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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.

Available Resources

To optimize 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. In this regard, available resources for adjustment of dosages of drugs in patients with renal insufficiency have been found to be 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 with regard to their recommendations for adjustments of dosage and dosage interval [1]. 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.

Commonly, official sources of information also have been shown to be inadequate and lacking completeness, especially with regard to medications prescribed for acutely ill patients. A recent evaluation of Food and Drug Administration (FDA)-approved product labeling for the 100 medications used most frequently in adult intensive care units (ICUs) revealed that information graded as minimally adequate to guide dose calculations for patients requiring hemodialysis or continuous renal replacement therapy (CRRT) was available for 22 (22%) and 1 (1%) of these medications, respectively [2]. Similarly, a review of 356 Summaries of Product Characteristics (SMPCs) approved by the European Medicines Agency found that 51% of SMPCs did not provide relevant or explicit information on medicine use in renal impairment and 80% of SMPCs did not provide information on use of the medicine in patients undergoing hemodialysis [3]. Further, frequent inconsistencies have been found not only among FDA-approved prescribing information concerning recommended renal dose adjustments for recently marketed medications but also clinicians' methods for interpretation and application of these recommendations [5]. One highly regarded authority concluded that despite the availability of numerous secondary sources of drug dosing information, drug prescribing in renal failure remains imprecise and relies on interpolation, extrapolation, and estimation [5].

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. Ideally, clinicians should be provided with convenient access to at least two reliable 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.

Controversy and Challenges

Dosage adjustment of medications eliminated by the kidneys is governed by measurement of excretory kidney function. This measure is best accomplished by direct determination of the glomerular filtration rate (GFR), which is the volume of blood plasma that is cleared of a solute that is freely filtered from the renal capillaries and is neither reabsorbed nor secreted by the kidneys per unit time. Classically, this may be accomplished by injection of inulin with measurement of its rate of urinary excretion or, more commonly, with use of radioactive tracers such as Tc^{99}-diethylenetriaminepentaacetic acid (DTPA), Cr^{51}-ethylenediaminetetraacetic acid (EDTA), I^{25}-iothalamate, or iohexol. In most patients, creatinine clearance (CrCL, the volume of blood plasma that is cleared of creatinine per unit time in a timed [usually 12- or 24-hour] urine collection) is a close approximation of GFR [6]. All of these techniques for measuring kidney function are procedurally demanding, technically complex, and, in acutely ill patients, often impractical. For these reasons, calculated estimates of GFR or CrCL based on serum creatinine (SCr) concentration are used in clinical practice.

For more than two decades, the FDA has imposed standardized labeling requirements for pharmaceutical products that are substantially eliminated by the kidneys [7]. Mandatory product labeling includes specific verbiage for recommended doses to be presented in tabular form according to categorical severity of renal impairment as determined by CrCL calculated with the Cockcroft–Gault (CG) equation ($CrCL = [(140 - age) \times Weight/(72 \times SCr)] \times 0.85$ if female) [8]. This equation was derived through analysis of relationships between measured CrCL and SCr in a Caucasian population housed at the Queen Mary Veterans' Hospital in Montreal, Quebec, Canada during the mid-1970s. Although it has served remarkably well through the years, at this time, use of the Cockcroft–Gault equation for determination of dose adjustments in patients with kidney disease may be less than optimal. Reasoning for this opinion is as follows:

- Similar to measured CrCL, the CG equation overestimates CrCL due to tubular secretion of creatinine.
- The CG equation was derived from a study population of 249 men aged 18 to 92 years with and without chronic kidney disease. Because no women were included in the population, the correction factor for female sex ($CrCL \times 0.85$) is hypothetical.
- The CG equation estimates CrCL that is not adjusted for body surface area. Modifications have been developed to overcome the variability and potential imprecision associated with use of measured body weight in the numerator of the CG equation. These modifications include use of ideal body weight [9], modified body weight [10], or no body weight [11]. Clinical evidence to suggest that weight modifications consistently improve accuracy and promote better dose recommendations is presently equivocal.
- Because creatinine production is influenced by muscle mass, diet, and physical activity, cachexia and frailty are often associated with subnormal SCr concentrations. Modifications of the CG equation were developed to overcome the potential for overestimation of CrCL associated with use of low SCr values in the denominator of the equation. These modifications typically comprise rounding of any SCr value <1.0 mg/dL upward to 1.0 mg/dL [12]. Clinical evidence to suggest that up-rounding of low SCr values improves accuracy and leads to better dose recommendations is presently equivocal.

- The assay methodology used in the development of the CG equation is no longer in use and samples from the study are not available. Therefore, the CG equation cannot be re-expressed for use with the standardized, isotope dilution mass spectroscopy-traceable SCr values now reported by clinical laboratories. Accuracy of the CG equation is worsened when standardized SCr values are utilized [13]. Because standardized SCr values on average are 5% to 20% lower than those used to derive the CG equation, generalized [14] and targeted techniques [15] have been proposed to individually increase standardized SCr values to levels that are suitable for use with the CG equation. However, the clinical utility of these methods remains unproven.

