy*

Tofacitinib: Immunosuppressants may enhance the immunosuppressive effect of Tofacitinib. Management: Concurrent use with antirheumatic doses of methotrexate or nonbiologic disease modifying antirheumatic drugs (DMARDs) is permitted, and this warning seems particularly focused on more potent immunosuppressants. *Risk X: Avoid combination*

Trastuzumab: May enhance the neutropenic effect of Immunosuppressants. *Risk C: Monitor therapy*

Vaccines (Inactivated): Immunosuppressants may diminish the therapeutic effect of Vaccines (Inactivated). Management: Vaccine efficacy may be reduced. Complete all age-appropriate vaccinations at least 2 weeks prior to starting an immunosuppressant. If vaccinated during immunosuppressant therapy, revaccinate at least 3 months after immunosuppressant discontinuation. *Risk D: Consider therapy modification*

Vaccines (Live): Immunosuppressants may enhance the adverse/toxic effect of Vaccines (Live). Immunosuppressants may diminish the therapeutic effect of Vaccines (Live). Management: Avoid use of live organism vaccines with immunosuppressants; live-attenuated vaccines should not be given for at least 3 months after immunosuppressants. *Risk X: Avoid combination*

Pregnancy Risk Factor

D (show table)

Pregnancy Implications

[US Boxed Warning]: Avoid exposure during pregnancy. Adverse effects have been observed in animal reproduction studies. Women of childbearing potential are advised not to become pregnant. When used for gestational trophoblastic neoplasm, unfavorable outcomes have been reported when subsequent pregnancies occur within 6 months of treatment. It is recommended to use effective contraception for 6 months to 1 year after therapy (Matsui 2004; Seckl 2013)

Breast-Feeding Considerations

It is not known if dactinomycin is excreted in human breast milk. According to the manufacturer labeling, due to the potential for serious adverse reactions in the nursing infant, the decision to discontinue dactinomycin or to discontinue breast-feeding during therapy should take into account the benefits of treatment to the mother.

Monitoring Parameters

CBC with differential and platelet count, liver function tests, and renal

function tests; monitor for signs/symptoms of hepatic SOS, including unexplained weight gain, ascites, hepatomegaly, or unexplained right upper quadrant pain (Arndt, 2004)

Mechanism of Action

Binds to the guanine portion of DNA intercalating between guanine and cytosine base pairs inhibiting DNA and RNA synthesis and protein synthesis

Pharmacodynamics/Kinetics

Distribution: Children: Extensive extravascular distribution (59 to 714 L) (Veal 2005); does not penetrate blood-brain barrier

Metabolism: Minimal

Half-life elimination: ~36 hours; Children: Range: 14 to 43 hours (Veal 2005)

Excretion: ~30% in urine and feces within 1 week

Pricing: US

Solution (reconstituted) (Cosmegen Intravenous)

0.5 mg (1): $1621.88

Disclaimer: The pricing data provide a representative AWP and/or AAWP price from a single manufacturer of the brand and/or generic product, respectively. The pricing data should be used for benchmarking purposes only, and as such should not be used to set or adjudicate any prices for reimbursement or purchasing functions. Pricing data is updated monthly.

International Brand Names

Ac-De (MX); Cosmegen (AR, AT, AU, BE, BG, BM, BR, CH, CR, DE, DO, EE, EG, FI, FR, GB, GR, GT, HN, IE, IT, KR, MT, NI, NL, NZ, PA, PH, PK, PT, PY, RU, SE, SI, SK, SV, TR, TW, VN); Cosmegen, Lyovac (GB, HK); Dacmozen (IN); Dacticin (VN); Dactilon (PE); Dactin (VN); Dactinomicina Ac-De (PE); Trepar (PH)

REFERENCES

1. *Arndt C, Hawkins, D, Anderson JR, et al, "Age is a Risk Factor for Chemotherapy-Induced Hepatopathy With Vincristine, Dactinomycin and Cyclophosphamide," J Clin Oncol, 2004, 22(10):1894-901. [PubMed 15143082]*
2. *Basch E, Prestrud AA, Hesketh PJ, et al; American Society of Clinical Oncology. Antiemetics: American Society of Clinical Oncology clinical practice guideline update. J Clin Oncol. 2011;29(31):4189-4198. [PubMed 21947834]*
3. *Cosmegen (dactinomycin) [prescribing information]. Lebanon, NJ: Recordati Rare Diseases Inc; February 2013.*
4. *Czauderna P, Katski K, Kowalczyk J, et al, "Venoocclusive Liver Disease (VOD) as a Complication of Wilms' Tumour Management in the Series of Consecutive 206 Patients," Eur J Pediatr Surg, 2000, 10(5):300-3. [PubMed 11194540]*
5. *D'Antiga L, Baker A, Pritchard J. et al, "Veno-Occlusive Disease With Multi-Organ Involvement Following Actinomycin-D," Eur J Cancer, 2001, 37(9):1141-8. [PubMed 11378345]*
6. *Dupuis LL, Boodhan S, Holdsworth M, et al; Pediatric Oncology Group of Ontario. Guideline for the prevention of acute nausea and vomiting due to antineoplastic medication in pediatric cancer patients. Pediatr Blood Cancer. 2013;60(7):1073-1082. [PubMed 23512831]*
7. *Dupuis LL, Boodhan S, Sung L, et al; Pediatric Oncology Group of Ontario. Guideline for the classification of the acute*

emetogenic potential of antineoplastic medication in pediatric cancer patients. Pediatr Blood Cancer. 2011;57(2):191-198. [PubMed 21465637]

