Dosage Adjustment in Renal Impairment

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Introduction

Careful dosage adjustment may reduce the risk of drug toxicity in patients with impaired renal function. The following is an approach to empiric dosage adjustments (dose and/or interval) in adult patients based on an estimate of renal function (see Figure 1, Table 1). This approach does not apply to patients on dialysis (consult specialized references).

Patient/Drug Considerations

The following questions should be answered prior to making empiric dosage adjustments. Table 2 provides drug-specific information.

Is the patient's renal function impaired?

Use the following formula[1] to estimate the *weight-corrected creatinine clearance* (ClCr) and to guide empiric dosage adjustments:

$$\text{Males: ClCr (mL/min/70 kg)} = \frac{(140 - \text{age}) \times 90}{\text{serum creatinine (μmol/L)}}$$

Females: ClCr (mL/min/70 kg) = 0.85 × above equation

Many clinicians may be more familiar with a ClCr formula that includes weight. When using formulas to estimate ClCr, first identify the reason for the ClCr determination. If an estimate of the patient's true ClCr (in mL/minute) is needed, then use a ClCr formula that includes weight. However, if the estimate of the degree of renal impairment is to guide dosage adjustments, use a weight-corrected estimate of ClCr rather than the patient's actual ClCr. This weight-corrected estimate is then compared to a "normal" ClCr for a 70 kg male (108–120 mL/min) to approximate the degree of renal dysfunction. Charts that suggest empiric dosage adjustments are usually based on the assumption that the baseline or normal ClCr is 108–120 mL/min. In addition, a weight-corrected ClCr is easier to calculate.

Elderly (>65 years) or malnourished patients may have relatively low muscle mass and therefore produce less creatinine. If the actual serum creatinine for such patients is used, the formula can often overestimate renal function. A general rule in such patients is not to use a serum creatinine <100 μmol/L in the above formula.

Other equations, such as the Modification of Diet in Renal Disease (MDRD) equation, can be used to estimate the glomerular filtration rate (GFR). The MDRD is recommended for staging chronic kidney disease because it has improved predictive performance over the Cockcroft-Gault equation in estimating the GFR. Some clinicians also use the MDRD to estimate the GFR in order to adjust medication doses in patients with renal impairment. However, in adjusting drug doses in patients with renal impairment, the improved accuracy of the MDRD equation to predict the GFR will not, in most cases, result in measurably improved outcomes such as enhanced medication safety or efficacy. This is because most recommendations for drug dosing in patients with renal impairment are not based on specific pharmacokinetic or pharmacodynamic outcome data. Instead, the dosage recommendations are based on somewhat broad and arbitrary GFR cut-off points. Given this, both the Cockcroft-Gault and MDRD equations provide sufficiently accurate estimates of renal function for use in drug dosage adjustment. Clinicians should likely choose the equation that is easiest to use or the one with which they are most familiar. Most importantly, clinicians need to determine rational starting doses using not only these equations, but also by basing their decision on the urgency of the need for a response to drug therapy. All these issues make the current debate about which formula to use to estimate renal

function somewhat irrelevant. However, regardless of the method used, there is a critical next step: *titrate the dose whenever possible, and determine the correct dose by monitoring a patient's response to the dose chosen*.

In general, if ClCr estimates are ≥60 mL/min/70 kg, empiric dosage adjustments are not required because reductions in ClCr to ≥60 mL/min/70 kg are associated with relatively small changes in the half-life of a drug or its active metabolite. However, as ClCr falls below 60 mL/min/70 kg, empiric dosage adjustments should be based on the following questions.

Is the drug effective/safe in patients with renal impairment?

Some drugs are ineffective or potentially toxic in patients with clinically important renal dysfunction (ClCr <30 mL/min/70 kg) and should be avoided (see Table 2, Comments column).

Is the drug nephrotoxic?

A number of drugs have the potential to worsen renal function and an alternative non-nephrotoxic agent should be used if possible (see Table 2, Comments column).

Is an immediate clinical effect required?

When failure to elicit an immediate response (e.g., life-threatening conditions or severe pain) poses a clinically important risk of mortality or morbidity, drug dosing should be aimed at obtaining a therapeutic response within minutes or hours irrespective of renal function. In an attempt to achieve a rapid response, usual initial doses should be used, followed by empiric dosage adjustments once the patient has responded.

If an immediate effect is not required, can the dose be titrated?

Many conditions do not require an immediate or maximal effect, and dose titration can often be used to determine the lowest effective dose. To identify the correct dose for any patient, but particularly in patients with renal impairment, start with a low dose (e.g., one-quarter or one-half of the typically recommended dose) and titrate up to a clinical effect.

Is the drug >50% renally eliminated or does it have active or toxic metabolites?

Drugs that are primarily eliminated by the kidney (>50%) require empiric dosage adjustments based on an estimate of renal function (see Table 2). In addition, some drugs are metabolized to active or toxic metabolites that may be excreted by the kidney and may need dosage adjustments. Some drugs should be avoided in patients with compromised renal function if toxic metabolites can accumulate, e.g., meperidine.

Approach to Empiric Dosage Adjustments

When dose titration is not possible or desired, base empiric dosage adjustments on estimates of renal function.

Interval versus Dose Adjustment

For drugs given intermittently, the dose or the dosing interval can be adjusted based on the desired goal. Often a combination of extending the interval and reducing the dose is effective and convenient. If the aim is to achieve steady-state maximum/peak and minimum/trough concentrations (e.g., aminoglycosides) similar to those seen in patients with normal renal function, extend the interval between doses. If a relatively constant steady-state concentration is desired (e.g., antihypertensives), reduce the dose.