In light of these concerns, authorities recommend that the most accurate estimating equation should be used not only for pharmacokinetic studies and investigational drug development but also for dose determination of approved medications by clinicians [16]. These authorities present evidence that currently the most accurate estimating equation is the 4-variable Modification of Diet in Renal Disease (MDRD) Study equation as re-expressed for use with standardized SCr values [17, 18]. Accordingly, they provide further commentary that the MDRD equation may be preferred for estimation of kidney function for drug dosing in a majority of patients [16].

These sentiments are reflected in official policy changes. Recently posted FDA guidelines for drug development indicate that study designs must include subjects with varying degrees of renal impairment whose renal function is determined with calculation of both CrCL via CG and GFR via MDRD [19]. Product labeling for several recently approved medications from various pharmaceutical classes includes renal dose recommendations based on estimated GFR calculated with the MDRD with dose breakpoints set at categorical chronic kidney disease (CKD) severity levels as established by the Kidney Disease: Improving Global Outcomes (KDIGO) organization [20] (for examples, see the antimicrobials delafloxacin/Baxdela® and meropenem and vaborbactam/Vabomere®, the sodium-glucose cotransporter 2 (SGLT2) inhibitors canagliflozin/Invokana®, dapagliflozin/Farxiga®, empagliflozin/Jardiance®, and ertugliflozin/Steglatro™, the androgen receptor inhibitor darolutamide/Nubeqa™, the tyrosine kinase inhibitor afatinib/Gilotrif®, the dopamine-2 (D_2) antagonist antiemetic amisulpride/Barhemsys®, the Janus kinase 1 and 2 inhibitor antirheumatic baricitinib/Olumiant®, the central α_2 agonist lofexidine/Lucemyra™, and the selective dopamine and norepinephrine reuptake inhibitor (DNRI) solriamfetol/Sunosi™). It is anticipated that planned revisions to FDA guidance documents will include broadened provisions for dose adjustment according to GFR and CKD category [21].

Results of an extensive simulation study comparing more than 5500 drug dosages determined through use of FDA-approved product guidelines and estimated GFR or CrCL calculated from standardized SCr values in a diverse patient population demonstrated 88% concordance [22]. This indicates that in approximately 9 out of 10 cases, there is no difference in the drug dose that would be administered when either the CG or the MDRD equation was used to discern an appropriate dose. Based on these and other considerations, the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK, formerly the National Kidney Diseases Program [NKDEP] Laboratory Working Group) currently suggests that either estimated GFR or CrCL may be utilized for drug dosing [23]. Contrastingly, similar considerations of comparative renal estimation data by members of the Nephrology Practice and Research Network of the American College of Clinical Pharmacy resulted in the development of a comprehensive algorithmic approach to drug dosing decisions that promotes optimization of individualized risk:benefit assessments through stepwise comparisons of CG and MDRD outputs balanced against acuity or disease severity and the medication's therapeutic index (Fig. 1) [24]. Presently, use of this algorithmic methodology affords what is arguably the optimal means by which to maximize therapeutic benefit from creatinine-based assessment of kidney function. This is particularly true in patients with serious or critical illnesses and rapidly changing kidney function. Clinicians must strive to meet the challenge of optimizing

