REMOVAL OF ONCOLOGY DRUGS BY HEMODIALYSIS [1-9]

DRUG	HEMODIALYSIS EFFECTIVENESS	SUMMARY OF DATA AVAILABLE
Aldesleukin	Ineffective	Slightly water soluble. Rapidly distributes to extravascular and extracellular space. Metabolized in proximal tubule (> 80%); remainder cleared by GF.
Alemtuzumab	Ineffective	Due to the large size of the molecule (150,000 daltons), [10] it is highly improbable that the drug could pass through a hemodialysis membrane. Molecules > 500 daltons are considered impassable for conventional hemodialysis. Antibody/antigen complexes are most likely eliminated in the liver and spleen after uptake by the reticular endothelial system.[11]
Altretamine	Minimally effective]	Not water soluble. Minimal protein binding of altretamine; active metabolites 25% -50% bound. Rapid distribution to all organs. Liver metabolism with some active metabolites; almost 90% of metabolites excreted renally.
Amifostine	Minimally effective	Water soluble. Prodrug, dephosphorylated by alkaline phosphatase to active free sulfhydryl metabolite and inactive metabolite. Active metabolite distributes into BM. < 1% of dose excreted renally as unchanged drug within 1st hour after administration; < 3% excreted renally as active metabolite.[12]
Aminogluteth-imide	[Ineffective]	Not water soluble. Vd (steady state) averages 1 L/kg; ≈ 24% bound to plasma proteins. Undergoes extensive hepatic metabolism. 10% to 20% excreted renally. Some clinicians recommend supplemental dosing after HD.[8,9]
Anagrelide	Ineffective	Very slightly water soluble. Vd (steady state) is 12 L/kg. Extensively metabolized. Less than 1% excreted renally as unchanged drug.[13]
Anastrozole	Minimally effective	Freely soluble in water. 40% bound to plasma proteins. Extensively metabolized with 10% excreted in urine.
Antithymocyte globulin	Ineffective	Due to the large size of the molecule (150,000 to 160,000 daltons), [14] it is highly improbable that the drug could pass through a HD membrane. Molecules > 500 daltons are considered impassable for conventional HD. Minimal amount excreted unchanged in urine (1%).
Arsenic trioxide	Ineffective, minimally effective [15-17]	Some removal after overdose in patients with significant renal impairment. Drug unlikely to be removed in patients with normal renal function, based on PK properties. [18] Sparingly water soluble. Metabolized to active moiety (trivalent arsenic) by hepatic methyltransferases. Trivalent arsenic is stored in the liver, kidneys, heart, lungs, hair, and nails. Inactivated by methyltransferase in the liver and excreted in the urine.
Asparaginase	Ineffective	Water soluble. Vd (steady state) 70% -80% of plasma volume in adults. Pattern of elimination unknown; excreted in urine (< 1%) and feces (trace).
Azathioprine	Minimally effective	Not water soluble. Rapidly cleared from blood, although Vd not fully characterized (ranges from 0.55 to 0.8 L/kg at steady state). Both drug and active metabolite (mercaptopurine) are ≈ 30% bound to serum proteins. Both compounds metabolized in liver; metabolites excreted renally. Only small amounts of azathioprine (< 2%) and mercaptopurine excreted in urine. Some clinicians recommend a supplemental dose of 0.25 mg/kg after HD. [1,2,8,9]
Bexarotene	Ineffective	Not water soluble. [19] Highly bound (> 99%) to plasma proteins. Tissue distribution unknown. Metabolized by CYP450 3A4; metabolites may be active. Primarily biliary excretion; minimal excretion in urine (< 1% of dose) as unchanged drug or metabolites.
Bicalutamide	Ineffective	Not water soluble. More than 90% bound to plasma protein. Extensively metabolized in liver to active and inactive metabolites. Drug and metabolites eliminated in urine and feces. [20]
Bleomycin	Minimally effective	Water soluble. Vd (steady state) 0.25 to 0.3 L/kg. < 5% bound to plasma proteins. Distributed to skin, lungs, kidneys, peritoneum, and lymphatics. Some metabolism by bleomycin hydrolase in tissue, but 60% to 70% excreted renally. Supplemental dosing is usually not required after HD. [1,2,8,9]
Busulfan	Ineffective	Water soluble. Vd (steady state) averages 1 L/kg in adults. Primarily metabolized in liver; renal excretion < 3%.

DRUG	HEMODIALYSIS EFFECTIVENESS	SUMMARY OF DATA AVAILABLE
Capecitabine	Minimally effective	Sparingly water soluble. Distribution characteristics of capecitabine unknown. Metabolized in liver to 5-fluorouracil (active). [21] Vd (steady state) of 5-fluorouracil averages 0.25 to 0.5 L/kg with distribution to tumors, intestinal mucosa, bone marrow, and liver. 5-fluorouracil crosses BBB and is 10% bound to plasma proteins. 5-fluorouracil is converted to other active metabolites in tissues and metabolized in liver. Renal excretion of unchanged 5-fluorouracil is 7% to 20% within 6 hours.
Carboplatin	Ineffective [22,23] Minimally effective [24,25] Moderately effective [26,27]	Efficacy of HD decreases with time after administration. Drug unlikely to be removed based on PK properties. Water soluble. Vd (steady state) averages 0.24 L/kg in adults. Platinum molecule highly protein bound (> 90%), although drug itself is not (< 10%). Almost 70% of drug excreted unchanged in urine; remainder of platinum eliminated with protein turnover. After HD, some clinicians recommend supplementing with 50% of the original dose. [1,2,8,9]
Carmustine	Moderately effective	Removed by dialysis in vitro and likely to be removed in vivo based on PK data. [28] Slightly water soluble. Vd (steady state) averages 3.3 L/kg. Crosses BBB. Metabolized in liver with some active metabolites. Undergoes enterohepatic circulation. Supplemental doses are usually not required after HD.[8,9]
Chlorambucil	Ineffective	Slightly water soluble. Vd (steady state) averages 0.86 L/kg in adults; 99% protein bound in plasma. Liver metabolism with some active metabolites. Drug and active metabolites undergo spontaneous degradation. Less than 1% of dose excreted renally. Supplemental doses are usually not required after HD.[8,9]
Cisplatin	Ineffective [29-31]	In case reports, coadministration with HD reduces AUC 46%. [32] Removed by dialysis in vitro but unlikely to be removed in vivo based on PK properties. [28] Water soluble. Vd (steady state) in adults ranges from 0.28 to 1.14 L/kg. Distributed to liver, kidney, and intestines. Platinum molecule highly protein bound (> 90%) although drug itself is not (< 10%). Eliminated by displacement of chloride ligands by water. Undergoes enterohepatic circulation. Renal excretion accounts for 15% to 50% of dose. Controversy exists whether or not supplemental doses are necessary after dialysis. [1,2,8,9]
Cladribine	Ineffective	Some removal in poorly documented case report. [33] Slightly water soluble. Vd (steady state) in adults averages 4.5 L/kg; 20% protein bound in plasma. Excreted in urine (41% to 44%); < 1% excreted in feces.