Drugs Eliminated ≥75% by the Kidney

Table 1 provides guidelines for the dosage of these drugs (see Table 2) based on the usual dosing interval. For frequently administered drugs (e.g., Q4H–Q12H), extending the interval may decrease the cost of administration or improve adherence.

Drugs Eliminated 50 to <75% by the Kidney

These drugs have a clinically important proportion of nonrenal clearance; therefore, empiric dosage adjustments are generally not required until renal function estimates are <45 mL/min/70 kg (see Table 1, Table 2).

Drugs Eliminated <50% by the Kidney

For drugs eliminated <50% by the kidney (see Table 2), empiric dosage adjustments are generally not required, assuming the drug has no active or toxic metabolites. However, these drugs may require dosage adjustment in patients with clinically important liver dysfunction.

Drugs with Active or Toxic Metabolites

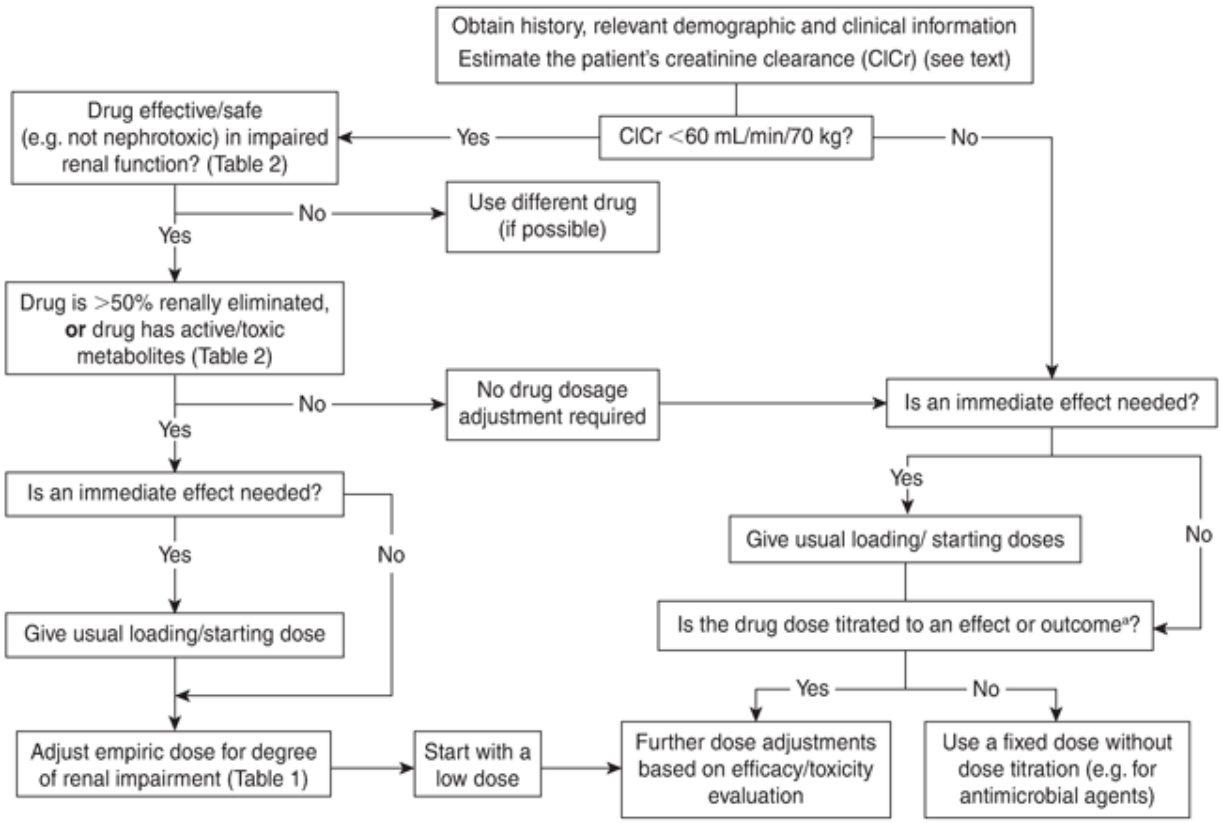
Empiric dosage adjustments for drugs with active or toxic metabolites that are dependent on renal elimination should be made as though the drug were 75–100% renally eliminated (see Table 2, Comments column).

Further Dosage Adjustments Based on Clinical Response

All of the above recommendations are for empiric dosage adjustments, and further dosage changes must always be made based on a patient-specific assessment of efficacy and toxicity. Serum drug concentration monitoring may guide dosage adjustments for certain drugs (see Table 2, Comments column).

Algorithms

Figure 1: Empiric Dosage Adjustment Based on Renal Function (Adults)



[a] For example, antihypertensives, antihyperglycemics, antidepressants.

