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Renal Pharmacotherapy

Dosage Adjustment of Medications Eliminated by the Kidneys

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Preface

For optimal effectiveness and safety, medications used to manage both acute and chronic diseases must be administered in dosages carefully tailored according to patient-specific metabolic and excretory functional capacity. Due to variably compromised ability to eliminate certain drugs from the body, patients with kidney disease often present with complex and potentially challenging clinical issues related to adjustment of drug dosages. In these patients, provision of effective and safe pharmacotherapy depends upon not only understanding the pharmacokinetic and pharmacodynamic actions of all prescribed medications but also comprehensive appreciation of each patient's current clinical status.

In this regard, additional challenges have been recently realized. As of 2009, clinical laboratories in North America and elsewhere are expected to report serum creatinine (SCr) concentrations that are consistent with reference values obtained by isotope dilution mass spectrometry [1]. For most laboratories, this has necessitated recalibration of autoanalyzers. Depending on analyzer manufacturer and model, recalibrated SCr levels are known to be 5–20 % lower than values reported prior to recalibration [2]. Use of recalibrated SCr values with the Cockroft-Gault equation [3] to calculate estimated creatinine clearance (CrCL) often results in a compounded error leading to a numerically exaggerated estimate of excretory kidney function. If this CrCL value is used as currently recommended by the US Food and Drug Administration [4] for the purpose of determining drug dosages for persons with renal impairment, risk for medication error and drug overdose is increased.

In order to improve the accuracy of measures of kidney function used for staging severity of kidney disease, clinical laboratories now are encouraged to utilize recalibrated SCr concentrations with the 4-variable Modification of Diet in Renal Disease (MDRD) equation [5] or the Chronic Kidney Disease Epidemiological (CKDepi) equation [6] to calculate estimated glomerular filtration rate (eGFR) in mL/min/1.73 m^2 and to report this number along with the SCr value to clinicians [1, 7]. Although this measure of excretory kidney function often is readily available, it is not fully compatible with FDA-mandated product labeling related to drug dosage adjustment in patients with renal insufficiency. These inconsistencies may lead to further confusion and additional potential errors.

Available resources for adjustment of dosages of drugs in patients with renal insufficiency have been found to be broadly inconsistent and imprecise. A systematic review of dosage recommendations for 100 commonly prescribed medications listed in four widely used compendia found disparities in all of these resources in their recommendations for adjustments of dosage and dosage interval [8]. These differences ranged from minor disagreement regarding suggested dosage amount for a specific medication to divergence as broad and conflicting as no adjustment needed versus contraindicated. The four sources varied in their definitions of renal impairment, and some were found to be qualitative and unclear. In response, authorities conceded that "despite numerous secondary sources of drug dosing information, drug prescribing in renal failure remains imprecise and relies on interpolation, extrapolation, and estimation" [9]. In similar fashion, frequent inconsistencies have been found not only among FDA-approved prescribing information concerning recommended dose adjustments for recently marketed medications but also clinicians' methods for interpretation and application of these recommendations [10].

Additional resource-related issues may be problematic concerning efforts to provide optimal drug therapy for patients with abnormal or rapidly changing renal function. At least as important as use of inconsistent or discrepant information concerning drug dosing is inability or failure to recognize disparate dosage recommendations. Clinicians should be provided with convenient access to at least two reputable, reliable, and evidence-based sources of information on renal drug dosing, thereby allowing individualized selection of the most relevant regimen based on clinical judgment in light of pharmacological concerns weighted for safety and effectiveness. We sought to satisfy this requirement by compiling a listing of dosing suggestions comprised of official and alternative recommendations.

Methods

Conduct oversight for this project was provided by the Colorado Multiple Institutional Review Board (COMIRB, Protocol № 10-1105). Our objective, based on a review of available resources, was to compile a comprehensive tabular listing of dosage recommendations for patients with compromised renal function.

Information concerning adjustment of selected drug dosages that is compatible with conventional and revised measures of kidney function was obtained from available tertiary, secondary, and primary literature sources. This information was compiled into an alphabetical listing according to the approved generic drug name. Information on drug dosage adjustment was included in the listing if, in the opinion of the authors, such adjustment is necessary.

For all medications included in the listing, FDA-mandated product information was obtained from the package insert. In every instance, careful attempt was made to directly quote or to remain entirely faithful to the actual language and/or meaning within the product information. Alternative dosage adjustment information routinely was obtained from commonly used compendia. Most often, this consisted of GFR-based adjustment recommendations taken from the professional standard *Drug Prescribing in Renal Failure* [11] (with permission) or any of its various derivatives [12–15]. In most cases, other tertiary [16–21], secondary [22–25], and primary references (or available Internet-based counterparts of these print media) were used. Use of these alternatives often was necessary to supply or, more commonly, to corroborate and/or expand evidence-based dosing information for antimicrobials, newly marketed medications, and drugs used in patients receiving renal replacement therapy. Specialized alternative resources also were used for certain drugs for which information other than that provided in standard compendia was considered preferable.

The primary literature related to drug dosing in kidney disease was reviewed for all renally eliminated medications. In the event that alternative dose recommendations differed from those provided by the manufacturer, information selected and subsequently included in the listing was believed to be the most clinically relevant based on original clinical research and experience. The primary literature also was utilized for all medications for which proprietary dosing information was believed to be inadequate or outmoded and in need of change. This was most often necessary for dose adjustment of medications used for patients receiving renal replacement therapy. Searches for information contained in the primary literature were performed with the US National Library of Medicine's PubMed indexing system and Elsevier's Embase using nonproprietary or preferred drug names.

Results

A review of available resources disclosed 349 medications that require or suggest need for dosage adjustment when administered to patients with acute or chronic kidney disease and 769 drug entities that normally do not require dose adjustment for renal impairment. From this review, salient data for each medication was extracted and incorporated into a pre-formatted computer file. This file comprises the listings shown below.