Cyclophos-phamide	Moderately effective	Active moiety removed by dialysis in vitro and likely to be removed in vivo based on PK properties. [28] Water soluble. Vd (steady state) averages 0.64 L/kg. < 15% bound to plasma proteins. Metabolized to active moiety in liver. Active metabolite is > 60% bound to plasma protein and is further metabolized in the liver. Renal excretion of unchanged drug ranges from 5% - 25%. After HD, some recommend supplementing with 50% of the original dose. [1,2,8,9]
Cyclosporine	Ineffective	Not water soluble. Vd (steady state) ranges from 1.45 to 7.26 L/kg; distributes into erythrocytes, granulocytes, and lymphocytes. > 90% protein bound, primarily to lipoproteins. Metabolized primarily in the liver with some minimally active metabolites. Excreted almost entirely in the feces as metabolites; ≈ 0.1% excreted unchanged in the urine. Supplemental doses are usually not required after HD. [2,8,9]
Cytarabine	Ineffective	Removed by dialysis in vitro but unlikely to be removed in vivo based on PK properties. [28] Water soluble. Vd (steady state) averages 2 to 3 L/kg in adults; crosses BBB. ≈ 13% protein bound. Metabolized in liver and degraded by cytidine deaminase. Renal excretion of unchanged drug < 10%.
Cytarabine liposome	Ineffective	NOTE: Product for intrathecal use only. Primarily confined to intrathecal space. Distribution from cerebrospinal fluid (CSF) to plasma occurs very slowly. Systemic exposure is insignificant. Cleared by CSF bulk flow. [34]
Dacarbazine	Moderately effective	Removed by dialysis in vitro and likely to be removed in vivo based on PK properties. [28] Slightly water soluble. Vd (steady state) exceeds total body water. Drug crosses BBB, but protein binding is minimal. Metabolized in liver, may have active metabolites. Much of dose (15% to 40%) is excreted unchanged by renal tubular secretion.

DRUG	HEMODIALYSIS EFFECTIVENESS	SUMMARY OF DATA AVAILABLE
Dactinomycin	Ineffective	Removed by dialysis in vitro but unlikely to be removed in vivo based on PK properties. [28] Slightly water soluble. Concentrates in bone marrow and nucleated cells; does not cross BBB. Minimally metabolized; 10% to 30% of dose is excreted unchanged in urine.
Daunorubicin	Ineffective	Not removed by dialysis in vitro and unlikely to be removed in vivo. [28] Water soluble. Vd (steady state) > 14 L/kg. Concentrates in spleen, kidneys, liver, lungs, and heart. Highly protein bound in plasma (percentage unknown). Crosses placenta, but not BBB. Metabolized in liver with some active metabolites and inactivated by cleavage of glycoside bonds. Biliary excretion of unchanged drug and active metabolite is ≈ 40% and renal excretion is 25%.
Daunorubicin citrate liposomal	Ineffective	Confined to extracellular space; Vd (steady state) averages 0.09 L/kg. Unknown if liposomal preparation crosses BBB. Metabolized in liver with some active metabolites. [35]
Denileukin diftitox	Ineffective	Due to the large size of the molecule (58,000 daltons), it is highly improbable the drug could pass through a HD membrane. Molecules > 500 daltons are considered impassable for conventional HD. Denileukin diftitox binds to the high affinity IL-2 receptor expressed on malignant cells, activated T lymphocytes, activated B lymphocytes, and activated macrophages. Distributes to the liver and kidneys. Metabolized by proteolytic degradation. Less than 25% excreted as low molecular weight breakdown products. [36]
Dexrazoxane	Minimally effective	Sparingly water soluble. Distributes primarily in total body water. Not bound to plasma proteins. 42% excreted renally.
Diethylstil-bestrol	Unknown	Effects of HD unknown. Not water soluble. Inactivated in the liver. Eliminated in urine and feces as glucuronide.
Docetaxel	Ineffective	Not water soluble. Vd (steady state) averages 1.6 L/kg; 94% to 97% protein bound. Urinary excretion of unchanged drug < 10%.