Abbreviations: ClCr = creatinine clearance

Dosage Adjustment Tables

Table 1: Suggested Empiric Dosage Adjustments in Adults for Drugs Primarily Renally Eliminated[a]

How to Use Table 1:

1. Estimate renal function (weight-corrected ClCr), *e.g., a patient with an estimated ClCr of 25 mL/min/70 kg is receiving IV ampicillin.*
2. Determine percentage of renal elimination of drug (Table 2), *e.g., ampicillin is 75–100% renally eliminated, according to Table 2.*
3. Determine normal dosing interval, *e.g., usual dosing interval for ampicillin is Q6H.*
4. Using above information, determine empiric dosage adjustment, *e.g., the patient's ClCr is between 15 and 30 mL/min/70 kg. Therefore, the empiric dosing adjustment is to administer the ampicillin Q12H.*

			Normal Dosing Interval				
% Renal Elimination of Drug:	**75–100%**	**50–74%**	**Q4H**	**Q6H**	**Q8H**	**Q12H**	**Q24H**
	>60	>45	No adjustment required	No adjustment required	No adjustment required	No adjustment required	No adjustment required
Estimated ClCr (mL/min/70 kg)	30–60	20–45	Q6H	Q8H	Q12H	Q24H	Reduce dose by 25%[b]
	15–30	10–20	Q8H	Q12H	Q24H	Q24H and reduce dose by 25%[b]	Reduce dose by 50%[b]
	<15	<10	Q12H	Q24H	Q24H and reduce dose by 25%[b]	Q24H and reduce dose by 50%[b]	Reduce dose by 75%[b]

[a] Based on percentage of renal elimination and estimated creatinine clearance (normal ClCr = 120 mL/min/70 kg).
[b] For certain drugs, decreasing the dose is not appropriate, or one may need to extend interval >Q24H if available dosage forms do not permit specific dose reductions.

Table 2: Dosage Adjustment in Renal Impairment—Adults[a]

	% Renal Elimination			
Drug	**<50**[b]	**50–74**[c]	**≥75**[c]	**Comments**

Drug	% Renal Elimination			Comments
	<50[b]	50–74[c]	≥75[c]	
5-aminosalicylic acid	•			
abacavir	•			
abatacept	•			
acamprosate			•	Avoid in severe renal impairment
acarbose	•			
acebutolol		•		Active metabolite; assume ≥75% renal elimination for dosage adjustment
acetaminophen	•			
acetazolamide			•	Avoid; ineffective when ClCr <10mL/min
acitretin	•			
acyclovir			•	
adalimumab	•			
adefovir dipivoxil	•			Nephrotoxic. Active metabolite; assume ≥75% renal elimination for dosage adjustment
adenosine	•			
albendazole	•			
alemtuzumab	•			
alendronate	•			Avoid in severe renal impairment
alfacalcidol	•			
alfuzosin	•			
alirocumab	•			
aliskiren	•			
allopurinol	•			Active metabolite; assume ≥75% renal elimination for dosage adjustment
almotriptan			•	

Drug	% Renal Elimination			Comments
	<50[b]	50–74[c]	≥75[c]	
alogliptin			•	Active metabolite
alprazolam	•			
alprostadil	•			
alteplase	•			
aluminum salts	•			Avoid in severe renal impairment as may accumulate
amantadine			•	
amikacin			•	Nephrotoxic; monitor serum drug concentrations
amiloride		•		Avoid in severe renal impairment
aminophylline	•			
amiodarone	•			Active metabolite but no dosage adjustment required
amitriptyline	•			Active metabolite but no dosage adjustment required
amlodipine	•			
amoxicillin		•		
amoxicillin/clavulanate		•		
amphetamine, mixed salts		•		Active metabolite but no dosage adjustment required
amphotericin B	•			Nephrotoxic
ampicillin			•	
anakinra			•	
anidulafungin	•			
apixaban	•			

Drug	% Renal Elimination			Comments
	<50[b]	50–74[c]	≥75[c]	
apomorphine	•			Manufacturer recommends lower starting doses in mild and moderate renal impairment and that the drug not be used in severe renal impairment
apremilast	•			Manufacturer recommends dose reduction in severe renal impairment
aprepitant	•			
aripiprazole	•			
ASA	•			Nephrotoxic
asenapine	•			
atazanavir	•			
atenolol			•	
atomoxetine	•			
atorvastatin	•			Active metabolite but no dosage adjustment required
atovaquone	•			
atropine	•			
auranofin			•	Avoid; nephrotoxic
azathioprine	•			Active metabolite; assume ≥75% renal elimination for dosage adjustment
azilsartan	•			
azithromycin	•			
baclofen			•	
baricitinib			•	Manufacturer recommends avoiding use if ClCr <60 mL/min
bazedoxifene	•			
belimumab	•			

Drug	% Renal Elimination			Comments
	<50[b]	50–74[c]	≥75[c]	
benazepril	•			
benralizumab	•			
benztropine	•			
bezafibrate		•		Avoid in renal impairment
bictegravir	•			Manufacturer recommends avoiding use if ClCr <30 mL/min
bilastine	•			
bisacodyl	•			Active metabolite but no dosage adjustment required
bismuth subsalicylate	•			
bisoprolol		•		
bivalirudin	•			Reduce dose in severe renal impairment
brexpiprazole	•			Manufacturer recommends reducing dose by 25–33% when ClCr <60 mL/min
brinzolamide		•		Eye drops; contraindicated in severe renal impairment
brivaracetam	•			
bromocriptine	•			
brompheniramine	•			
budesonide	•			
bumetanide	•			Larger doses may be required in severe renal impairment
buprenorphine	•			
bupropion	•			Active metabolite; assume ≥75% renal elimination for dosage adjustment
buserelin	•			
buspirone	•			