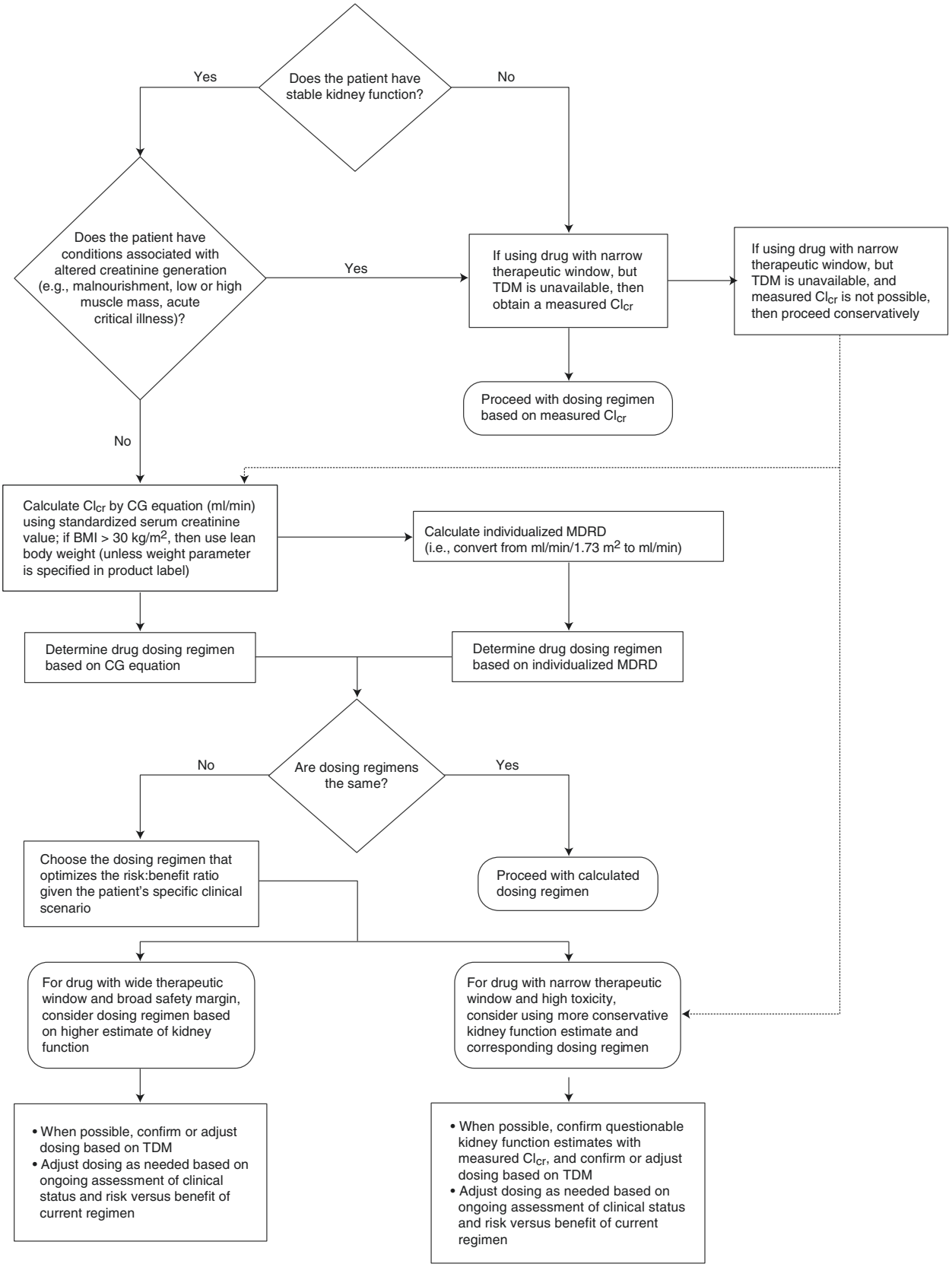

Fig. 1 Algorithm for use of serum creatinine–based kidney function assessments in drug dosing. Cl_{cr} denotes creatinine clearance, CG denotes Cockcroft–Gault, BMI denotes body mass index, MDRD denotes Modification of Diet in Renal Disease, TDM denotes therapeutic drug monitoring. (Adapted from Nyman et al. [24] with permission)

pharmacotherapy for these patients through the development of a personalized strategy of preemptive action that utilizes the algorithm and other tools as part of a constantly evolving plan of care.

Limitations

The appendant listing was designed to close some identified gaps in information concerning dosage adjustment of medications eliminated by the kidneys. This resource listing displays several strengths including alphabetical format, completeness, referencing, and alternative dosage recommendations based on GFR. In 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 vetted evidence-based recommendations. Secondly, our information was compiled with use of secondary or tertiary data sources with corroboration of the primary literature. In most cases, access to the primary literature was limited to use of only the National Library of Medicine's PubMed indexing system. Thirdly, dosage information is provided for adults receiving systemic medications. No neonatal, pediatric, or adolescent dose recommendations are provided, and no information is included on inhalational, topical, transdermal, or implanted drugs. Fourthly, for many drugs, dose finding studies have not been performed using actual or estimated GFR. Consequently, in the appendant listing, dosage suggestions that are displayed according to GFR represent categorical approximations based upon existing information. These approximations are commonly based on information that is considered reliable but taken from previously available CrCL-related data. 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.

References

1. Vidal L, Shavit M, Fraser A, Paul M, Leibovici L. Systematic comparison of four sources of drug information regarding adjustment of dose for renal function. BMJ. 2005;331:263–5.
2. Eastman C, Erstad BL. Availability of information for dosing commonly use medications in special ICU populations. Am J Health Syst Pharm. 2020;77:529–31.
3. Dowling TC, Matzke GR, Murphy JE, Burckhart GJ. Evaluation of renal drug dosing: prescribing information and clinical pharmacist approaches. Pharmacotherapy. 2010;30:776–86.
4. Salgado TM, Arguello B, Martinez-Martinez F, Benrimoj SI, Fernandez-Llimos F. Clinical relevance of information in the Summaries of Product Characteristics for dose adjustment in renal impairment. Eur J Clin Pharmacol. 2013;69:1973–9.
5. Aronoff GA. Dose adjustment in renal impairment: response from Drug Prescribing in Renal Failure [letter]. BMJ. 2005;331:293–4.
6. Bennett WM, Porter GA. Endogenous creatinine clearance as a clinical marker of glomerular filtration rate. Br Med J. 1971;4:84–6.
7. U.S. Department of Health and Human Services, Food and Drug Administration and the Center for Drug Evaluation and Research (CDER). Guidance for Industry. Pharmacokinetics in patients with impaired renal function: study design, data analysis, and impact on dosing and labeling. https://www.fda.gov/media/71334/download. Accessed 10 Apr 2020.
8. Cockcroft DW, Gault MH. Prediction of creatinine clearance from serum creatinine. Nephron. 1976;16:31–41.
9. Demirovic, JA, Pai, AB, Pai, MP. Estimation of creatinine clearance in morbidly obese patients. Am J Health Syst Pharm 2009;66:642–8.
10. Winter MA, Guhr KN, Berg GM. Impact of various body weights and serum creatinine concentrations on the bias and accuracy of the Cockcroft-Gault equation. Pharmacotherapy. 2012;32:604–12.
11. Ariano RE, Zelenitsky SA, Poncsak KR, Davis JC, Vercaigne LM. No role for patient body weight on renal function assessment for drug dosing. J Antimicrob Chemother. 2017;72:1802–11.