Dolasetron	Minimally effective	Water soluble. Distribution characteristics of dolasetron not fully characterized. Completely metabolized to active metabolite (hydrodolasetron) by carbonyl reductase. Volume of distribution (steady state) of hydrodolasetron averages 5.8 L/kg. 69% to 77% bound to plasma proteins; α_1-acid glycoprotein accounts for 50% of bound drug. Active moiety further metabolized in liver. 53% dose excreted in urine as unchanged hydrodolasetron; 33% of dose recovered in feces as hydrodolasetron and metabolites. [37]
Doxorubicin	Ineffective [38]	In PK studies; removed by dialysis in vitro but unlikely to be removed in vivo based on pharmacokinetic properties. [28] Water soluble. Vd (steady state) is 21.5 L/kg; ≈ 80% protein bound in plasma. Does not cross BBB. Metabolized in liver with active metabolites and inactivated by cleavage of glycoside bonds. Biliary excretion of unchanged drug is 40% to 50% and renal excretion < 15%. Supplemental doses are usually not required after HD. [2,8,9]
Doxorubicin hydrochloride liposome	Minimally effective	Vd (steady state) is 0.07 L/kg, primarily limited to intravascular space. Protein binding has not been determined. Does not cross BBB. Metabolized in liver with active metabolites; decreased metabolism to active metabolites compared with nonliposomal doxorubicin.[39]
Epirubicin	Ineffective	Water soluble. Vd (steady state) is 21 to 27 L/kg; ≈ 77% protein bound in plasma. Concentrates in red blood cells. Metabolized in liver, red blood cells, and other organs with active metabolites and inactivated by cleavage of glycosidic bonds. Unchanged drug and metabolites excreted in the feces (34%) and urine (27%). Approximately 11% of dose excreted in urine as unchanged drug. [40] , [41] Supplemental doses are usually not required after HD. [2]
Epoetin alfa	Ineffective	Does not appear to be removed by HD. Apparent Vd equals or slightly exceeds plasma volume. Metabolic fate has not been determined although nonrenal mechanisms are predominant. <10% excreted renally as unchanged drug. Supplemental doses are not required after HD.[8,9]
Estramustine	Unknown	Effects of HD unknown. Water soluble. Vd is unknown. Primarily excreted in feces; cleaved to mustard and estrogen components.

DRUG	HEMODIALYSIS EFFECTIVENESS	SUMMARY OF DATA AVAILABLE
Etoposide	Ineffective [26,27,42]	Not removed by dialysis in vitro in case reports. [28] Minimally water soluble. Vd (steady state) averages 0.17 to 0.5 L/kg. Concentrates in kidneys, small intestine, and liver; poorly crossed the BBB. Over 90% protein bound in plasma. Metabolized in liver; excreted in urine (30% to 45%) and feces (2% to 16%). Supplemental doses are not required after HD.[2,8,9]
Exemestane	Ineffective	Practically insoluble. Distributes extensively into tissues. Binds to both albumin and α_1-acid glycoprotein; $\approx$ 90% bound in plasma. Extensively metabolized in liver, primarily by cytochrome P450 3A. Unchanged drug and metabolites excreted in the feces (42%) and urine (42%). Less than 1% of dose excreted in urine as unchanged drug. [43]
Fentanyl	Ineffective [44]	Sparingly water soluble. Vd (steady-state) averages 4 L/kg. Distributes rapidly into lungs and skeletal muscle; also stored in body fat. Highly protein bound (80% to 85%) in plasma, primarily to α_1-acid glycoprotein. Metabolized extensively by hepatic and intestinal CYP450 3A4 to inactive metabolites, which are excreted renally. Small amounts excreted unchanged in urine (< 10%) and feces (< 1%).
Filgrastim	Ineffective	Very water soluble. Vd (steady state) averages 0.15 L/kg. Concentrates in BM, adrenal glands, kidney, and liver; unknown if filgrastim crosses the BBB. Metabolic fate not fully determined. Supplemental doses not required after HD.[8,9]
Floxuridine	Minimally effective	Effectively removed by dialysis in vitro and some removal predicted in vivo based on PK properties. [28] Water soluble. Distribution characteristics of floxuridine unknown. Metabolized in liver to 5-fluorouracil (active). Volume of distribution (steady state) of 5-fluorouracil averages 0.25 to 0.5 L/kg with distribution to tumors, intestinal mucosa, bone marrow, and liver. 5-fluorouracil crosses BBB and is 10% bound to plasma proteins. 5-fluorouracil is converted to other active metabolites in tissues and metabolized in liver. Renal excretion of unchanged 5-fluorouracil is 7% to 20% within 6 hours.
Fludarabine	Ineffective	Slightly water soluble. Vd (steady state) averages 1.08 to 2.42 L/kg; drug concentrates in kidney, liver, and spleen. Metabolic rate is largely unknown, although 23% to 24% is excreted renally as unchanged drug.
Fluorouracil	Minimally effective	Effectively removed by dialysis in vitro and likely to be removed in vivo based on PK properties. [28] Minimally water soluble. Vd (steady state) averages 0.25 to 0.5 L/kg. Drug distributes to tumors, intestinal mucosa, bone marrow, and liver; crosses the BBB. Only 10% protein bound in plasma. Converted to active metabolite in tissues and metabolized in liver. Renal excretion of unchanged drug is 7% to 20% within 6 hours. After HD, some clinicians recommend supplementing with 50% of the original dose.[1,2,8,9]
Flutamide	Ineffective [45]	Plasma protein binding > 90% for both flutamide (94% to 96%) and active metabolite (92% to 94%). Extensively metabolized to active and inactive metabolites. Supplemental doses are not required after HD.[8,9]
Gemcitabine	Minimally effective	Water soluble. Vd (steady state) averages 8.62 L/kg. Plasma protein binding is negligible. Metabolized with 92% to 98% of dose excreted renally as drug or inactive metabolite; < 10% as unchanged drug.
Gemtuzumab ozogamicin	Ineffective	Because of the large size of the molecule (151,000 to 153,000 daltons), [46] it is highly improbable that the drug could pass through a HD membrane. Molecules > 500 daltons are considered impassable for conventional HD. Gemtuzumab ozogamicin binds to CD33 antigen on leukemic blasts and immature normal myelomonocytes. Antibody/antigen complex is internalized after binding, releasing calicheamicin. The exact metabolic pathways of calicheamicin and gemtuzumab ozogamicin are unknown, although hepatic metabolism may occur.

DRUG	HEMODIALYSIS EFFECTIVENESS	SUMMARY OF DATA AVAILABLE
Goserelin	Moderately effective	Water soluble. Vd (steady state) averages 0.63 L/kg in men and 0.29 L/kg in women; < 30% bound to plasma proteins. Metabolized by hydrolysis of C-terminal amino acids with ≈ 20% excreted unchanged in urine.
Granisetron	Minimally effective	Water soluble. Vd (steady state) ranges from 3 to 4 L/kg in adults. 65% bound to plasma proteins. Undergoes hepatic metabolism, including N-demethylation, aromatic ring oxidation, and conjugation; may have active metabolites. Approximately 11% - 12% of dose excreted unchanged in urine.