Drug	% Renal Elimination			Comments
	<50[b]	50–74[c]	≥75[c]	
butalbital	•			Active metabolite; assume ≥75% renal elimination for dosage adjustment
cabotegravir	•			
caffeine	•			Active metabolite; assume ≥75% renal elimination for dosage adjustment
calcitonin	•			
calcitriol	•			
calcium salts	•			
canagliflozin	•			Less effective in moderate and ineffective in severe renal impairment
candesartan	•			
captopril		•		
carbamazepine	•			Active metabolite but no dosage adjustment required
carvedilol	•			Active metabolite but no dosage adjustment required
cascara				Route of elimination unknown
caspofungin	•			
cefadroxil			•	
cefazolin			•	
cefepime			•	
cefixime		•		
cefotaxime		•		Active metabolite; assume ≥75% renal elimination for dosage adjustment
cefoxitin			•	
cefprozil		•		
ceftazidime			•	

Drug	% Renal Elimination			Comments
	<50[b]	50–74[c]	≥75[c]	
ceftriaxone	•			
cefuroxime			•	
celecoxib	•			Nephrotoxic
cephalexin			•	
certolizumab pegol	•			Polyethylene glycol component renally eliminated
cetirizine		•		
chloral hydrate	•			Avoid. Active metabolite; assume ≥75% renal elimination for dosage adjustment
chlordiazepoxide	•			Active metabolite; assume ≥75% renal elimination for dosage adjustment
chloroquine		•		
chlorpheniramine	•			
chlorpromazine	•			Active metabolite but no dosage adjustment required
chlorthalidone		•		Avoid; ineffective when ClCr <30 mL/min
chlorzoxazone	•			
chromium			•	
cidofovir			•	Avoid; nephrotoxic. Active metabolite; assume ≥75% renal elimination for dosage adjustment
cilazapril	•			Active metabolite; assume ≥75% renal elimination for dosage adjustment
cimetidine		•		
cinacalcet	•			
ciprofloxacin		•		
citalopram	•			
cladribine	•			Not recommended if ClCr <60 mL/min

Drug	% Renal Elimination			Comments
	<50[b]	50–74[c]	≥75[c]	
clarithromycin	•			Active metabolite; assume ≥75% renal elimination for dosage adjustment
clindamycin	•			
clobazam	•			
clodronate			•	Avoid; nephrotoxic
clomiphene	•			
clomipramine	•			Active metabolite but no dosage adjustment required
clonazepam	•			
clonidine	•			
clopidogrel	•			
cloxacillin	•			
clozapine	•			Active metabolite but no dosage adjustment required
cobicistat	•			
codeine	•			Active metabolite; assume ≥75% renal elimination for dosage adjustment
coenzyme Q10	•			
colchicine	•			Avoid in renal impairment
cyanocobalamin		•		% renal elimination increased with large doses
cyclobenzaprine	•			
cyclophosphamide	•			Active metabolite; dosage adjustment recommended in severe renal impairment
cyclosporine	•			Nephrotoxic; monitor serum drug concentrations
cyproheptadine	•			
cyproterone acetate	•			

Drug	% Renal Elimination			Comments
	<50[b]	50–74[c]	≥75[c]	
cytisine				Route of elimination unknown
dabigatran			•	Contraindicated in severe renal impairment
dalteparin			•	
danazol	•			
dantrolene	•			
dapagliflozin	•			Contraindicated in moderate to severe renal impairment
dapsone	•			
daptomycin			•	
darbepoetin alfa	•			
darifenacin	•			
darunavir	•			
deferoxamine			•	
delavirdine	•			
delta-9-tetrahydrocannabinol/ cannabidiol	•			
denosumab	•			
desipramine	•			Active metabolite but no dosage adjustment required
desloratadine	•			Active metabolite; assume ≥75% renal elimination for dosage adjustment
desmopressin			•	
desvenlafaxine	•			Manufacturer recommends dosage adjustment if ClCr <30 mL/min, although <50% renal elimination
dexamethasone	•			
dexbrompheniramine	•			

Drug	% Renal Elimination			Comments
	<50[b]	50–74[c]	≥75[c]	
dexlansoprazole	•			
dexrazoxane	•			Reduce dose by 50% in patients with moderate to severe renal impairment
dextroamphetamine		•		Active metabolite but no dosage adjustment required
dextromethorphan	•			Active metabolite; assume ≥75% renal elimination for dosage adjustment
diazepam	•			Active metabolite but no dosage adjustment required
diclofenac	•			Nephrotoxic
dicyclomine			•	
didanosine	•			Active metabolite; assume ≥75% renal elimination for dosage adjustment
dienogest	•			
diflunisal	•			Nephrotoxic
digoxin			•	Monitor serum concentrations
dihydroergotamine	•			Active metabolite; no data on renal elimination
diltiazem	•			Active metabolite but no dosage adjustment required
dimenhydrinate	•			
dimethyl fumarate	•			
diphenhydramine	•			
diphenoxylate	•			Active metabolite
dipyridamole	•			
disulfiram	•			
divalproex	•			
dobutamine	•			

Drug	% Renal Elimination			Comments
	<50[b]	50–74[c]	≥75[c]	
docusate	•			
dofetilide			•	
dolutegravir	•			
domperidone	•			
donepezil	•			Active metabolite but no dosage adjustment required
doravirine	•			
doxazosin	•			
doxepin	•			Active metabolite but no dosage adjustment required
doxycycline	•			
doxylamine	•			
dronedarone	•			
dulaglutide	•			
duloxetine	•			Use contraindicated by manufacturer if ClCr <30 mL/min
dutasteride	•			
edoxaban		•		
efavirenz	•			
elagolix	•			
eletriptan	•			
eluxadoline	•			
elvitegravir	•			
empagliflozin		•		Less effective in moderate and ineffective in severe renal impairment
emtricitabine			•	