Discussion

To promote effectiveness and minimize possible toxicity, the dosage of certain medications must be adjusted in persons with compromised kidney function. Convenient and comprehensive evidence-based resources are needed to enable consistent application of such adjustments.

Failure to enjoin appropriate dosage adjustments in patients with abnormal or rapidly changing kidney function continues to lead to reports of drug toxicity involving a broad array of renally eliminated medications [26–37]. Better resources clearly are needed to facilitate dose optimization. Means to ensure that patients whose current medications need adjustment are consistently identified also are vitally necessary.

Computerized assessment and consequent-directed recommendations concerning drug dosage have proven capable of improving prescribing patterns. A recent meta-analysis that evaluated 26 controlled comparisons of behavioral prescriber changes and/or health outcomes of patients associated with computerized interventions targeted to affect prescribing documented significant benefit of computerized advice by increasing the initial dose, increasing serum drug concentrations, reducing the time to therapeutic stabilization, reducing the risk of toxic drug levels, and reducing the length of hospital stay [38]. In patients with renal insufficiency, automated clinical decision support (CDS) systems have proven capable of detecting potentially dangerous and costly exposure to excess dosages of antimicrobial and other drugs that occurs frequently despite the intensive monitoring afforded to critically ill patients [39] and those attended in the emergency department [40]. Perhaps most convincing of the value of CDS are data showing that, as compared with pre-implementation figures, implementation of a CDS system was associated with a statistically and clinically significant 39 % increase in the fraction of delivered prescriptions for renally eliminated or nephrotoxic medications deemed appropriate according to previously published and/or expert evaluation standards when the system was applied to approximately 100,000 orders for these medications in hospitalized patients with renal insufficiency [41]. CDS systems for renally eliminated medications may be most effective if supplemented with academic detailing [42].

The appendant listing was designed to close some identified gaps in information concerning dosage adjustment of medications eliminated by the kidneys. More importantly, it was composed with the intent that this was to be adapted and used as part of an automated system that would display each patient's identification, location, and kidney function. Ultimately, the listing is to be used with CDS as described above, thereby enabling provider alerting to need for attention based on determination of specific clinically relevant dosing cusps or breakpoints for prescribed medications with individualized information displayed concerning suggested dose modifications and recommended actions.

This resource listing displays several strengths including alphabetical format, completeness, referencing, and, when available, dosage recommendations based on eGFR [43]. In glaring contrast, it also has significant weaknesses and limitations. First and foremost, we fully understand and appreciate that no single reference related to medication management in patients with kidney disease can provide truly comprehensive, completely accurate, totally unbiased, and thoroughly evidence-based recommendations. Secondly, our information was largely compiled with use of secondary or tertiary data sources with corroboration of the primary literature. Thirdly, alternative dosage adjustment recommendations that include breakpoints set in terms of eGFR often are listed in our information. The authors of the original guidelines in which this standard was established concede that calculated CrCL, an approximation useful in clinical dosimetry, may be used to simulate GFR [44]. These measures of kidney function thusly were considered essentially interchangeable, as demonstrated in earlier clinical investigations [45], and this bias currently persists in the dosing guidelines used as our foremost source of alternative dosage adjustment recommendations [11]. This relationship likely will not hold true if currently available measures of SCr are used to calculate CrCL or if eGFR is not corrected for body surface area in unusually small or large adults. Lastly, other than an

informal acceptability survey of clinicians at the University of Colorado Hospital, the utility of this resource has not been clinically tested. Nonetheless, the appendant listing is believed to satisfy some, if not most, of the dosing information needs of busy clinicians involved in pharmacotherapy for patients with kidney disease.

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Disclaimer

Information presented is designed to facilitate clinical assessment of drug therapy and to enable discernment and determination of optimal drug dosing in persons with kidney disease. This information is intended to aid clinical decision making. This information must not be substituted for sound clinical judgment. Rather, it should be used with comprehensive understanding of pathological, pharmacological, and patient-specific clinical issues in order to provide the best treatment for seriously ill patients.

This document was originally designed for use by those who are competent healthcare professionals employed by or directly connected and having privileges with University of Colorado Hospital who rely on their clinical judgment and discretion. User assumes full responsibility for ensuring the appropriate use and reliance upon the information in view of all attendant circumstances, indications, and contraindications.

Abbreviations and Keys

CAPD	Chronic ambulatory peritoneal dialysis
CrCL	Creatinine clearance (mL/min)
CRRT	Continuous renal replacement therapy
CVVH	Continuous venovenous hemofiltration
CVVHD	Continuous venovenous hemodialysis
CVVHDF	Continuous venovenous hemodiafiltration
dL	Deciliter
doi	Digital object identifier
eCrCL	Estimated CrCL in mL/min using the Cockroft-Gault equation $CrCL = (140 - age) \times Weight/(72 \times SCr)$ for males and $0.85 \times CrCL$ for females where SCr is derived from rSCr in our hospital as follows: $SCr = (rSCr + 0.07)/0.99$; alternatively, this value may be approximated by increasing rSCr by 8 %. This may facilitate use of CrCL equations that were developed prior to availability and reporting of rSCr by clinical laboratories. In many patients, this may be closely approximated by eGFR with correction for body surface area [$eGFR \times (1.73\ m^2/BSA)$]. Other laboratories differ.
eGFR	Estimated GFR as calculated by the clinical laboratory using the 4-variable MDRD equation
ESRD	End-stage renal disease
FDA	United States Food and Drug Administration
g	Gram
GFR	Glomerular filtration rate in mL/min, usually determined by iohexol or ^{125}I-iothalamate clearance
IM	Intramuscular
IV	Intravenous
kg	Kilogram (actual body weight unless otherwise specified)
L	Liter
mg	Milligram
mL	Milliliter
NR	Non-renal
PRN	Pro re nata (as occasion requires; as necessary)
rSCr	Recalibrated serum creatinine (traceable to IDMS reference standard, mg/dL)
℞	Treatment
SCr	Serum creatinine (mg/dL)

Common systemic medications that normally do not require significant downward dose adjustment in the presence of renal impairment in adults (NR). Cautions are described if present in proprietary information.