Hydroxyurea	Moderately effective	Water soluble. Vd (steady state) averages 0.5 L/kg in adults. Crosses BBB. Liver metabolism and renal excretion of unchanged drug each account for ≈ 50% of dose. Metabolites excreted in urine and as respiratory carbon dioxide. Supplemental doses are not required after HD.[8,9]
Idarubicin	Ineffective	Water soluble. Widely distributed throughout body; Vd (steady state) ranges from 11.6 to 45.4 L/kg. Both drug and active metabolite cross BBB. > 90% bound to proteins in plasma and tissue. Extrahepatic metabolism with ≥ 1 active metabolite. Most of dose eliminated by biliary excretion with minimal renal excretion.[47]
Ifosfamide	Moderately effective	Removed by dialysis in vitro and likely to be removed in vivo based on PK properties. [28] Water soluble. Vd (steady state) averages 0.71 L/kg in adults. No information on protein binding. Metabolized in liver to active moiety via saturable pathways; active agent further metabolized in liver. Urinary excretion of unchanged drug varies with dose; following doses of 1.6 to 2.4 g/m ^{2} and 5 g/m ^{2} , 12% to 18% and 61% excreted renally, respectively. Some clinicians recommend a supplemental dose after HD, although specific recommendations are not available.[8,9]
Imatinib	Ineffective	Because of the large size of the molecule (590 daltons), [48] it is highly improbable that the drug could pass through a HD membrane. Molecules > 500 daltons are considered impassable for conventional HD. Very water soluble. Highly bound (95%) to plasma protein. Metabolized by CYP450 3A4 to active and inactive metabolites. Some elimination of unchanged drug in urine (5%) and feces (20%), but primarily excreted in feces as metabolites.
Interferon Alfa-2a, Alfa-2b, Alfa-n3	Ineffective	Continuous ambulatory peritoneal dialysis also ineffective in case report.[49] Water soluble. Vd (steady state) averages 0.4 L/kg in adults. IFN's concentrate in spleen, kidney, and liver. Filtered through glomeruli and eliminated by proteolytic degradation in renal tubule. Supplemental doses are not required after HD.[8,9]
Irinotecan	Ineffective	Slightly water soluble. Vd (steady state) averages 2.56 L/kg. Active metabolite highly protein bound (95%) although drug itself is moderately protein bound (30% to 68%). Metabolized to active lipophilic moiety. Urinary excretion of irinotecan ranges from 11% to 20%; < 1% of active metabolite excreted renally.
Isotretinoin	Ineffective[50]	In a single case report, isotretinoin was effective at usual doses in a HD patient. Drug unlikely to be removed based on PK properties. Not water soluble. Extensive distribution to liver, ureters, adrenal glands, ovaries, lacrimal glands, and other tissues. Highly bound (> 99%) to plasma protein. Metabolized in liver to 4-oxo-derivative, which may be active. Excreted in urine (32% to 42%) and feces (32% to 42%) as metabolites and unchanged drug. May undergo enterohepatic circulation.
Letrozole	Ineffective	Practically insoluble. Vd averages 1.9 L/kg. Weakly protein bound. Primarily metabolized to inactive carbinol metabolite. Urinary excretion accounts for 75% of the inactive metabolite and 6% of active drug.[51]
Leucovorin	Ineffective	Slightly water soluble. Distributes to all body tissues as THF derivatives (exact volume of distribution unknown). Half of body folate stores deposited in the liver. Rapidly and extensively converted to THF derivatives for transport and storage. Excreted in urine as THF derivatives.

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Leuprolide	Minimally effective	Slightly water soluble. Vd (steady state) averages 0.38 L/kg in men; may concentrate in kidney, liver, pineal, and pituitary tissue. Approximately 43% to 49% bound to plasma proteins, mainly albumin. Metabolic fate largely unknown, although it may undergo some enzymatic degradation in the hypothalamus and anterior pituitary to inactive peptides. Less than 5% excreted unchanged in urine.
Levamisole	Unknown	Effects of HD unknown. Water soluble. Vd is unknown. Primarily metabolized in liver. < 5% excreted unchanged in urine and < 0.2% in bile.
Lomustine	Unknown	Effects of HD unknown. Not water soluble. Widely distributed throughout body. Crosses BBB and is taken up by cells. Metabolized in liver with some active metabolites; unknown quantity excreted in urine. Supplemental doses are not required after HD.[8,9]
Mechloreth-amine	Ineffective	Water soluble. Vd is unknown. Reacts extensively with water and cellular compounds, undergoing rapid chemical transformation. <0.01% excreted unchanged in urine. Supplemental doses are not required after HD.[8,9]
Medroxy-progesterone	Ineffective	Not water soluble. Approximately 90% bound to plasma proteins. Extensively metabolized in liver and excreted in urine, primarily as metabolites.[52,53]
Megestrol	Unknown	Effects of HD unknown. Not water soluble. Extensively metabolized in the liver. 50-70% excreted unchanged in urine; 5% - 8% of dose eliminated in the urine as metabolites.[54,55]
Melphalan	Minimally effective	Removed by dialysis in vitro and likely to be removed in vivo based on PK properties. [28] Not water soluble. Vd (steady state) averages 0.5 to 0.75 L/kg in adults and drug is 60% - 90% protein bound; 30% is irreversibly bound. Undergoes spontaneous hydrolysis. Unchanged drug excreted in feces and in urine (10%). Supplemental doses not required after HD.[8,9]
Mercapto-purine	Minimally effective	Not water soluble. Distributes throughout total body water and crosses BBB. 19% protein bound in plasma. Metabolized by xanthine oxidase in liver and 11% excreted unchanged in urine. Some clinicians recommend a supplemental dose after HD, although specific recommendations are not available.[8,9]
Mesna	Moderately effective	Water soluble. Remains in intravascular compartment (volume of distribution is 0.652 L/kg in adults). Oxidized to dimesna in systemic circulation. Does not undergo hepatic metabolism. Excreted unchanged in urine within 24 hours: 32% as mesna, 33% as dimesna.