Drug	% Renal Elimination			Comments
	<50[b]	50–74[c]	≥75[c]	
enalapril	•			Active metabolite; assume ≥75% renal elimination for dosage adjustment
enfuvirtide	•			
enoxaparin			•	
entacapone	•			
entecavir		•		
eplerenone	•			Use contraindicated by manufacturer if ClCr <30 mL/min
epoetin alfa	•			
eprosartan	•			
eptifibatide	•			Dosage adjustment recommended for patients with renal impairment
eptinezumab	•			
erenumab	•			
ertapenem			•	
ertugliflozin		•		Less effective in moderate, and ineffective in severe renal impairment
erythromycin	•			
escitalopram	•			Active metabolite but no dosage adjustment required
esketamine	•			Active metabolite; assume ≥75% renal elimination for dosage adjustment
eslicarbazepine			•	
esmolol	•			
esomeprazole	•			
estrogens	•			
eszopiclone			•	

Drug	% Renal Elimination			Comments
	<50[b]	50–74[c]	≥75[c]	
etanercept	•			
ethacrynic acid	•			Avoid in severe renal impairment
ethambutol		•		
ethopropazine				Route of elimination unknown
ethosuximide	•			
etidronate		•		Nephrotoxic
etodolac	•			Nephrotoxic
etravirine	•			
evolocumab	•			
exenatide			•	Avoid in severe renal impairment
ezetimibe	•			
famciclovir	•			Active metabolite; assume ≥75% renal elimination for dosage adjustment
famotidine			•	
fampridine			•	Use contraindicated by manufacturer if ClCr <60 mL/min
fatty acids, omega-3	•			
febuxostat	•			
felodipine	•			
fenofibrate	•			Active metabolite; assume ≥75% renal elimination for dosage adjustment
fentanyl	•			
fesoterodine		•		Active metabolite
fexofenadine	•			Active metabolite; assume ≥75% renal elimination for dosage adjustment
fidaxomicin	•			

Drug	% Renal Elimination			Comments
	<50[b]	50–74[c]	≥75[c]	
filgrastim	•			
finasteride	•			
fingolimod	•			
flecainide	•			Active metabolite; assume ≥75% renal elimination for dosage adjustment
fluconazole		•		
flucytosine			•	
fludrocortisone	•			
flunarizine	•			
fluoxetine	•			Active metabolite but no dosage adjustment required
flupentixol	•			
fluphenazine	•			
flurazepam	•			Active metabolite but no dosage adjustment required
flurbiprofen	•			Nephrotoxic
flutamide	•			
fluvastatin	•			
fluvoxamine	•			
folic acid	•			% renal elimination increased with large doses
fondaparinux			•	
fosamprenavir	•			
fosaprepitant	•			
foscarnet			•	Avoid; nephrotoxic
fosfomycin	•			

Drug	% Renal Elimination			Comments
	<50[b]	50–74[c]	≥75[c]	
fosinopril	•			Active metabolite but no dosage adjustment required
fremanezumab	•			
frovatriptan	•			
furosemide		•		Larger doses may be required in severe renal impairment
gabapentin			•	
galantamine	•			Manufacturer recommends a maximum daily dose of 16 mg if ClCr <60 mL/min
galcanezumab	•			
ganciclovir			•	
gemfibrozil	•			Active metabolite; assume ≥75% renal elimination for dosage adjustment
gentamicin			•	Nephrotoxic; monitor serum drug concentrations
glatiramer	•			
gliclazide	•			
glimepiride	•			Active metabolite; assume ≥75% renal elimination for dosage adjustment
glucosamine	•			
glyburide	•			Avoid. Active metabolite but no dosage adjustment required
glycopyrrolate	•			
golimumab	•			
goserelin	•			
granisetron	•			
guaifenesin				Route of elimination unknown

Drug	% Renal Elimination			Comments
	<50[b]	50–74[c]	≥75[c]	
guanfacine		•		
guselkumab	•			
haloperidol	•			
heparin	•			
hydralazine	•			
hydrochlorothiazide			•	Avoid; ineffective when ClCr <30 mL/min
hydrocodone	•			Active metabolite; assume ≥75% renal elimination for dosage adjustment
hydrocortisone	•			
hydromorphone	•			
hydroxychloroquine	•			Active metabolite; assume ≥75% renal elimination for dosage adjustment
hydroxyzine		•		
hyoscine	•			
ibuprofen	•			Nephrotoxic
ibutilide	•			Active metabolite but no dosage adjustment required
icosapent ethyl	•			
imipenem/cilastatin		•		
imipramine	•			Active metabolite but no dosage adjustment required
indapamide	•			Avoid; ineffective when ClCr <30 mL/min
indomethacin	•			Nephrotoxic
infliximab	•			
insulin	•			
interferon alfa	•			