Abacavir/Ziagen®
Abatacept/Orencia®
Abciximab/ReoPro®
Abiraterone/Zytiga™
AbobotulinumtoxinA/Dysport™
Acetylcysteine/Acetadote®
Adalimumab/Humira®
Adenosine/Adenocard®, Adenoscan®
Aflibercept (intravitreal)/Eylea™
Agalsidase beta/Fabrazyme®
Albendazole/Albenza®
Albumin/Albuminar®
Albuterol/Proventil®
Aldesleukin/Proleukin®
Alefacept/Amevive®
Alemtuzumab/Campath®
Alfentanil/Alfenta®
Alglucerase/Ceredase®
Alglucosidase alfa/Lumizyme™, Myozyme®
Alosetron/Lotronex®
$Alpha_1$-Proteinase Inhibitor ($Alpha_1$ Antitripsin)/Prolastin® C
Alpha galactosidase/Beano®
Alprazolam/Xanax®
Alprostadil/Caverject®
Alteplase/Activase®
Altretamine/Hexalen®
Aluminum hydroxide/Amphogel®, Alternagel®
Aluminum hydroxide and magnesium trisilicate or carbonate and alginic acid/Gaviscon®—Caution, contains small amounts of magnesium
Alvimopan/Entereg®
Ambenonium/Mytelase®
Ambrisentan/Letairis®
Amifostine/Ethyol®
Aminobenzoate potassium/Potaba®
Aminocaproic acid/Amicar®
Aminohippurate sodium
Aminolevulinic acid/Levulan®, Kerastick®
Aminophylline
Amiodarone/Cordarone®, Nexterone®
Amitriptyline/Elavil®
Amlodipine/Norvasc®
Amobarbital/Amytal®
Amoxapine/Asendin®
Amphotericin B/Fungizone®
Amphotericin B liposome/Ambisome®
Amyl nitrate
Anagrelide/Agrylin®
Anastrozole/Arimidex®
Anidulafungin/Eraxis™
Antihemophilic factor, human/Monoclate P®, Koate DVI®
Antihemophilic factor, recombinant/Recombinate®, Hexilate®
Antihemophilic factor/von Willebrand factor complex/Humate-P®
Anti-inhibitor coagulant complex/Feiba NF
Antithrombin III/Thrombate III®
Antithymocyte globulin, equine/Atgam®
Antithymocyte globulin, rabbit/Thymoglobulin®
Antivenin lactrodectus mactans
Aprepitant/Emend®
Argatroban
Arginine/R-gene®
Aripiprazole/Abilify®
Artemether and lumefantrine/Coartem®—Caution in severe renal impairment
Articaine 4 % and epinephrine/Orabloc™, Septocaine®
Ascorbic acid/Vitamin C
Asenapine/Saphris®
Asparaginase/Elspar®
Asparaginase *Erwinia chrysanthemi*/Erwinase™
Atomoxetine/Strattera®
Atorvastatin/Lipitor®
Atovaquone/Mepron®
Atracurium
Atropine
Avanafil/Stendra™
Axitinib/Inlyta®
Azficel-T/LaViv®
Azilsartan/Edarbi™
Azithromycin/Zithromax®—Caution in severe renal impairment (GFR < 10 mL/min)
Baclofen/Lioresal®—Caution in severe renal impairment
Balsalazide/Colazal®—Caution in severe renal impairment
Barium sulfate/Barobag™, Barosperse™, Cheetah™, Enhancer™, Entrobar™, HD 85™, HD™ 200 Plus, Intropaste™, Prepcat™, Scan C™, Tonojug™, Tonopaque™
Basiliximab/Simulect®
Beclomethasone/QVAR®, Beconase®
Belatacept/Nulojix®
Belimumab/Benlysta®
Belladonna and opium/B&O®
Benzphetamine/Didrex®
Benzonatate/Tessalon®
Benztropine/Cogentin®
Beta-carotene
Betamethasone/Celestone®
Betaxolol/Kerlone®—Caution, reduce dose in severe renal impairment
Bethanechol/Urecholine®
Bevacizumab/Avastin®
Bexarotene/Targretin®—Caution in severe renal impairment
Bicalutamide/Casodex®
Bisacodyl/Dulcolax®
Boceprevir/Victrelis™
Bortezomib/Velcade®
Bosentan/Tracleer®
Brentuximab/Adcetris™—Caution, the effects or risks imposed by renal impairment have not been determined
Bromocriptine/Cycloset®, Parlodel®
Brompheniramine/Brovex™
Budesonide/Entocort®
Bumetanide/Bumex®
Bupivacaine/Marcaine®
Buprenorphine/Buprenex®
Bupropion/Wellbutrin®—Caution in severe renal impairment
Busulfan/Myleran®
Butabarbital/Butisol®
C1 esterase inhibitor/Berinert®, Cinryze™
Cabazitaxel/Jevtana®—Caution in severe renal impairment
Cabergoline/Dostinex®
Caffeine sodium benzoate
Calcitonin/Miacalcin®
Calcitriol/Rocaltrol®
Calcium acetate/PhosLo®