Methotrexate	Moderately effective[56]	In case report, effectively removed by dialysis in vitro and likely to be removed in vivo based on PK properties. [28] Water soluble. Vd (steady state) averages 0.4 to 0.8 L/kg. Concentrates in kidneys, gallbladder, spleen, liver, and skin; does not cross the BBB. Fifty percent protein bound in plasma. Metabolized hepatically and intracellularly to active metabolites, which are converted back to parent drug by hydrolase enzymes. Eighty percent to 90% excreted renally as unchanged drug by filtration and active transport. Less than 10% removed by biliary excretion. After HD, some clinicians recommend supplementing with 50% of the original dose.[2,8,9]
Mitomycin	Minimally effective	Removed by dialysis in vitro and likely to be removed in vivo based on PK properties. [29] Water soluble. Vd (steady state) averages 0.5 L/kg; concentrates in kidneys, muscles, eyes, lungs, intestines, and stomach. Inactivated by saturable enzymes in liver, kidneys, spleen, brain, and heart. Some excreted in urine (< 10%) and bile.
Mitotane	Ineffective	Not water soluble. Distributed to all tissues and stored in body fat. May cross BBB. Metabolized in liver then metabolite eliminated in bile (< 17%) and urine (≈ 10%). No unchanged drug found in urine or feces.
Mitoxantrone	Ineffective [57]	In a case report, not removed by dialysis in vitro and unlikely to be removed in vivo. [28] Minimally water soluble. Vd (steady state) is > 24.3 L/kg; 80% to 90% protein bound in plasma. Metabolized in liver; also eliminated by renal excretion (≈ 7%) and biliary excretion (18%). Supplemental doses are not required after HD.[8,9]

DRUG	HEMODIALYSIS EFFECTIVENESS	SUMMARY OF DATA AVAILABLE
Muromonab-CD3	Ineffective	Due to the large size of the molecule (75,000 daltons) it is highly improbable the drug could pass through a HD membrane. Molecules > 500 daltons are considered impassable for conventional HD.
Nilutamide	Ineffective	Slightly water soluble. Moderately bound to plasma proteins with minimal binding to erythrocytes. Distribution kinetics not fully characterized. Extensively metabolized with ≥ 1 active metabolite. Less than 2% excreted unchanged in urine; fecal elimination negligible.
Octreotide	Minimally effective	Water soluble. Vd (steady state) averages 0.19 L/kg. 65% bound to lipoprotein and albumin. Excreted unchanged in urine (32%). Some recommend a supplemental dose after HD, although specific recommendations are not available.[8,9]
Ondansetron	Minimally effective	Water soluble. Distributes into erythrocytes. Protein binding 70% to 76% in plasma. Metabolized in liver; only 5% eliminated renally.
Oprelvekin	Unknown	Effects of HD unknown. Rapidly distributes to highly perfused organs (i.e., kidney, heart, brain). Distribution kinetics not fully characterized. Protein binding has not been determined. Metabolic fate not determined although nonrenal mechanisms are predominant; minimal urinary excretion of unchanged drug.[58]
Paclitaxel	Ineffective	No decrease in effect in case report. [59] Drug unlikely to be removed based on PK properties. Not water soluble. Vd (steady state) averages 0.35 to 1.34 L/kg in adults; 89% to 98% protein bound in plasma. Distributes into biliary tract. Primarily metabolized in liver. Some (1.3% to 12.6%) excreted unchanged in urine. May be eliminated by biliary excretion also. Supplemental doses are not required after HD.[9]
Pamidronate	Ineffective	Water soluble. Concentrates in bone, liver, spleen, teeth, and tracheal cartilage. Adsorbs to hydroxyapatite crystals in bone (54% of dose within 120 hours). Not metabolized; 46% eliminated unchanged in urine.
Pegaspargase	Unknown	Effects of HD unknown. Vd (steady state) equivalent to plasma volume. No unchanged drug detected in urine. [60] Pattern of elimination unknown.
Pentostatin	Moderately effective	Water soluble. Vd ranges from 0.51 to 0.6 L/kg; 4% protein bound in plasma. Poorly crosses BBB. Excreted renally as unchanged drug (30% to 90%).
Plicamycin	Ineffective	Slightly water soluble. Distributes to liver, kidneys, and bone surfaces. Crosses BBB. Protein binding minimal. Pattern of elimination is unknown. Drug is rapidly cleared from plasma but may persist in areas of bone resorption.
Procarbazine	Minimally effective	Water soluble. Concentrates in liver, kidneys, intestinal wall, and skin. Crosses BBB. Metabolized in liver with some active metabolites. 5 - 20% of dose is excreted unchanged in urine.
Rituximab	Ineffective	Due to the large size of the molecule (145,000 daltons) it is highly improbable the drug could pass through a HD membrane. Molecules > 500 daltons are considered impassable for conventional HD. Rituximab binds to CD20 antigen on B-cell non-Hodgkin's lymphomas, pre-B lymphocytes, and mature B lymphocytes. Antibody/antigen complex concentrates in the thymus, spleen, peripheral blood, and lymph nodes.[61]
Sargramostim	Ineffective	Very water soluble. Concentrates in liver, spleen, and kidney; unknown if sargramostim crosses the BBB. Metabolic fate not fully determined.
Scopolamine	Unknown	Effects of HD unknown. Freely soluble in water. Vd is not known. Primarily excreted unchanged in urine.
Streptozocin	Minimally effective	Water soluble. Vd (steady state) averages 0.63 L/kg in adults. Distributes into liver, kidneys, intestine, and pancreas but does not cross BBB. Metabolized in liver and kidneys. 10-20% excreted unchanged in urine; < 1% excreted in feces.
Tacrolimus	Ineffective	Practically insoluble in water. Vd (steady state) averages 0.85 L/kg. Protein binding ranges from 75% to 99%. Highly bound to albumin, α_1-acid glycoproteins and erythrocytes. Extensively metabolized primarily by cytochrome P450 3A, with ≈ 1% of drug excreted in urine. Supplemental doses are not required after HD.[8,9]

DRUG	HEMODIALYSIS EFFECTIVENESS	SUMMARY OF DATA AVAILABLE
Tamoxifen	Ineffective	Freely soluble in water. Distributes into uterine tissue; volume of distribution (steady state) averages 20 L/kg. Protein binding > 90% in plasma. Rapidly and extensively metabolized. Less than 30% excreted in feces as unchanged drug and unconjugated metabolites. Small amounts excreted unchanged in urine.