Drug	% Renal Elimination			Comments
	<50[b]	50–74[c]	≥75[c]	
interferon beta	•			
iodine			•	
irbesartan	•			
iron salts	•			
isoniazid	•			
isosorbide dinitrate or 5-mononitrate	•			Active metabolite but no dosage adjustment required
isotretinoin	•			Avoid in renal impairment
itraconazole	•			
ivabradine	•			Active metabolite; no data available for ClCr <15 mL/min
ixekizumab	•			
ketoconazole	•			
ketoprofen	•			Nephrotoxic
ketorolac			•	Nephrotoxic
ketotifen		•		
L-carnitine			•	
L-tryptophan	•			
labetalol	•			
lacosamide			•	Manufacturer recommends a maximum daily dose of 300 mg in patients with end-stage renal disease
lamivudine		•		Active metabolite; assume ≥75% renal elimination for dosage adjustment
lamotrigine	•			
lanreotide	•			

Drug	% Renal Elimination			Comments
	<50[b]	50–74[c]	≥75[c]	
lansoprazole	•			
leflunomide	•			Active metabolite; assume ≥75% renal elimination for dosage adjustment
lemborexant	•			
letermovir	•			
letrozole	•			
leuprolide	•			
levetiracetam		•		
levodopa	•			Active metabolite but no dosage adjustment required
levofloxacin			•	
levomilnacipran		•		
levonorgestrel	•			
levothyroxine	•			
lidocaine	•			Active metabolite but no dosage adjustment required
linagliptin	•			
linezolid	•			
liothyronine				No data on renal elimination
liraglutide	•			
lisdexamfetamine	•			
lisinopril			•	
lithium			•	Nephrotoxic; monitor serum drug concentrations
lixisenatide		•		No dosage adjustment required if ClCr >30 mL/min; no data available for ClCr <30 mL/min

Drug	% Renal Elimination			Comments
	<50[b]	50–74[c]	≥75[c]	
loperamide	•			
lopinavir/ritonavir	•			
loratadine	•			Active metabolite; consider dosage adjustment in severe renal impairment
lorazepam	•			
losartan	•			Active metabolite but no dosage adjustment required
lovastatin	•			
loxapine	•			
lurasidone	•			Active metabolite; assume ≥75% renal elimination for dosage adjustment
magnesium salts	•			Avoid in severe renal impairment as may accumulate
maraviroc	•			Modify dose when taking concurrent potent CYP3A4 inhibitors
mebendazole	•			
medroxyprogesterone	•			
mefenamic acid	•			Nephrotoxic
mefloquine	•			
megestrol	•			
melatonin	•			
meloxicam	•			Nephrotoxic
memantine			•	
meperidine	•			Active metabolite; assume ≥75% renal elimination for dosage adjustment
mepolizumab	•			

Drug	% Renal Elimination			Comments
	<50[b]	50–74[c]	≥75[c]	
mercaptopurine	•			Active metabolite; assume ≥75% renal elimination for dosage adjustment
meropenem		•		
mesna			•	
metformin			•	Avoid in severe renal impairment
methadone	•			
methazolamide	•			Avoid; ineffective in severe renal impairment
methimazole	•			
methocarbamol	•			
methotrexate			•	Avoid; nephrotoxic
methotrimeprazine	•			Active metabolite but no dosage adjustment required
methyldopa	•			Active metabolite; assume ≥75% renal elimination for dosage adjustment
methylnaltrexone		•		
methylphenidate	•			
methylprednisolone	•			
metoclopramide			•	Active metabolite; assume ≥75% renal elimination for dosage adjustment
metolazone		•		Dosage reduction not necessary in renal impairment
metoprolol	•			
metronidazole	•			Active metabolite but no dosage adjustment required
mexiletine	•			Active metabolite but no dosage adjustment required
micafungin	•			

Drug	% Renal Elimination			Comments
	<50[b]	50–74[c]	≥75[c]	
miconazole	•			
midazolam	•			
midodrine	•			Active metabolite; assume ≥75% renal elimination for dosage adjustment
milrinone			•	
minocycline	•			
mirabegron	•			Manufacturer recommends a maximum daily dose of 25 mg in patients with severe renal impairment
mirtazapine			•	
misoprostol	•			
mitoxantrone	•			
moclobemide	•			
montelukast	•			
morphine	•			Active metabolite; assume ≥75% renal elimination for dosage adjustment
moxifloxacin	•			
mycophenolate	•			
nabilone	•			
nabumetone	•			Nephrotoxic. Active metabolite; assume ≥75% renal elimination for dosage adjustment
nadolol			•	
nadroparin			•	
nafarelin	•			
naloxegol	•			Manufacturer recommends 50% reduction of initial dose in moderate or severe renal impairment

Drug	% Renal Elimination			Comments
	<50[b]	50–74[c]	≥75[c]	
naloxone	•			
naltrexone	•			Active metabolite but no dosage adjustment required
naproxen	•			Nephrotoxic
naratriptan		•		
natalizumab	•			
nebivolol	•			Active metabolite; assume ≥75% renal elimination for dosage adjustment
nelfinavir	•			Active metabolite but no dosage adjustment required
nevirapine	•			
niacin	•			
nicotine	•			
nifedipine	•			
nimodipine	•			
nitazoxanide	•			Active metabolite
nitrofurantoin	•			Avoid in renal impairment
nitroglycerin	•			
nitroprusside	•			
nizatidine		•		
norethindrone	•			
norfloxacin			•	
nortriptyline	•			Active metabolite but no dosage adjustment required
ocrelizumab	•			
octreotide	•			Reduce dose in severe renal impairment