Calcium carbonate/Tums®
Calcium citrate/Citracal®
Calcium polycarbophil/FiberCon®
Candesartan/Atacand®
Carbamazepine/Tegretol®
Carbidopa/Lodosyn®
Carbinoxamine/Palgic®
Carboprost/Hemabate®
Carisoprodol/Soma®
Carvedilol/Coreg®
Cascara sagrada
Caspofungin/Cancidas®
Castor oil
Cefaclor/Ceclor®
Ceftriaxone/Rocephin®
Certolizumab/Cimzia®—Caution, inadequate data to recommend dose in renal impairment
Cetrorelix/Cetrotide®
Cetuximab/Erbitux®
Cevimeline/Evoxac®
Chloramphenicol/Chloromycetin®—Caution in severe renal impairment
Chlordiazepoxide/Librium®
Chloroprocaine/Nesacaine®
Chloroquine/Aralen®
Chlorpheniramine/Chlor-trimeton®
Chlorpromazine/Thorazine®
Chlorzoxazone/Parafon®
Cholecalciferol/Vitamin D_3
Cholestyramine/Questran®
Choline magnesium trisalicylate/Trilisate®—Caution, monitor salicylate levels
Cilostazol/Pletal®—Caution in severe renal impairment (GFR < 25 mL/min)
Cinacalcet/Sensipar®
Cisatracurium/Nimbex®
Citalopram/Celexa®
Citric acid, sodium, and potassium citrate/Polycitra®—Caution with low urine output
Clemastine/Tavist®
Clevidipine/Cleviprex™
Clidinium and chlordiazepoxide/Librax®
Clindamycin/Cleocin®
Clobazam/Onfi™—Caution, no experience in severe renal impairment
Clomiphene/Clomid®, Serophene®
Clonazepam/Klonopin®
Clonidine/Catapres®
Clopidogrel/Plavix®
Clorazepate/Tranxene®
Cocaine
Collagenase *Clostridium histolyticum* injection/Xiaflex™
Colesevelam/Welchol®
Colestipol/Colestid®
Corticorelin/Acthrel®
Cortisone acetate
Cosyntropin/Cortrosyn®
Crizotinib/Xalkori®
Cromolyn/Gastrocrom®—Caution, consider dose reduction
Cyanocobalamin/Vitamin B_{12}
Cyclobenzaprine/Flexeril®
Cyclophosphamide/Cytoxan®—Caution, consider dose reduction in severe renal impairment (GFR < 10 mL/min) and/or chronic oral administration
Cyclosporine/Gengraf®, Neoral®, Sandimmune®
Cyproheptadine/Periactin®
Cytarabine/Cytosar®
Cytomegalovirus immune globulin/Cytogam®
Dacarbazine/DTIC®
Daclizumab/Zenapax®
Dactinomycin/Cosmegen®
Danazol/Cyclomen®
Dantrolene/Dantrium®
Dapsone
Darbepoetin alfa/Aranesp®
Darifenacin/Enablex®
Darunavir/Prezista®
Dasatinib/Sprycel®
Decitabine/Dacogen™
Deferiprone/Ferriprox®—Caution, not evaluated in patients with kidney disease
Degarelix/Firmagon®—Caution in severe renal impairment
Delavirdine/Rescriptor®
Denileukin/Ontak®
Denosumab/Prolia™, Xgeva™—Caution, patients with CrCL < 30 mL/min or on hemodialysis are at increased risk for hypocalcemia
Desflurane/Suprane®
Desipramine/Norpramin®
Desloratadine/Clarinex®—Caution in renal impairment, consider initiation with 5 mg every 48 h
Dexamethasone/Decadron®
Dexlansoprazole/Kapidex™
Dexmedetomidine/Precedex®
Dexmethylphenidate/Focalin®
Dextran 40/Gentran®—Caution in renal impairment
Dextroamphetamine/Dexedrine®
Dextroamphetamine and amphetamine/Adderall®
Dextromethorphan/Robitussin DM®
Diatrizoate/Gastrografin™, MD-Gastroview®
Diazepam/Valium®
Diazoxide/Proglycem®—Caution, consider reduced dosage in renal impairment
Dicloxacillin/Pathocil®
Dicyclomine/Bentyl®
Diethylpropion/Tenuate®
Diflunisal—Caution, no data in renal impairment
Digoxin immune Fab/Digibind®
Dihydrotachysterol/DHT™
Diltiazem/Cardizem®, Cartia®, Dilacor®, Taztia®, Tiazac®
Dimenhydrinate/Dramamine®
Dimercaprol/BAL®
Dinoprostone/Cervidil®, Prepidil®, Prostin E_2®
Diphenhydramine/Benadryl®
Diphenoxin and atropine/Motofen®
Diphenoxylate and atropine/Lomotil®
Diphtheria and tetanus toxoids and acellular pertussis vaccine/Adacel®, Boostrix®
Dipyridamole/Persantine®
Disulfiram/Antabuse®
Divalproex/Depakote®
Dobutamine/Dobutrex®
Docetaxel/Taxotere®
Docusate/Colace®
Dolasetron/Anzemet®
Donepezil/Aricept®
Dopamine/Intropin®
Doxapram/Dopram®
Doxazosin/Cardura®
Doxepin/Sinequan®
Doxercalciferol/Hectorol®
Doxorubicin/Adriamycin®
Doxylamine/Unisom®