Temozolo-mide	Ineffective	Vd (steady state) averages 0.4 L/kg. Plasma protein binding is ≈ 15%. Undergoes pH-dependent nonenzymatic hydrolysis to active moiety. Hepatic oxidative metabolism is a minor route of elimination. Approximately 38% of dose excreted in urine as unchanged drug (< 6%) and inactive metabolites (≈ 31%).[62]
Teniposide	Ineffective	Not removed by dialysis in vitro and unlikely to be removed in vivo based on PK properties. [28] Minimally water soluble. Vd (steady state) averages 0.2 to 0.7 L/kg in adults. Does not cross BBB. Over 90% protein bound in plasma. Metabolized in liver. Some eliminated by renal excretion (4% to 12%) and by biliary excretion (< 10%). Supplemental doses are not required after HD.[2]
Thalidomide	Ineffective	Not water soluble. [63] Little information about Vd or plasma protein binding. Undergoes nonenzymatic hydrolysis in plasma; no significant hepatic metabolism. Minimally excreted in urine unchanged (< 0.7%) or as metabolites (< 0.02%).
Thioguanine	Ineffective	Not water soluble. Rapidly incorporated into and stored in bone marrow. Metabolized in liver with trace amounts excreted renally.
Thiotepa	Ineffective	Water soluble. Vd is unknown; < 10% protein bound in plasma. Metabolized in liver with trace amounts excreted unchanged in urine.
Topotecan	Moderately effective	Water soluble. Vd (steady state) ranges from 0.5 to 4.6 L/kg. [64] Thirty-five percent bound to plasma proteins. Undergoes reversible pH-dependent hydrolysis to active moiety. Thirty percent of dose excreted in urine.
Toremifene	Ineffective	Vd (steady state) averages 8.3 L/kg in adults. Almost completely protein bound in plasma (> 99.5%), primarily to albumin. Extensively metabolized in liver with 1 active metabolite. Undergoes enterohepatic circulation. Eliminated in urine (10%) and in feces as metabolites.
Trastuzumab	Ineffective	Because of the large size of the molecule (≈ 148,000 daltons) it is highly improbable the drug could pass through a HD membrane. Molecules > 500 daltons are considered impassable for conventional HD. Trastuzumab binds to the extracellular domain of the human epidermal growth factor receptor 2 protein (HER2), which is present in the tumor and in the circulation as shed antigen. Antibody/antigen complexes are thought to be removed by phagocytosis.[65,66]
Tretinoin	Unknown	Effects of HD unknown. Volume of distribution is unknown. Approximately 63% of active drug is recovered unchanged in urine.[67]
Trimetrexate	Ineffective	Water soluble as glucuronate salt; not water soluble as base. Volume of distribution is 0.62 L/kg at steady state. Plasma protein binding ≈ 95%. Metabolized by hepatic cytochrome P450. Excreted in the urine as unchanged drug (5% to 33%) and metabolites. Minimal amounts excreted in the feces (< 10%).
Uracil mustard	Unknown	Effects of HD unknown. Very slightly water soluble. Vd is unknown. Less than 1% excreted unchanged in the urine.
Valrubicin	Ineffective	NOTE: Product for intravesical use only. Not water soluble. Vd is unknown. Minimal systemic exposure with intravesical use. If bladder wall is perforated, systemic exposure may approximate that seen with IV administration. [68] Supplemental doses are not required after HD.[8]
Vinblastine	Ineffective	Not removed by dialysis in vitro and unlikely to be removed in vivo. [28] Water soluble. Vd (steady state) ranges from 13 to 40 L/kg in adults. Concentrates in liver, lung, spleen, and kidney. Poorly crosses BBB; 75% protein bound in plasma. Metabolized in liver to active metabolite. Breakdown products and drug excreted in urine and feces.

DRUG	HEMODIALYSIS EFFECTIVENESS	SUMMARY OF DATA AVAILABLE
Vincristine	Ineffective	Not removed by dialysis in vitro and unlikely to be removed in vivo. [28] Water soluble. Vd (steady state) ranges from 5 to 11 L/kg. Rapidly distributed into bile. Protein bound in plasma (75%) and in tissues. Poorly crosses BBB. Extensively metabolized in liver with some drug being spontaneously decomposed. Breakdown products and drug excreted in urine (10% to 15% as unchanged drug) and feces.
Vinorelbine	Ineffective	No decrease in efficacy in case report when given concurrently with HD. [69] Unlikely to be removed by HD based on PK properties. Water soluble. Vd (steady state) ranges from 25.1 to 40.1 L/kg. Highly bound (79.6% to 91.2%) to plasma constituents, including platelets and lymphocytes. Extensively metabolized in liver with ≥ 1 active metabolite. Large amounts of drug and metabolites excreted in the feces with ≈ 10.9% excreted unchanged in urine.

Vd = Volume of distribution; BBB = blood brain barrier; PK = pharmacokinetic; GF = glomerular filtration.

1. Bennett WM. Guide to drug dosage in renal failure. In: Holford N, ed. *Clinical pharmacokinetics. Drug Data Handbook* . 3rd ed. USA: ADIS Press, 1998:49-112.
2. Aronoff GR, Berns JS, Brier ME, et al. Drug prescribing in renal failure. *Dosing Guidelines for Adults.* 4th ed. Philadelphia, PA: American College of Physicians, 1999.
3. McEvoy GK, Litvak K, Welsh OH, Miller JL, Snow EK. *AHFS 2001 Drug Information.* Bethesda, MD: American Society of Health-System Pharmacists, 2001.
4. Burnham TH, Short RM, eds. *Drug Facts and Comparisons.* St. Louis, MO: Facts and Comparisons, 2001.
5. Schrier RW, Gambertoglio JG. *Handbook of Drug Therapy in Liver and Kidney Disease.* Boston, MA: Little, Brown and Company, 1991.