12. Robert, S, Zarowitz, BJ, Peterson, EL, Dumler, F. Predictability of creatinine clearance estimates in critically ill patients. Crit Care Med 1993;21:1487–95.
13. Stevens LA, Manzi J, Levey AS, et al. Impact of creatinine calibration on performance of GFR estimating equations in a pooled individual patient database. Am J Kidney Dis. 2007;50:21–35.
14. Wade WE, Spruill WJ. New serum creatinine assay standardization: implications for drug dosing. Ann Pharmacother 2007;41:475–80.
15. Jones MA, Golightly LK, Stolpman NM. Use of recalibrated serum creatinine concentrations for adjustment of drug dosages: determination of values compatible with conventional dosing recommendations. Ann Pharmacother 2011;45:748–56.
16. Stevens LA, Levey AS. Use of the MDRD Study equation to estimate kidney function for drug dosing. Clin Pharmacol Ther. 2009;85:465–7.
17. Levey AS, Coresh J, Greene T, et al. Expressing the Modification of Diet in Renal Disease Study equation for estimating glomerular filtration rate with standardized serum creatinine values. Clin Chem. 2007;53:766–72.
18. Levey AS, Coresh J, Greene T, et al. Using standardized serum creatinine values in the Modification of Diet in Renal Disease Study equation for estimating glomerular filtration rate. Ann Intern Med. 2006;145:247–54.
19. Gieser G. Clinical pharmacology 1: phase 1 studies and early drug development. https://www.fda.gov/media/84920/download. Accessed 10 Apr 2020.
20. Stevens PE, Levin A, Bilous RW, et al. Evaluation and management of chronic kidney disease: synopsis of the Kidney Disease: Improving Global Outcomes 2012 clinical practice guideline. Ann Intern Med. 2013;158:825–30.
21. New & revised draft guidances CDER plans to publish during calendar year 2020. Pharmacokinetics in patients with impaired renal function: study design, data analysis and impact on dosing and labeling. https://www.fda.gov/media/134778/download. Accessed 10 Apr 2020.
22. Stevens LA, Nolin TD, Richardson MM, et al. Comparison of drug dosing recommendations based on measured GFR and kidney function estimating equations. Am J Kidney Dis. 2009;54:33–42.
23. National Institute of Diabetes and Digestive and Kidney Diseases. CKD & Drug Dosing. Information for providers: estimation of kidney function for prescription medication dosage in adults. https://www.niddk.nih.gov/health-information/professionals/advanced-search/ckd-drug-dosing-providers. Accessed 10 Apr 2020.
24. Nyman HA, Dowling TC, Hudson JQ, St Peter WL, Joy MS, Nolin TD. Comparative evaluation of the Cockcroft-Gault equation and the Modification of Diet in Renal Disease (MDRD) Study equation for drug dosing: an opinion of the Nephrology Practice and Research Network of the American College of Clinical Pharmacy. Pharmacotherapy. 2011;31:1130–44.

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Contents

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 the 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