Drug	% Renal Elimination			Comments
	<50[b]	50–74[c]	≥75[c]	
olanzapine	•			
olmesartan	•			Not recommended in severe renal impairment
olsalazine	•			
omalizumab	•			
omeprazole	•			
ondansetron	•			
orlistat	•			
orphenadrine	•			Active metabolite; assume ≥75% renal elimination for dosage adjustment
oseltamivir	•			Active metabolite; dosage adjustment recommended in severe renal impairment
oxazepam	•			
oxcarbazepine	•			Active metabolite; assume ≥75% renal elimination for dosage adjustment
oxtriphylline	•			
oxybutynin	•			Active metabolite but no dosage adjustment required
oxycodone	•			
oxymetazoline				Route of elimination unknown
paliperidone		•		Manufacturer recommends dosage adjustment in renal impairment
palonosetron			•	Active metabolite but no dosage adjustment required
pamidronate		•		Nephrotoxic
pantoprazole	•			
paroxetine	•			

Drug	% Renal Elimination			Comments
	<50[b]	50–74[c]	≥75[c]	
pegfilgrastim	•			Polyethylene glycol component renally eliminated
peginterferon alfa	•			Polyethylene glycol component renally eliminated
penicillamine	•			Avoid; nephrotoxic
penicillin G/V		•		
pentamidine	•			Nephrotoxic when given IV
pentazocine	•			
pentoxifylline	•			
perampanel	•			
perindopril	•			Active metabolite; assume ≥75% renal elimination for dosage adjustment
perphenazine	•			
phenelzine	•			
pheniramine			•	
phenobarbital	•			Active metabolite but no dosage adjustment required
phenylephrine	•			
phenytoin	•			
pilocarpine	•			
pimozide	•			
pinaverium bromide	•			
pindolol	•			
pioglitazone	•			
piperacillin			•	
piperacillin/tazobactam			•	

Drug	% Renal Elimination			Comments
	<50[b]	50–74[c]	≥75[c]	
piroxicam	•			Nephrotoxic
pizotifen	•			
posaconazole	•			
potassium salts			•	May accumulate in renal impairment
pramipexole			•	
prasugrel	•			Active metabolite but no dosage adjustment required
pravastatin	•			
prazosin	•			
prednisone	•			
pregabalin			•	
primaquine	•			
primidone	•			Active metabolite but no dosage adjustment required
probenecid			•	Ineffective when ClCr <50 mL/min
procainamide		•		Active metabolite; assume ≥75% renal elimination for dosage adjustment
prochlorperazine	•			Active metabolite; assume ≥75% renal elimination for dosage adjustment
procyclidine	•			Active metabolite; assume ≥75% renal elimination for dosage adjustment
progesterone	•			
proguanil	•			Active metabolite but no dosage adjustment required
promethazine	•			
propafenone	•			
propranolol	•			

Drug	% Renal Elimination			Comments
	<50[b]	50–74[c]	≥75[c]	
propylthiouracil	•			
prucalopride		•		
pseudoephedrine			•	
pyrazinamide	•			Avoid in severe renal impairment
pyridoxine		•		% renal elimination increased with large doses
quetiapine	•			
quinapril	•			Active metabolite; assume ≥75% renal elimination for dosage adjustment
quinidine	•			Active metabolite but no dosage adjustment required
quinine	•			
quinupristin/dalfopristin	•			
rabeprazole	•			
raloxifene	•			
raltegravir	•			
ramipril	•			Active metabolite; assume ≥75% renal elimination for dosage adjustment
ranitidine		•		
rasagiline	•			Conclusive data not available for renally impaired patients
rasburicase	•			
remdesivir	•			Active metabolite. The excipient betadex sulfobutyl ether may accumulate in severe renal impairment
repaglinide	•			
reslizumab	•			
ribavirin	•			Avoid in renal impairment

Drug	% Renal Elimination			Comments
	<50[b]	50–74[c]	≥75[c]	
riboflavin		•		
rifabutin	•			Active metabolite but no dosage adjustment required
rifampin	•			Active metabolite but no dosage adjustment required
rilpivirine	•			
risankizumab	•			
risedronate			•	Avoid in severe renal impairment
risperidone	•			Active metabolite; assume ≥75% renal elimination for dosage adjustment
ritonavir	•			Active metabolite but no dosage adjustment required
rituximab	•			Nephrotoxic
rivaroxaban	•			Avoid in severe renal impairment
rivastigmine	•			
rizatriptan	•			Active metabolite but no dosage adjustment required
roflumilast	•			
romosozumab	•			
ropinirole	•			
rosiglitazone	•			
rosuvastatin	•			
rotigotine	•			
rufinamide	•			
rupatadine	•			Active metabolite; not studied in renal impairment
sacubitril/valsartan		•		

Drug	% Renal Elimination			Comments
	<50[b]	50–74[c]	≥75[c]	
safinamide	•			
saquinavir	•			
sarilumab	•			
saxagliptin	•			Active metabolite; assume ≥75% renal elimination for dosage adjustment
scopolamine	•			
secukinumab	•			
selegiline	•			Active metabolite but no dosage adjustment required
semaglutide	•			
senna				% renally eliminated unknown
sertraline	•			
sildenafil	•			
silodosin	•			
simvastatin	•			
siponimod	•			
sitagliptin			•	
sodium phosphates				% renally eliminated unknown; may accumulate in renal impairment
sofosbuvir			•	No dose adjustment recommended in mild and moderate renal impairment
solifenacin		•		Active metabolite
sotalol		•		
spectinomycin			•	Dosage adjustment unnecessary
spironolactone	•			Avoid. Active metabolite; assume ≥75% renal elimination for dosage adjustment