6. *Mosby's GenRx. The Complete Reference for Generic and Brand Drugs.* St. Louis, MO: Mosby-Year Book Inc., 1999.
7. Evans WE, Schentag JJ, Jusko WJ. *Applied Pharmacokinetics. Principles of Therapeutic Drug Monitoring.* 3rd ed. Vancouver, WA: Applied Therapeutics, Inc., 1992.
8. Subach RA. 2001 Clinical considerations in drug dialysis. *Pharmacy Practice News* December 2000.
9. Johnson CA, Simmons WD. 2000 Dialysis of Drugs . Thousand Oaks, CA: Amgen / Nephrology Pharmacy Associates; 2000.
10. Millennium and ILEX Partners. Campath (Alemtuzumab) package insert. Cambridge, MA: Millennium and ILEX Partners, LP, 2001.
11. Williams E. Personal communication. Richmond, CA: Berlex Laboratories. May 2001.
12. U.S. Bioscience Inc. Ethyol (amifostine) for injection package insert. Pennsylvania, PA: U.S. Bioscience, Inc., 1997
13. Roberts Laboratories, Inc. Agrylin (anagrelide hydrochloride) capsules package insert. Eatontown, NJ: Roberts Pharmaceutical Group, 1998.
14. Lymphocyte immune globulin, anti-thymocyte globulin (equine). In: Grabenstein JD. ImmunoFacts: Vaccines & Immunologic Drugs. St. Louis, MO: Facts and Comparisons, Inc;1998:291-295.
15. Vaziri ND, Upham T, Barton CH. Hemodialysis clearance of arsenic. *Clin Toxicol* . 1980;17:451-456.
16. Mathieu D, Mathieu-Nolf M, Germain-Alonso M, et al. Massive arsenic poisoning - effect of hemodialysis and dimercaprol on arsenic kinetics. *Intensive Care Med* . 1992;18:47-50.
17. Smith SB, Wombolt DG. Results of hemodialysis and hemoperfusion in the treatment of acute arsenic ingestion. *Clin Exp Dial Apheresis* . 1981;5:399-404.
18. Cell Therapeutics Inc. Trisenox (arsenic trioxide) injection package insert. Seattle, WA: Cell Therapeutics, Inc., 2000.
19. Ligand Pharmaceuticals Inc. Targretin (bexarotene) capsules, 75 mg package insert. San Diego, CA: Ligand Pharmaceuticals Inc., 2001.
20. Zeneca Pharmaceuticals. Casodex (bicalutamide) tablets package insert. Wilmington, DE: Zeneca Inc., 1997.
21. Roche Pharmaceuticals. Xeloda (capecitabine) tablets package insert. Nutley, NJ: Roche Laboratories Inc., 1998.
22. Chatelut E, Rostaing L, Gualano V, et al. Pharmacokinetics of carboplatin in a patient suffering from advanced ovarian carcinoma with hemodialysis-dependent renal insufficiency. *Nephron*. 1994;66:157-161.
23. El-Yazigi A, Alfurayh O, Amer M. Pharmacokinetics of carboplatin in a patient with cervical cancer with ureteric obstruction before, during, and after hemodialysis. *J Clin Pharmacol*. 1995;35:1003-1007.
24. Yanagawa H, Takishita Y, Bando H, Sumitani H, Okada S. Carboplatin-based chemotherapy in patients undergoing hemodialysis. *Anticancer Res*. 1996;16:533-536.
25. Motzer RJ, Niedzwiecki D, Isaacs M, et al. Carboplatin-based chemotherapy with pharmacokinetic analysis for patients with hemodialysis-dependent renal insufficiency. *Cancer Chemother Pharmacol*. 1990;27:234-238.
26. English M, Lowis S, Peng B, et al. Pharmacokinetically guided dosing of carboplatin and etoposide during peritoneal dialysis and hemodialysis. *Br J Cancer*. 1996;73:776-780.
27. Suzuki S, Koide M, Sakamoto S, Matsuo T. Pharmacokinetics of carboplatin and etoposide in a hemodialysis patient with Merkel-cell carcinoma. *Nephrol Dial Transplant*. 1997;12:137-140.
28. Sauer H, Fuger K, Blumenstein M. Modulation of cytotoxicity of cytostatic drugs by hemodialysis *in vitro* and *in vivo*.

Cancer Treat Rev. 1990;17:293-300.
29. Tanabe N, Goto M, Morita H, et al. Pharmacokinetics of cis-diammine-dichlor-platin in a hemodialysis patient. *Cancer Investigation* 1991;9:629-635
30. Gorodetsky R, Vexler A, Bar-Khaim Y, Biran H. Plasma platinum elimination in a hemodialysis patient treated with cisplatin. *Ther Drug Monit* 1995; 17:203-206.
31. Rebibou J, Chauffert B, Dumas M, et al. Combined chemotherapy and radiotherapy for esophageal carcinoma in a hemodialyzed patient. Long-term survival. *Nephron* 1996; 74:611-612.
32. Yura T, Badr K, Yuasa S, et al. Alleviation of cisplatin nephrotoxicity: efficacy of local intra-arterial injection concomitant with hemodialysis. *Blood Purif* 1996; 14:146-156.
33. Poschl J, Klaus G, Querfeld R, Ludwig R, Mehls O. Chemotherapy with cytosine arabinoside in a child with Burkitt's lymphoma on maintenance hemodialysis and hemofiltration. *Ann Hematol* 1993;67:37-39.
34. DepoTech Inc./Chiron Corporation. DepoCyt (cytarabine liposome injection) package insert. San Diego, CA/Emeryville, CA: DepoTech Inc./Chiron Corporation, 1999.
35. NeXstar Pharmaceuticals Inc. DaunoXome (daunorubicin citrate liposome injection) package insert. San Dimas, CA: NeXstar Pharmaceuticals Inc., 1996.
36. Seragen, Incorporated/Ligand Pharmaceuticals Incorporated. Ontak (denileukin diftitox) package insert. Hopkinton, MA/San Diego, CA: Seragen, Inc./Ligand Pharmaceuticals, February 1999.