A1C	Glycosylated hemoglobin (%)
ACE	Angiotensin converting enzyme
AKI	Acute kidney injury
APD	Automated peritoneal dialysis
ARB	Angiotensin receptor blocker
AUC	Area under the plasma concentration/time curve
BMI	Body mass index {weight (kg)/[height (m)]^2}
BSA	Body surface area (m^2)
BUN	Blood urea nitrogen (mg/dL)
CAPD	Chronic ambulatory peritoneal dialysis
CKD	Chronic kidney disease
Stage 1	Normal or high kidney function: GFR ≥90 mL/min
Stage 2	Mildly decreased kidney function: GFR 60–89 mL/min
Stage 3a	Mildly to moderately decreased kidney function: GFR 45–59 mL/min
Stage 3b	Moderately to severely decreased kidney function: GFR 30–44 mL/min
Stage 4	Severely decreased kidney function: GFR 15–29 mL/min
Stage 5	Kidney failure: GFR <15 mL/min
CKDepi	Chronic Kidney Disease Epidemiology equation
C_{max}	Maximal or peak post-dose plasma drug concentration
CNS	Central nervous system
CrCL	Creatinine clearance (mL/min)
CRRT	Continuous renal replacement therapy
CVVH	Continuous venovenous hemofiltration
CVVHD	Continuous venovenous hemodialysis
CVVHDF	Continuous venovenous hemodiafiltration
dL	Deciliter (100 mL)
https://doi.org/	Digital object identifier
CrCL	Estimated CrCL in mL/min using the Cockcroft–Gault equation [CrCL = (140 - age) × Weight / (72 × SCr) for males and 0.85 × CrCL for females where SCr is derived from recalibrated (isotope dilution mass spectroscopy {IDMS} standardized) SCr in our hospital as follows: SCr = (recalibrated SCr + 0.07) / 0.99]; alternatively, this value may be approximated by increasing recalibrated SCr by 8%. This may facilitate use of CrCL equations that were developed prior to availability and reporting of recalibrated SCr by clinical laboratories. In many patients, this may be closely approximated by the estimated GFR with correction for body surface area [GFR × (1.73 m^2/BSA)].
doi	Digital object identifier
e	Electronic format identifier prefix or estimated sign
EGFR	Endothelial growth factor receptor
ESRD	End-stage renal disease
et al.	And others

FDA	United States Food and Drug Administration
g	Gram
h or hr	Hour
GFR	Glomerular filtration rate in mL/min, formally determined by iohexol, ^{125}I-iothalamate, or Cr^{51}-EDTA clearance. Throughout the monographs in this publication, use of GFR for dosage determination represents either actual GFR as above or, more commonly, the estimated GFR as calculated by the clinical laboratory using the 4-variable MDRD equation. Although units of dosing GFR are shown in this reference as mL/min, the MDRD results in units of mL/min/1.73 m^2. In unusually small or large or overweight/obese patients, dosing GFR should be corrected by multiplying the GFR as determined with the MDRD equation by the division product of 1.73 m^2/BSA.
HbA1c	Glycosylated hemoglobin
HER	Human epidermal growth factor receptor
HIV	Human immunodeficiency virus
https	Hypertext transfer protocol secure
IBW	Ideal body weight
IM	Intramuscular
IP	Intraperitoneally
IV	Intravenous
kg	Kilogram (actual body weight unless otherwise specified)
KDIGO	Kidney Disease: Improving Global Outcomes
L	Liter
m	Meter
m^2	Square meter
MDRD	Modification of Diet in Renal Disease equation
mg	Milligram
MIC	Minimum inhibitory concentration
mL	Milliliter
NKF	National Kidney Foundation
NR	Nonrenal
PIRRT	Prolonged intermittent renal replacement therapy
PRN	Pro re nata (as occasion requires; as necessary)
Q or q	Every
qs	Quantity sufficient or enough
®	Registered trademark symbol
RAAS	Renin angiotensin aldosterone system
℞	Take or treatment
SCr	Serum creatinine (mg/dL)
SLED	Sustained or slow low-efficiency dialysis
TBW	Total body weight
™	Trademark symbol
VEGF	Vascular endothelial growth factor