Drug	% Renal Elimination			Comments
	<50[b]	50–74[c]	≥75[c]	
stavudine	•			Active metabolite; assume ≥75% renal elimination for dosage adjustment
stiripentol	•			
streptomycin			•	Nephrotoxic; monitor serum drug concentrations
sucralfate	•			Al^{++} may accumulate
sulfadiazine		•		Nephrotoxic
sulfamethoxazole/trimethoprim		•		
sulfasalazine	•			Active metabolite but no dosage adjustment required
sulfinpyrazone	•			Avoid; nephrotoxic
sulindac	•			Nephrotoxic. Active metabolite but no dosage adjustment required
sumatriptan	•			
tacrolimus	•			
tadalafil	•			Active metabolite; assume ≥75% renal elimination for dosage adjustment
tamsulosin	•			
tapentadol	•			Not recommended in severe renal impairment
telbivudine			•	
telmisartan	•			
temazepam	•			
tenecteplase	•			
tenofovir			•	Nephrotoxic
tenoxicam	•			Nephrotoxic
terazosin	•			

Drug	% Renal Elimination			Comments
	<50[b]	50–74[c]	≥75[c]	
terbinafine		•		
teriflunomide	•			
teriparatide	•			Do not use if ClCr <30 mL/min
tetracycline		•		Nephrotoxic
theophylline	•			
thiamine	•			
tiaprofenic acid			•	Nephrotoxic
ticagrelor	•			
tigecycline	•			
timolol	•			
tinzaparin			•	
tipranavir	•			
tirofiban		•		
tizanidine	•			
tobramycin			•	Nephrotoxic; monitor serum drug concentrations
tocilizumab	•			
tofacitinib	•			Manufacturer recommends dosage adjustment in moderate or severe renal impairment
tolbutamide	•			
tolterodine	•			
topiramate			•	
tramadol	•			Active metabolite; assume ≥75% renal elimination for dosage adjustment
trandolapril	•			Active metabolite; assume ≥75% renal elimination for dosage adjustment

Drug	% Renal Elimination			Comments
	<50[b]	50–74[c]	≥75[c]	
tranexamic acid			•	
tranylcypromine	•			Active metabolite; assume ≥75% renal elimination for dosage adjustment
trazodone	•			
triamterene	•			Avoid; nephrotoxic. Active metabolite but no dosage adjustment required
triazolam	•			
trientine	•			
trifluoperazine	•			
trihexyphenidyl			•	
trimeprazine	•			
trimethoprim			•	
trimipramine	•			
triprolidine	•			
triptorelin	•			Conclusive data not available for renally impaired patients but dosage adjustment may be required
trospium	•			Conclusive data not available for renally impaired patients but dosage adjustment may be required
ulipristal	•			
upadacitinib	•			
ursodeoxycholic acid	•			
ustekinumab	•			
valacyclovir	•			Active metabolite; assume ≥75% renal elimination for dosage adjustment
valganciclovir		•		Nephrotoxic. Active metabolite; assume ≥75% renal elimination for dosage adjustment

Drug	% Renal Elimination			Comments
	<50[b]	50–74[c]	≥75[c]	
valproic acid	•			
valsartan	•			
vancomycin			•	Nephrotoxic; monitor serum drug concentrations
vardenafil	•			
varenicline			•	
vasopressin	•			
vedolizumab	•			
venlafaxine	•			Active metabolite; assume ≥75% renal elimination for dosage adjustment
verapamil	•			Active metabolite but no dosage adjustment required
verteporfin	•			
vigabatrin			•	
vilazodone	•			
vitamin C			•	
vitamin D	•			
vitamin E	•			
voriconazole	•			Avoid IV formulation in renal impairment; nephrotoxic vehicle
vortioxetine	•			
warfarin	•			
xylometazoline				Route of elimination unknown
yohimbine				Avoid. Route of elimination unknown
zanamivir	•			
zidovudine	•			Reduce dose in severe renal impairment

Drug	% Renal Elimination			Comments
	<50[b]	50–74[c]	≥75[c]	
ziprasidone	•			
zoledronic acid			•	
zolmitriptan	•			Active metabolite but no dosage adjustment required
zolpidem	•			
zopiclone	•			
zuclopenthixol	•			

[a] Omission of a drug from this table does not imply that dosage adjustment is NOT required in renal impairment. Refer to specific references for dosing in dialysis.
[b] Dosage adjustment usually not required unless there are active or toxic metabolites (see Comments column).
[c] See Table 1 for suggested dose adjustment.

Abbreviations: ASA = acetylsalicylic acid; ClCr = creatinine clearance; CYP3A4 = cytochrome P450 3A4

Suggested Readings

Dersch D, McCormack J. Estimating renal function for drug dosing: rewriting the gospel? *Can J Hosp Pharm* 2008;61(2):138-43. Available from: www.cjhp-online.ca/index.php/cjhp/article/view/31.

Vidal L, Shavit M, Fraser A et al. Systematic comparison of four sources of drug information regarding adjustment of dose for renal function. *BMJ* 2005;331(7511):263.

Wilhelm SM, Kale-Pradhan PB. Estimating creatinine clearance: a meta-analysis. *Pharmacotherapy* 2011;31(7):658-64.

References

1. McCormack JP Cooper J, Carleton B. Simple approach to dosage adjustment in patients with renal impairment. *Am J Health Syst Pharm* 1997;54(21):2505-9.