Doxycycline/Vibramycin®
Dronabinol/Marinol®
Dronedarone/Multaq®
Droperidol/Inapsine®
Drotrecogin alfa/Xigris®
Dutasteride/Avodart®
Ecallantide/Kalbitor®—Caution, no data in renal impairment
Eculizumab/Soliris®
Edrophonium/Enlon®
Efalizumab/Raptiva®
Eletriptan/Relpax®
Eltrombopag/Promacta®—Caution, no data in renal impairment; monitor closely
Enflurane/Ethrane®
Enfuvirtide/Fuzeon®
Entacapone/Comtan®
Ephedrine
Epinephrine/Adrenalin®
Epirubicin/Ellence®
Epoetin alfa/Epogen®, Procrit®
Epoprostenol/Flolan®
Eprosartan/Teveten®
Ergocalciferol/Drisdol®
Ergoloid mesylates
Ergonovine/Ergotrate®
Ergotamine/Ergotrate®
Erlotinib/Tarceva™—Caution, no data in renal impairment
Erythromycin/EES®, Erythrocin®
Escitalopram/Lexapro®—Caution in severe renal impairment
Esmolol/Brevibloc®
Esomeprazole/Nexium®
Estazolam/ProSom®
Estradiol/Estrace®
Estramustine/Emcyt®
Estrogens, conjugated/Premarin®
Estrogens, esterified/Menest®
Estropipate/Ogen®
Eszopiclone/Lunesta®
Etanercept/Enbrel®
Ethanolamine/Ethamolin®
Ethinyl estradiol/Estinyl®
Ethosuximide/Zarontin®
Ethotoin/Peganone®
Ethosuximide/Zarontin®—Caution in patients with known renal disease
Etidronate/Didronel®—Caution, consider dosage decrease with reduction in GFR
Etomidate/Amidate®
Etravirine/Intelence™
Everolimus/Afinitor®, Zortress®
Exemestane/Aromasin®
Ezetemibe/Zetia®
Ezogabine/Potiga™—Caution, dose initiation should follow a conservative approach
Factor VIIa (recombinant)/NovoSeven®
Factor IX complex, human/Profilnine®
Fat emulsion/Intralipid®
Febuxostat/Uloric®—Caution in severe renal impairment
Felodipine/Plendil®
Fenoldopam/Corlopam®
Fentanyl/Sublimaze®, Subsys™
Ferric gluconate/Ferrlecit®
Ferrous sulfate/Feosol®
Ferumoxsil/GastroMARK™ Ferumoxytol/Feraheme™
Fesoterodine/Toviaz™—Caution, in severe renal impairment (CrCL < 30 mL/min) max dose = 4 mg/day
Fidaxomicin/Dificid™
Filgrastim/Neupogen®
Finasteride/Proscar®
Fingolimod/Gilenya™
Flavoxate/Urispas®
Floxuridine/FUDR®
Fludrocortisone/Florinef®
Flumazenil/Romazicon®
Fluorescein/AK-Fluor®, Fluorescite®
Fluorouracil/Adrucil®—Caution in severe renal impairment
Fluoxetine/Prozac®
Fluoxymesterone/Androxy®
Fluphenazine/Prolixin®
Flurazepam/Dalmane®
Flurbiprofen/Ansaid®
Fluvastatin/Lescol®—Caution in severe renal impairment
Fulvestrant/Faslodex®
Fluvoxamine/Luvox®
Folic acid/Folvite®
Follitropin alfa/Gonal-f®
Fosamprenavir/Lexiva®
Fosaprepitant/Emend®
Fosinopril/Monopril®
Fosphenytoin/Cerebyx®—Caution, see phenytoin
Fospropofol/Lusedra™
Frovatriptan/Frova®
Furosemide/Lasix®
Galsulfase/Naglazyme®
Ganirelix
Gefitinib/Iressa®
Gemcitabine/Gemzar®—Caution, no data in severe renal impairment
Gemtuzumab/Mylotarg®—Caution, no data in renal impairment
Glatiramer/Copaxone®—Caution, no data in renal impairment
Glimepiride/Amaryl®
Glucagon
Glucarpidase/Voraxaze®
Glutamine/Sympt-X®
Glycerin
Glycopyrrolate/Robinul®
Golimumab/Simponi™—Caution, no data in renal impairment
Goserelin/Zoladex®
Granisetron/Kytril®
Griseofulvin/Grifulvin®
Guaifenesin/Robitussin®
Guanabenz/Wytensin®
Guanfacine/Tenex®
Haloperidol/Haldol®
Hemin/Panhematin®
Heparin—Caution, monitor carefully; renal dysfunction may reduce clearance
Hepatitis B immune globulin/HepaGam B™
Hepatitis B vaccine (recombinant)/Engerix-B®
Histrelin/Vantas™
Human chorionic gonadotropin/Pregnyl®
Hyaluronate/Hylaform®, Juvederm®, Orthovisc®, Restylane®, Supartz™, Synvisc®
Hydralazine/Apresoline®
Hydrocodone and acetaminophen/Vicodin®
Hydrocortisone/Cortef®, Solu-Cortef®
Hydromorphone/Dilaudid®
Hydroxocobalamin/Cyanokit®
Hydroxychloroquine/Plaquenil®
Hydroxyzine/Atarax®, Vistaril®
Hyoscyamine/Levsin®
Hyoscyamine, atropine, scopolamine, and phenobarbital/Donnatal®
Ibritumomab/Zevalin®
Ibuprofen/Motrin®, Advil®—Caution, no data in advanced renal disease; not recommended