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

Abacavir/Ziagen®
Abaloparatide/Tymlos™
Abatacept/Orencia®
Abciximab/ReoPro®
Abemaciclib/Verzenio®—Caution, pharmacokinetics in patients with CrCL <30 mL/min or ESRD are unknown
Abiraterone/Zytiga™
Abobotulinumtoxin A/Dysport™
Acalabrutinib/Calquence®—Caution, has not been evaluated in patients with GFR <29 mL/min or those requiring hemodialysis
Acetylcysteine/Acetadote®
Adalimumab/Humira®
Adenosine/Adenocard®, Adenoscan®
ado-Trastuzumab emtansine/Kadcyla®
Afamelanotide/Scenesse®
Aflibercept (intravitreal)/Eylea™
Agalsidase beta/Fabrazyme®
Air polymer-type A/ExEm® Foam
Albendazole/Albenza®
Albiglutide/Tanzeum®
Albumin/Albuminar®
Albuterol/Proventil®
Aldesleukin/Proleukin®
Alectinib/Alecensa®—Caution, safety has not been studied in patients with CrCL <30 mL/min
Alefacept/Amevive®
Alemtuzumab/Campath®
Alendronate/Fosamax®, Binosto®—Caution, not recommended in patients with CrCL <35 mL/min
Alfentanil/Alfenta®
Alglucerase/Ceredase®
Alglucosidase alfa/Lumizyme™, Myozyme®
Alirocumab/Praluent®
Alosetron/Lotronex®
Alpelisib/Piqray®
Alpha 1-proteinase inhibitor (alpha 1 antitrypsin)/Prolastin® C
Alpha galactosidase/Beano®
Alprazolam/Xanax®
Alprostadil/Caverject®
Alteplase/Activase®
Altretamine/Hexalen®
Aluminum hydroxide/Amphogel®, Alternagel®
Aluminum hydroxide/magnesium trisilicate or carbonate/alginic acid/Gaviscon®—Caution, contains small amounts of magnesium
Alvimopan/Entereg®
Ambenonium/Mytelase®
Ambrisentan/Letairis®
Amifampridine/Firdapse®—Caution, starting dose should be the lower of the usual range, 15 mg orally 3 times daily; no dose recommendation can be made for patients with ESRD
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®
Angiotensin II/Giapreza™
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 *Latrodectus mactans*
Apalutamide/Erleada®
Apixaban/Eliquis®—Caution, although dosage reductions are not recommended for patients with any degree of renal impairment including those with ESRD on chronic hemodialysis for most indications, for reduction of risk of stroke and systemic embolism in patients with nonvalvular atrial fibrillation, the recommended dose should be limited to 2.5 mg orally twice daily in patients >80 years of age, body weight ≤ 60 kg, and those with SCr ≥1.5 mg/dL
Aprepitant/Emend®
Argatroban
Arginine/R-Gene®
Aripiprazole/Abilify®
Aripiprazole lauroxil/Aristada®
Artemether and lumefantrine/Coartem®—Caution in severe renal impairment
Articaine and Epinephrine/Orabloc™, Septocaine®
Ascorbic acid/vitamin C
Asenapine/Saphris®
Asfotase alfa/Strensiq®
Asparaginase/Elspar®
Asparaginase *Erwinia chrysanthemi*/Erwinase™
Atezolizumab/Tecentriq®
Atomoxetine/Strattera®
Atorvastatin/Lipitor®
Atovaquone/Mepron®
Atracurium
Atropine
Avanafil/Stendra™—Pharmacokinetics in patients with severe renal disease or on renal dialysis have not been studied; do not use in such patients
Avapritinib/Ayvakit™
Avatrombopag/Doptelet®
Avelumab/Bavencio®
Axitinib/Inlyta®
Azficel-T/LaViv®
Azilsartan/Edarbi™