8. *Floyd J, Mirza I, Sachs B, et al, "Hepatotoxicity of Chemotherapy," Semin Oncol, 2006, 33(1):50-67. [PubMed 16473644]*
9. *Gershenson DM, Copeland LJ, Kavanagh JJ, et al, "Treatment of Malignant Nondysgerminomatous Germ Cell Tumors of the Ovary With Vincristine, Dactinomycin, and Cyclophosphamide," Cancer, 1985, 56(12):2756-61. [PubMed 2996746]*
10. *Goorin AM, Schwartzentruber DJ, Devidas M, et al, "Presurgical Chemotherapy Compared With Immediate Surgery and Adjuvant Chemotherapy for Nonmetastatic Osteosarcoma: Pediatric Oncology Group Study POG-8651," J Clin Oncol, 2003, 21(8):1574-80. [PubMed 12697883]*
11. *Green DM, Breslow NE, Beckwith JB, et al, "Effect of Duration of Treatment on Treatment Outcome and Cost of Treatment for Wilms' Tumor: A Report From the National Wilms' Tumor Study Group," J Clin Oncol, 1998, 16(12):3744-51. [PubMed 9850017]*
12. *Grier HE, Krailo MD, Tarbell NJ, et al, "Addition of Ifosfamide and Etoposide to Standard Chemotherapy for Ewing's Sarcoma and Primitive Neuroectodermal Tumor of Bone," N Engl J Med, 2003, 348(8):694-701. [PubMed 12594313]*
13. *Griggs JJ, Mangu PB, Anderson H, et al, "Appropriate Chemotherapy Dosing For Obese Adult Patients With Cancer: American Society of Clinical Oncology Clinical Practice Guideline," J Clin Oncol, 2012, 30(13):1553-61. [PubMed 22473167]*
14. *Matsui H, Iitsuka Y, Suzuka K, et al. Early pregnancy outcomes after chemotherapy for gestational trophoblastic tumor. J Reprod Med. 2004;49(7):531-534. [PubMed 15305824]*
15. *Moncrieff MD, Kroon HM, Kam PC, et al. Isolated limb infusion for advanced soft tissue sarcoma of the extremity. Ann Surg Oncol. 2008;15(10):2749-2756. [PubMed 18648882]*
16. *Morgan C, Tillett T, Braybrooke J, et al, "Management of Uncommon Chemotherapy-Induced Emergencies," Lancet Oncol, 2011, 12(8):806-14. [PubMed 21276754]*
17. *Osborne RJ, Filiaci V, Schink JC, et al. Phase III trial of weekly methotrexate or pulsed dactinomycin for low-risk gestational trophoblastic neoplasia: a gynecologic oncology group study. J Clin Oncol. 2011;29(7):825-831. [PubMed 21263100]*
18. *Paulussen M, Craft AW, Lewis I, et al. Results of the EICESS-92 Study: two randomized trials of Ewing's sarcoma treatment--cyclophosphamide compared with ifosfamide in standard-risk patients and assessment of benefit of etoposide added to standard treatment in high-risk patients. J Clin Oncol. 2008;26(27):4385-4393. [PubMed 18802150]*
19. *Pérez Fidalgo JA, García Fabregat L, Cervantes A, et al, "Management of Chemotherapy Extravasation: ESMO-EONS Clinical Practice Guidelines," Ann Oncol, 2012, 23(Suppl 7):167-73. [PubMed 22997449]*
20. *Pritchard J, Imeson J, Barnes J, et al, "Results of the United Kingdom Children's Cancer Study Group First Wilms' Tumor Study," J Clin Oncol, 1995, 13(1):124-33. [PubMed 7799012]*
21. *Raney RB, Walterhouse DO, Meza JL, et al, "Results of the Intergroup Rhabdomyosarcoma Study Group D9602 Protocol, Using Vincristine and Dactinomycin With or Without Cyclophosphamide and Radiation Therapy, for Newly Diagnosed Patients With Low-Risk Embryonal Rhabdomyosarcoma: A Report From the Soft Tissue Sarcoma Committee of the Children's Oncology Group," J Clin Oncol, 2011, 29(10):1312-8. [PubMed 21357783]*
22. *Seckl MJ, Sebire NJ, Fisher RA, et al. Gestational trophoblastic disease: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2013 Oct;2(Suppl 6):vi39-50. [PubMed 23999759]*
23. *Slayton RE, Park RC, Silverberg SG, et al, "Vincristine, Dactinomycin, and Cyclophosphamide in the Treatment of Malignant Germ Cell Tumors of the Ovary. A Gynecologic Oncology Group Study (A Final Report)," Cancer, 1985, 56(2):243-8. [PubMed 2988740]*
24. *Sulis ML, Bessmertny O, Granowetter L, et al, "Veno-Occlusive Disease in Pediatric Patients Receiving Actinomycin D and Vincristine Only for the Treatment of Rhabdomyosarcoma, J Pediatr Hematol Oncol, 2004, 26(12):843-6.*
25. *US Department of Health and Human Services; Centers for Disease Control and Prevention; National Institute for Occupational Safety and Health. NIOSH list of antineoplastic and other hazardous drugs in healthcare settings 2016. http://www.cdc.gov/niosh/topics/antineoplastic/pdf/hazardous-drugs-list_2016-161.pdf. Updated September 2016. Accessed October 5, 2016.*
26. *Veal GJ, Cole M, Errington J, et al, "Pharmacokinetics of Dactinomycin in a Pediatric Patient Population: A United Kingdom Children's Cancer Study Group Study," Clin Cancer Res, 2005, 11(16):5893-9. [PubMed 16115931]*

Topic 9318 Version 147.0