Ibutilide/Corvert®
Icatibant/Firazyr®
Iloperidone/Fanapt™
Iloprost/Ventavis®
Imiglucerase/Cerezyme®
Imipramine/Tofranil®
Immune globulin/Gamastan®, Flebogamma®, Gammagard®, Gamunex®, Octagam®, Vivaglobin®
Indinavir/Crixivan®
Indocyanine green
Indigo Carmine
Infliximab/Remicade®
Influenza virus vaccine (inactivated)/ Fluarix®, Fluzone®
Interferon alfa-2B/Intron® A
Interferon alfacon-1/Infergen®—Caution, no data available in patients with renal impairment
Interferon beta-1a/Avonex®, Rebif®
Interferon beta-1b/Betaseron®
Interferon beta-1b/Extavia®
Interferon gamma-1b/Actimmune®
Iodipamide meglumine/Cholografin™
Iodixanol/Visipaque®—Caution, possible contrast induced nephropathy
Iodoquinol/Yodoxin®
Iopamidol/Isovue®—Caution, possible contrast induced nephropathy
Iothalamate ^{125}I/Glofil®-125
Iothalamate meglumine/Conray®, Cysto-Conray™—Caution, possible contrast induced nephropathy
Ipecac
Ipilimumab/Yervoy™
Irbesartan/Avapro®
Irinotecan/Camptosar®—Caution, no data in renal impairment; not recommended in hemodialysis
Iron dextran/Dexferrum®, INFeD®
Iron sucrose/Venofer®
Isoniazid/Nydrazid®
Isoflurane/Forane®
Isoproterenol/Isuprel®
Isosorbide dinitrate/Isordil®
Isosorbide mononitrate/Imdur®
Isotretinoin/Accutane®
Isradipine/DynaCirc®—Caution, in renal impairment; starting dose is 5 mg daily
Ivacaftor/Kalydeco™
Ivermectin/Stromectol®
Ixabepilone/Ixempra®
Japanese encephalitis virus vaccine/ JE-Vax®
Ketamine/Ketalar®
Ketoconazole/Nizoral®
Labetalol/Trandate®
Lactulose/Enulose®
Lamotrigine/Lamictal®—Caution, minimal data available in patients with renal impairment
Lansoprazole/Prevacid®
Lanthanum/Fosrenol®
Lapatinib/Tykerb®
Leflunomide/Arava®—Caution in renal impairment
Letrozole/Femara®—No dosage adjustment required if CrCL ≥10 mL/min
Leucovorin calcium
Leuprolide/Lupron®
Levocarnitine/Carnitor®
Levodopa/Larodopa®
Levoleucovorin/Fusilev™
Levonorgestrel/Plan B®
Levorphanol/Levo-Dromoran®
Levothyroxine/Synthroid®
Lidocaine/Xylocaine®
Linagliptin/Tradjenta™
Linezolid/Zyvox®
Liothyronine/Cytomel®
Liotrix/Thyrolar®
Liraglutide/Victoza®
Lisdexamfetamine/Vyvanse™
Loperamide/Imodium®
Lopinavir and ritonavir/Kaletra®
Loratadine/Claritin®—Caution, if GFR < 30 mL/min starting dose is 10 mg every other day
Lorazepam/Ativan®—Caution, renal impairment contributes to risk of propylene glycol accumulation in patients receiving high-dose continuous infusion
Losartan/Cozaar®
Lovastatin/Mevacor®
Loxapine/Loxitane®
Lubiprostone/Amitiza®—Caution, no data in renal impairment
Maprotiline/Ludiomil®
Measles, mumps, and rubella virus vaccine/MMR® II
Mebendazole/Vermox®
Mechlorethamine/Mustargen®
Meclizine/Antivert®
Medroxyprogesterone/Provera®
Mefloquine/Lariam®
Megestrol/Megace®—Caution, no data in renal impairment
Menotropins/Repronex®
Mephobarbital/Mebaral®—Caution, reduce dose in renal impairment
Mepivacaine/Carbocaine®
Mesalamine/Asacol®, Pentasa®, Rowasa™—Caution, renal impairment may increase risk for blood and kidney problems; monitor blood counts and renal function
Mesna/Mesnex®—Caution, no data in renal impairment
Metaproterenol/Alupent®
Methamphetamine/Desoxyn®—Caution in renal impairment
Methimazole/Tapazole®
Methocarbamol (oral)/Robaxin®
Methoxsalen/Oxsoralen®
Methsuximide/Celontin®
Methyclothiazide/Enduron®
Methylene blue
Methylergonovine/Methergine®
Methylphenidate/Methylin™, Ritalin®
Methylprednisolone/Solu-Medrol®, Depo-Medrol®
Metolazone/Zaroxolyn®
Metoprolol/Lopressor®, Toprol-XL®
Metronidazole/Flagyl®
Metyrosine/Demser®
Mexiletine/Mexitil®
Micafungin/Mycamine®
Midazolam/Versed®
Mifepristone/Mifeprex®, Korlym™
Minocycline/Minocin®
Minoxidil/Loniten®
Mirtazapine/Remeron®—Caution, consider dose reduction in renal impairment; clearance is decreased 50 % if CrCL is <10 mL/min
Misoprostol/Cytotec®
Mitotane/Lysodren®
Mitoxantrone/Novantrone®—Caution, no data in renal impairment
Modafinil/Provigil®—Safety not established in renal impairment