Azithromycin/Zithromax®—Caution in severe renal impairment (GFR <10 mL/min)
Baloxavir/Xofluza®
Balsalazide/Colazal®, Giazo®—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®
Bedaquiline/Sirturo®
Belatacept/Nulojix®
Belimumab/Benlysta®
Belinostat/Beleodaq®—Caution, there is insufficient data to recommend a dose in patients with CrCL ≤39 mL/min
Belladonna and opium/B&O®
Bempedoic acid/Nexletol™—Caution, clinical trials did not include patients with severe renal impairment (stage 4, GFR <30 mL/min) or patients with ESRD on dialysis
Benralizumab/Fasenra®
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
Bezlotoxumab/Zinplava™
Bicalutamide/Casodex®
Bictegravir, emtricitabine, and tenofovir alafenamide/Biktarvy®—Caution, not recommended in patients with CrCL <30 mL/min
Binimetinib/Mektovi®
Bisacodyl/Dulcolax®
Blinatumomab/Blincyto®—Caution, there is no information available in patients with CrCL <30 mL/min or patients on hemodialysis
Boceprevir/Victrelis™
Bortezomib/Velcade®
Bosentan/Tracleer®
Bremelanotide/Vyleesi™—Caution, use with caution in patients with GFR <30 mL/min because these patients may have an increase in the incidence and severity of adverse reactions
Brentuximab/Adcetris™—Caution, the effects or risks imposed by renal impairment have not been determined
Brexanolone/Zulresso™—Caution, avoid use in ESRD because of the potential accumulation of the solubilizing agent, betadex sulfobutyl ether sodium
Brexpiprazole/Rexulti™—Caution, with CrCL <60 mL/min, the maximum recommended dose is 2 mg once daily for patients with major depressive disorder and 3 mg once daily for patients with schizophrenia
Brigatinib/Alunbrig™—Caution, pharmacokinetics and safety have not been studied in patients with CrCL <30 mL/min
Brivaracetam/Briviact®—Caution, there is no data in patients with ESRD undergoing dialysis; use not recommended
Brodalumab/Siliq™
Brolucizumab-dbll/Beovu®
Bromocriptine/Cycloset®, Parlodel®
Brompheniramine/Brovex™
Budesonide/Entocort® EC, Uceris®
Bumetanide/Bumex®
Bupivacaine/Marcaine®
Buprenorphine/Buprenex®
Buprenorphine and naloxone/Bunavail®
Buprenorphine and naloxone/Zubsolv®
Buprenorphine and naltrexone/Contrave®
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®
Cabozantinib/Cometriq®
Caffeine sodium benzoate
Calaspargase pegol-mknl/Asparlas™
Calcitonin/Miacalcin®
Calcitriol/Rocaltrol®
Calcium acetate/PhosLo®
Calcium carbonate/Tums®
Calcium citrate/Citracal®
Calcium polycarbophil/FiberCon®
Candesartan/Atacand®
Cangrelor/Kengreal®
Cannabidiol/Epidiolex®
Caplacizumab-yhdp/Cablivi®
Carbamazepine/Tegretol®
Carbidopa/Lodosyn®
Carbinoxamine/Palgic®, Karbinal® ER
Carboprost/Hemabate®
Carfilzomib/Kyprolis®
Cariprazine/Vraylar®—Caution, has not been evaluated in patients with CrCL <30 mL/min; use is not recommended in this patient population
Carisoprodol/Soma®
Carvedilol/Coreg
Cascara sagrada
Caspofungin/Cancidas®
Castor oil
Cefaclor/Ceclor®
Ceftriaxone/Rocephin®
Cemiplimab-rwlc/Libtayo®
Cenobamate/Xcopri®—Caution, has not been studied in ESRD and use is not recommended
Ceritinb/Zykadia®
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®
Cholic acid/Cholbam™
Choline magnesium trisalicylate/Trilisate®—Caution, monitor salicylate levels
Ciclesonide/Zetonna®
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, there is essentially no experience in severe renal impairment or ESRD
Clomiphene/Clomid®, Serophene®
Clonazepam/Klonopin®
Clonidine/Catapres®
Clopidogrel/Plavix®
Clorazepate/Tranxene®
Cocaine
Collagenase
Clostridium histolyticum injection/Xiaflex™
Cobimetinib/Cotellic®
Colesevelam/Welchol®
Colestipol/Colestid®
Copanlisib/Aliqopa™
Corticorelin/Acthrel®
Cortisone acetate
Cosyntropin/Cortrosyn®
Crizanlizumab-tmca (NR)/Adakveo®
Crizotinib/Xalkori®
Crofelemer/Mytesi®
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®
Cysteamine/Procysbi®
Cytarabine/Cytosar®
Cytomegalovirus immune globulin/Cytogam®
Dabrafenib/Tafinlar®
Dacarbazine/DTIC®
Daclatasvir/Daklinza®
Daclizumab/Zenapax®
Dacomitinib/Vizimpro®
Dactinomycin/Cosmegen®
Danazol/Cyclomen®
Dantrolene/Dantrium®, Ryanodex®
Dapsone
Daratumumab/Darzalex®
Darbepoetin alfa/Aranesp®
Darifenacin/Enablex®
Darunavir/Prezista®
Dasatinib/Sprycel®
Decitabine/Dacogen™
Deferiprone/Ferriprox®—Caution, not evaluated in patients with kidney disease
Defibrotide/Defitelio®
Deflazacort/Emflaza™
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
Deoxycholic acid/Kybella®
Desflurane/Suprane®
Desipramine/Norpramin®
Desloratadine/Clarinex®—Caution in renal impairment, consider initiation with 5 mg every 48 h
Deutetrabenazine/Austedo®
Dexamethasone/Decadron®
Dexlansoprazole/Kapidex™
Dexmedetomidine/Precedex®
Dexmethylphenidate/Focalin®
Dextran 40/Gentran®—Caution in renal impairment
Dextroamphetamine/Dexedrine®
Dextroamphetamine/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 E2®
Diphenhydramine/Benadryl®
Diphenoxin/atropine/Motofen®
Diphenoxylate/atropine/Lomotil®
Diphtheria and tetanus toxoids/acellular pertussis vaccine/Adacel®, Boostrix®
Dipyridamole/Persantine®
Diroximel/Vumerity™—Caution, not recommended in moderate or severe renal impairment due to an increase in the exposure of a major inactive metabolite, 2-hydroxyethyl succinimide
Disulfiram/Antabuse®
Divalproex/Depakote®
Dobutamine/Dobutrex®
Docetaxel/Taxotere®
Docusate/Colace®
Dolasetron/Anzemet®
Dolutegravir/Tivicay®
Donepezil/Aricept®
Dopamine/Intropin®
Doravirine/Pifeltro™
Doxapram/Dopram®
Doxazosin/Cardura®
Doxepin/Sinequan®
Doxercalciferol/Hectorol®
Doxorubicin/Adriamycin®
Doxylamine/Unisom®
Doxylamine and pyridoxine/Diclegis®
Doxycycline/Vibramycin®, Acticlate®
Dronabinol/Marinol®