37. The Pharmaceutical Company of Hoechst. Anzemet Injection (dolasetron mesylate injection) prescribing information. Kansas City, MO: Hoechst Marion Roussel, 1997.
38. Yoshida H, Goto M, Honda A, et al. Pharmacokinetics of doxorubicin and its active metabolite in patients with normal renal function and in patients on hemodialysis. *Cancer Chemother Pharmacol* 1994; 35:450-454.
39. Sequus Pharmaceuticals Inc. Doxil (doxorubicin HCl liposome injection) for intravenous infusion only package insert. Menlo Park, CA: Sequus Pharmaceuticals Inc, 1997.
40. Pharmacia & Upjohn. Ellence (epirubicin hydrochloride injection) package insert. Kalamazoo, MI: Pharmacia & Upjohn Company, September 1999.
41. Epirubicin. In: Dorr RT, von Hoff DD. *Cancer Chemotherapy Handbook*, 2nd edition. Norwalk, CT: Appleton & Lange, 1994:434-439.
42. Stewart C. Use of etoposide in patients with organ dysfunction: pharmacokinetic and pharmacodynamic considerations. *Cancer Chemother Pharmacol* . 1994;34(Suppl):S76-S83.
43. Pharmacia & Upjohn. Aromasin (exemestane) tablets package insert. Kalamazoo, MI: Pharmacia & Upjohn Company, October 1999.
44. Bastani B, Jamal JA. Removal of morphine but not fentanyl during hemodialysis. *Nephrol Dial Transplant* 1997;12: 2802-2804.
45. Schering Corporation. Eulexin (brand of flutamide) capsules package insert. Kenilworth, NJ: Schering Corporation, 1999.
46. Wyeth Laboratories. Mylotarg (gemtuzumab ozogamicin for injection) package insert. Philadelphia, PA: Wyeth-Ayerst Pharmaceuticals, 2000.
47. Adria Laboratories. Idamycin (Idarubicin HCl) for injection Product Monograph. Columbus, OH: Adria Laboratories Division of Erbamont Inc., 1991.
48. Novartis. Gleevec (imatinib mesylate) capsules package insert. East Hanover, NJ: Novartis Pharmaceuticals Corporation, 2001.
49. Grimbert P, Deray G, Lebon P, et al. Pharmacokinetics of recombinant leukocyte interferon in a patient on continuous ambulatory peritoneal dialysis. *Am J Nephrol* 1995;15:175.
50. Beightler EL, Tyring SK. The use of isotretinoin in a patient undergoing kidney hemodialysis. *J Am Acad Dermatol*. 1990;23(4 Pt 1):758.
51. Novartis. Femara (letrozole tablets) 2.5 mg tablets package insert. East Hanover, NJ: Novartis Pharmaceuticals Corporation, 1997
52. Ayerst Laboratories Inc. Premphase (conjugated estrogens/medroxyprogesterone acetate tablets) package insert. Philadelphia, PA: Wyeth-Ayerst Laboratories, 1997.
53. Ayerst Laboratories Inc. Prempro (conjugated estrogens/medroxyprogesterone acetate tablets) package insert. Philadelphia, PA: Wyeth-Ayerst Laboratories, 1997.
54. MeadJohnson Oncology Products. Megace Oral Suspension (megestrol acetate) package insert. Princeton, NJ: MeadJohnson Oncology Products, 1996.
55. MeadJohnson Oncology Products. Megace (megestrol acetate tablets) package insert. Princeton, NJ: MeadJohnson Oncology Products, 1996.
56. Thomson A, Daly M, Knepil J, Harden P, Symonds P. Methotrexate removal during haemodialysis in a patient with advanced laryngeal carcinoma. *Cancer Chemother Pharmacol.* 1996; 38:566-570.
57. Boros L, Cacek T, Pine R, Battaglia A. Distribution characteristics of mitoxantrone in a patient undergoing hemodialysis. *Cancer Chemother Pharmacol* 1992; 31:57-60.
58. Genetics Institute Inc. Neumega (oprelvekin) package insert. Cambridge, MA: Genetics Institute Inc., 1997.
59. Balat O, Kudelka A, Edwards C et al. A case report of paclitaxel administered to a patient with platinum-refractory ovarian cancer on long-term hemodialysis. *Eur J Gynaec Oncol* 1996; 17:232-233.
60. Rhone-Poulenc Rorer Pharmaceuticals Inc. Oncospar (pegaspargase) package insert. Collegeville, PA: Rhone-Poulenc Rorer Pharmaceuticals Inc., 1994.
61. IDEC Pharmaceuticals Corporation and Genentech Inc. Rituxan (rituximab) package insert. South San Francisco, CA: Genentech Inc., 1997.

62. Schering Corporation. Temodar (temozolomide) capsules package insert. Kenilworth, NJ: Schering Corporation, 1999.
63. Celgene Corporation. Thalomid capsules (thalidomide) package insert. Warren, NJ: Celgene Corporation, 1998.
64. Creemers G, Lund B, Verweij J. Topoisomerase I inhibitors: topotecan and irinotecan. *Cancer Treat Rev.* 1994; 20:73-96.
65. Genentech, Inc. Herceptin (trastuzumab) anti-HER2 monoclonal antibody package insert. South San Francisco, CA: Genentech, Inc., 1998.
66. Fung S. Personal communication. South San Francisco, CA: Genentech, Inc. April 1999.
67. Roche Laboratories. Vesanoid (tretinoin) capsules package insert. Nutley, NJ: Hoffmann-LaRoche Inc., 1995.
68. Anthra Pharmaceuticals, Inc./Medeva Pharmaceuticals, Inc. Valstar (valrubicin) sterile solution for intravesical instillation package insert. Princeton, NJ/Rochester, NY: Anthra Pharmaceuticals, Inc./Medeva Pharmaceuticals, Inc., June 1998.
69. Rollino C, Milongo R, Schaerer R, Cordonnier D. Vinorelbine therapy in a hemodialyzed patient. *Nephron* 1992; 61:232-233.

Reference: Facts and Comparisons eFacts 2005.