Molindone/Moban®
Montelukast/Singulair®
Moxifloxacin/Avelox®
Multivitamins/Hexavitamin
Muromonab-CD3/Orthoclone OKT3®
Nabilone/Cesamet™—Caution, no data in renal impairment
Nafarelin/Synarel®
Nafcillin/Unipen®
Nalbuphine/Nubain®—Caution in renal impairment; consider use of reduced doses
Nalmefene/Revex®
Naloxone/Narcan®
Naltrexone/ReVia®
Natalizumab/Tysabri®
Nateglinide/Starlix®
Nefazodone/Serzone®
Nelarabine/Arranon®
Nelfinavir/Viracept®
Nesiritide/Natrecor®
Nevirapine/Viramune®
Niacin/Niaspan®—Caution in renal disease
Nicardipine/Cardene®—Caution, in renal insufficiency initiate oral therapy with 20 mg three times daily or extended release 30 mg twice daily
Nicotine/Nicorette®, Nicoderm®
Nifedipine/Procardia®, Adalat®
Nilotinib/Tasigna®
Nilutamide/Nilandron®
Nimodipine/Nimotop®
Nisoldipine/Sular®
Nitazoxanide/Alinia®—Caution, no data in renal impairment
Nitroglycerin/Nitrostat®
Nitroprusside/Nitropress®
Norepinephrine/Levophed®
Norethindrone/Aygestin®
Nortriptyline/Pamelor®
Nystatin/Nilstat®, Mycostatin®
Octreotide/Sandostatin®
Ofatumumab/Arzerra™
Olanzapine/Zyprexa®
Olmesartan/Benicar®
Olsalazine/Dipentum®—Caution, monitor renal function
Omalizumab/Xolair®
Omega-3-acid esters/Lovaza®
Omeprazole/Prilosec®
Omeprazole and sodium bicarbonate/Zegerid®
OnabotulinumtoxinA/Botox®
Ondansetron/Zofran®
Opium tincture
Orlistat/Xenical®, Alli™
Orphenadrine/Norflex™
Oxaliplatin/Eloxatin®—Caution in renal impairment; safety not established
Oxandrolone/Oxandrin®
Oxazepam/Serax®
Oxybutynin/Ditropan®
Oxycodone/Roxicodone®, Oxecta™, OxyContin®
Oxymetholone/Anadrol®-50
Oxytocin/Pitocin®
Paclitaxel/Taxol®
Palifermin/Kepivance®
Palivizumab/Synagis®
Palonosetron/Aloxi®
Pancrelipase/Creon®, Zenpep®
Panitumumab/Vectibix®—Caution, no data in renal impairment
Pantoprazole/Protonix®
Papaverine
Papillomavirus vaccine, human, recombinant/Gardasil®
Paregoric
Paricalcitol/Zemplar®
Paromomycin/Humatin®
Pazopanib/Votrient™
Pegaptanib/Macugen®
Pegaspargase/Oncaspar®
Pegfilgrastim/Neulasta®
Peginesatide/Omontys®—Caution, not indicated in patients with chronic kidney disease not on dialysis
Pegloticase/Krystexxa™
Pegvisomant/Somavert®—Caution, no data in renal impairment
Penbutolol/Levatol®
Penicillin G benzathine/Bicillin LA®
Penicillin G procaine/Wycillin®
Penicillin V potassium/Pen VK®
Pentamidine (inhaled)/Nebupent®
Pentobarbital/Nembutal®
Pentosan polysulfate/Elmiron®
Perphenazine/Trilafon®
Pertuzumab/Perjeta™
Phenelzine/Nardil®
Phenol
Phenoxybenzamine/Dibenzyline®
Phentermine/Ionamin®
Phentolamine/Regitine®
Phenylephrine/Neo-Synephrine®
Phosphorated carbohydrate solution/Emetrol(c)
Physostigmine
Phytonadione/AquaMephyton®, Mephyton®
Pilocarpine/Salagen®
Pimozide/Orap®
Pindolol/Visken®
Pioglitazone/Actos®
Perflutren/Definity®
Pneumococcal conjugate vaccine (7-valent)/Prevnar®
Pneumococcal polysaccharide vaccine/Pneumovax 23®
Polidocanol/Asclera®
Poliovirus vaccine (inactivated)/IPOL®
Polyethylene glycol 3350/Miralax®, MoviPrep®
Polyethylene glycol-electrolyte solution/Colyte®, Golytely®, Nulytely®
Porfimer/Photofrin®
Posaconazole/Noxafil®
Potassium iodide/SSKI®
Pralatrexate/Folotyn®
Pramlintide/Symlin®—Caution, no data in hemodialysis
Prasugrel/Effient™
Pravastatin/Pravachol®—Caution, with history of significant renal dysfunction, starting dose is 10 mg daily
Praziquantel/Biltricide®
Prazosin/Minipress®
Prednisolone/Orapred®, Prelone®
Prednisone/Deltasone®
Prilocaine/Citanest®
Primaquine
Procaine/Novocain®
Procarbazine/Matulane®
Prochlorperazine/Compazine®
Progesterone/Prometrium®
Promethazine/Phenergan®
Propafenone/Rythmol®
Propantheline/Pro-Banthine®
Propofol/Diprivan®
Propranolol/Inderal®
Propylthiouracil
Protamine
Protriptyline/Vivactil®

Pseudoephedrine/Sudafed®
Psyllium/Metamucil®
Pyrantel pamoate/Combantrin™
Pyrazinamide
Pyrethrins and piperonyl butoxide/Rid®
Pyridoxine
Pyrimethamine/Daraprim®
Quazepam/Doral®
Quetiapine/Seroquel®
Quinupristin and dalfopristin/Synercid®
Rabeprazole/AcipHex®
Rabies immune globulin/HyperRab®
Raloxifene/Evista®
Raltegravir/Isentress®
Ramelteon/Rozerem®
Ranibizumab/Lucentis®
Rasagiline/Azilect®—Caution, no data in severe renal impairment
Rasburicase/Elitek®
Regadenoson/Lexiscan®
Remifentanil/Ultiva®—Caution, in patients >65 years, decrease starting dose by 50 %
Reteplase/Retavase®
Rh_o(D) immune globulin/RhoGam®
Ribavirin (inhaled)/Virazole®
Rilpivirine/Endurant™
Riboflavin
Rifapentine/Priftin®
Rifaximin/Xifaxan™
Rilpivirine/Edurant™
Riluzole/Rilutek®
RimabotulinumtoxinB/Myobloc®
Risperidone injection/Risperdal® Consta®
Ritonavir/Norvir®
Rituximab/Rituxan®—Caution, minimal data in renal impairment
Rivastigmine/Exelon®
Rizatriptan/Maxalt®
Rocuronium/Zemuron®
Roflumilast/Daliresp™
Romidepsin/Istodax®
Romiplostim/Nplate™
Ropinirole/Requip®
Ropvivacaine/Naropin®
Rosiglitazone/Avandia®
Rufinamide/Banzel™
Sacrosidase/Sucraid®
Saquinavir/Invirase®
Sargramostim/Leukine®
Scopolamine/Transderm Scōp®
Secobarbital/Seconal®
Selegiline/Eldepryl®
Selenium (homeopathic)/Male Libido™
Sertraline/Zoloft®
Sevelamer/Renagel®
Sevoflurane/Ultane®
Sildenafil/Revatio®, Viagra®—Caution, if CrCL < 30 mL/min, consider starting dose at Viagra 25 mg
Simethicone/Mylicon®
Simvastatin/Zocor®
Sipuleucel-T/Provenge®
Sirolimus/Rapamune®
Sodium bicarbonate
Sodium bicarbonate/Alka Seltzer® Heartburn and Acid Indigestion Relief
Sodium citrate and citric acid/Bicitra®
Sodium oxybate/Xyrem®
Sodium polystyrene sulfonate/Kayexalate®
Sodium tetradecyl sulfate/Sotradecol®
Somatropin/Humatrope®
Sorbitol
Succimer/Chemet®—Caution in renal impairment
Succinylcholine/Anectine®
Sucralfate/Carafate®
Sufentanil/Sufenta®
Sulfadiazine
Sulfasalazine/Azulfidine®—Caution, 37 % cleared renally
Sulindac/Clinoril®—Caution, not recommended in advanced renal disease
Sumatriptan/Imitrex®
Tacrine/Cognex®
Tacrolimus/Prograf®—Caution, careful monitoring indicated in renal dysfunction
Tamoxifen/Nolvadex®
Telaprevir/Incivek™
Telmisartan/Micardis®
Temazepam/Restoril™
Temozolomide/Temodar®—Caution in severely impaired renal function (CrCL < 36 mL/min); no data in hemodialysis
Temsirolimus/Torisel®
Tenecteplase/TNKase®
Teniposide/Vumon®
Terazosin/Hytrin®
Teriparatide/Forteo®
Tesamorelin/Egrifta™—Caution, safety not established in renal impairment
Testosterone/Delatestryl®, Depo-Testosterone®
Tetanus immune globulin/HyperTet™
Tetrabenazine/Xenazine®
Tetracaine/Pontocaine®
Thalidomide/Thalomid®
Theophylline/Elixophyllin®, Uniphyl®
Thiabendazole/Mintezol®—Caution in renal impairment
Thiamine
Thioguanine/Tabloid®
Thioridazine/Mellaril®
Thiotepa—Caution, use in low dosage, monitor carefully
Thiothixene/Navane®
Thyroid/Armour Thyroid®
Thyrotropin alfa/Thyrogen®
Tiagabine/Gabitril®
Ticagrelor/Brilinta™
Ticlopidine/Ticlid®
Tigecycline/Tygacil®
Timolol/Blocadren®
Tinidazole/Tindamax®
Tipranavir/Aptivus®
Tocilizumab/Actemra®
Tolazamide/Tolinase®
Tolbutamide/Orinase®
Tolcapone/Tasmar®—Caution in severe renal impairment (CrCL < 25 mL/min)
Tolvaptan/Samsca™
Toremifene/Fareston®
Torsemide/Demadex®
Tranylcypromine/Parnate®
Trastuzumab/Herceptin®
Trazodone/Desyrel®
Treprostinil/Remodulin®
Tretinoin/Vesanoid®—Caution, no data in renal impairment
Triamcinolone/Kenalog®, Aristospan®
Triazolam/Halcion®
Trientine/Syprine®
Trifluoperazine/Stelazine®
Trihexyphenidyl/Artane®
Trimethobenzamide/Tigan®
Trimipramine/Surmontil®

Triprolidine and pseudoephedrine/Actifed®
Triptorelin/Trelstar®—Caution, rate of elimination is diminished in renal impairment
Typhoid Vaccine/Vivotif®
Urofollitropin/Bravelle®
Ursodiol/Actigall®, Urso®
Ustekinumab/Stelara®—Caution, minimal data in renal impairment
Valproic acid/Depacon®, Depakene®
Valsartan/Diovan®
Vancomycin (oral)/Vancocin®
Vardenafil/Levitra®
Varicella virus vaccine/Varivax®
Varicella-zoster immune globulin/VariZIG™
Vasopressin/Pitressin®
Vecuronium/Norcuron®
Vemurafenib/Zelboraf™
Verapamil/Calan®, Isoptin®—Caution in renal impairment
Verteporfin/Visudyne®
Vilazodone/Viibryd™
Vinblastine/Velban®
Vincristine/Oncovin®
Vinorelbine/Navelbine®
Vismodegib/Erivedge™
Vitamin A/Aquasol A®
Vitamin E/Aquasol E®
Vorinostat/Zolinza®
Warfarin/Coumadin®
Yohimbine/Yocon®
Zafirlukast/Accolate®
Zaleplon/Sonata®
Zanamivir/Relenza®
Zileuton/Zyflo®
Zinc sulfate/Zincate®
Ziprasidone/Geodon®
Zolmitriptan/Zomig®
Zolpidem/Ambien®, Intermezzo®
Zoster vaccine/Zostavax®

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Dosage Adjustment of Medications Eliminated by the Kidneys

Acamprosate/Campral®	**{Alcohol deterrent; putative glutamate/GABA receptor modifier}**	
Usual initial dose:	666 mg orally	
Usual maintenance dose:	666 mg (two 333 mg tablets) orally three times daily	
Typical maximum dose:	1,998 mg/day	
Proportion eliminated unchanged:	~90 %	

Adjustment for Kidney Disease

FDA-approved product labeling:	*CrCL >50 mL/min*	*666 mg orally three times daily*
	CrCL 30–50 mL/min	*333 mg orally three times daily*
	CrCL <30 mL/min	*Contraindicated*
Alternative adjustment:	*Data not available*	

Acarbose - Selected References

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Dosage Adjustment of Medications Eliminated by the Kidneys

Acarbose/Precose®	**{Antidiabetic; α-glucosidase inhibitor}**	
Usual initial dose:	25 mg orally one to three times daily with meals	
Usual maintenance dose:	50–100 mg orally three times daily with meals	
Typical maximum dose:	50 mg orally three times daily (weight ≤60 kg); 100 mg orally three times daily (weight >60 kg)	
Proportion eliminated unchanged:	35 %	
Adjustment for Kidney Disease		
FDA-approved product labeling:	*SCr >2.0 mg/dL*	*Clinical trials in diabetic patients with significant renal dysfunction (SCr >2.0 mg/dL) have not been conducted; therefore, treatment of these patients with (acarbose) is not recommended.*
Alternative adjustment:	*GFR >50 mL/min*	*50 mg orally three times daily with meals*
	GFR 10–50 mL/min	*Data not available. Preferably avoid unless no suitable alternative exists; if indeed necessary, begin with low doses and monitor carefully.*
	GFR <10 mL/min	*Data not available. Preferably avoid unless no suitable alternative exists; if indeed necessary, begin with low doses and monitor carefully.*
	Hemodialysis	*Data not available. Avoid unless no suitable alternative exists; if indeed necessary, begin with low doses and monitor carefully.*
	CAPD	*Data not available. Preferably avoid unless no suitable alternative exists; if indeed necessary, begin with low doses and monitor carefully.*
	CRRT	*Not applicable; preferably avoid unless no suitable alternative exists.*

Acebutolol - Selected References

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