Dronedarone/Multaq®
Droperidol/Inapsine®
Drotrecogin alfa/Xigris®
Droxidopa/Northera®
Dulaglutide/Trulicity®
Dupilumab/Dupixent®
Durvalumab/Imfinzi™
Duvelisib/Copiktra™
Dutasteride/Avodart®
Ecallantide/Kalbitor®—Caution, no data in renal impairment
Eculizumab/Soliris®
Edaravone/Radicava®
Edrophonium/Enlon®
Efalizumab/Raptiva®
Elagolix/Orilissa®
Elapegademase-lvlr/Revcovi™
Elbasvir and grazoprevir/Zepatier®
Eletriptan/Relpax®
Elexacaftor, tezacaftor, and ivacaftor/Trikafta®
Eligulstat/Cerdelga®
Elosulfase alfa/Vimizim™
Elotuzumab/Empliciti®
Eltrombopag/Promacta®—Caution, no data in renal impairment; monitor closely
Eluxadoline/Viberzi®
Elvitegravir/Tybost®
Emapalumab-lzsg/Gamifant™
Emicizumab-kxwh/Hemlibra®
Enasidenib/Idhifa®
Encorafenib/Braftovi®
Enflurane/Ethrane®
Enfortumab vedotin-ejfv/Padcev™
Enfuvirtide/Fuzeon®
Entacapone/Comtan®
Entrectinib/Rozlytrek™
Enzalutamide/Xtandi®
Ephedrine
Epinephrine/Adrenalin®, Auvi-Q®, EpiPen®
Epirubicin/Ellence®
Epoetin alfa/Epogen®, Procrit®
Epoprostenol/Flolan®
Eprosartan/Teveten®
Eptinezumab-jjmr/Vyepti™
Eravacycline/Xerava™
Erdafitinib/Balversa™
Erenumab-aooe/Aimovig®
Ergocalciferol/Drisdol®
Ergoloid mesylates
Ergonovine/Ergotrate®
Ergotamine/Ergomar®
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®, Minivelle®
Estramustine/Emcyt®
Estrogens, conjugated/Premarin®
Estrogens, conjugated/bazedoxifene/Duavee®—Caution, pharmacokinetics have not been evaluated in patients with renal impairment and use not recommended
Estrogens, esterified/Menest®
Estropipate/Ogen®
Eszopiclone/Lunesta®
Etanercept/Enbrel®
Etelcalcetide/Parsabiv®
Eteplirsen/Exondys 51™
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®
Evolocumab/Repatha®
Exemestane/Aromasin®
Exenatide/Bydureon®
Ezetemibe/Zetia®
Ezogabine/Potiga™—Caution, dose initiation should follow a conservative approach
Factor VIIa (recombinant)/NovoSeven®
Factor IX complex, human/Profilnine®
Fam-trastuzumab deruxtecan-nxki/Enhertu®
Fat emulsion/Intralipid®
Febuxostat/Uloric®—Caution in severe renal impairment
Felodipine/Plendil®
Fenoldopam/Corlopam®
Fentanyl/Sublimaze®, Subsys™
Ferric gluconate/Ferrlecit®
Ferric maltol/Accrufer™
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®
Filgrastim-aafi/Nivestym™
Filgrastim-sndz/Zarxio®
Finasteride/Proscar®
Fingolimod/Gilenya™
Flavoxate/Urispas®
Flibanserin/Addyi™
Florbetaben F 18/Neuraceq™
Florbetapir F 18/Amyvid™
Floxuridine/FUDR®
Fluciclovine F^{18}/Axumin™
Fludrocortisone/Florinef®
Flumazenil/Romazicon®
Fluorescein/AK-Fluor®, Fluorescite®
Fluorodopa F 18
Fluorouracil/Adrucil®—Caution in severe renal impairment
Fluoxetine/Prozac®
Fluoxymesterone/Androxy®
Fluphenazine/Prolixin®
Flurazepam/Dalmane®
Flurbiprofen/Ansaid®
Flutemetamol F 18/Vizamyl™
Fluvastatin/Lescol®—Caution in severe renal impairment
Fulvestrant/Faslodex®
Fluvoxamine/Luvox®
Folic acid/Folvite®
Follitropin alfa/Gonal-f®
Fosamprenavir/Lexiva®
Fosaprepitant/Emend®
Fosinopril/Monopril®
Fosnetupitant and palonosetron/Akynzeo®—Caution, the pharmacokinetics of neither netupitant (the active constituent derived from metabolic hydrolysis of the prodrug fosnetupitant) nor palonosetron have been studied in ESRD; the manufacturer advises avoidance of use in patients with severe renal impairment and ESRD

Fosphenytoin/Cerebyx®—Caution, see phenytoin
Fospropofol/Lusedra™
Fostamatinib/Tavalisse™
Fremanezumab-vfrm/Ajovy®
Frovatriptan/Frova®
Furosemide/Lasix®
Ga 68 DOTATOC
Galcanezumab-gnlm/Emgality®
Gallium Ga^{68} dotatate/Netspot™
Galsulfase/Naglazyme®
Ganirelix acetate
Gefitinib/Iressa®
Gemcitabine/Gemzar®—Caution, no data in severe renal impairment
Gemtuzumab/Mylotarg®—Caution, no data in renal impairment
Gilteritinib/Xospata®
Givosiran/Givlaari™
Glasdegib/Daurismo™
Glatiramer/Copaxone®—Caution, no data in renal impairment
Glecaprevir and pibrentasvir/Mavyret™
Glimepiride/Amaryl®
Glucagon/Baqsimi™
Glucarpidase/Voraxaze®
Glutamine/Sympt-X®
Glycerin
Glycerol phenylbutyrate/Ravicti®
Glycopyrrolate/Robinul®
Golimumab/Simponi®, Simponi Aria®—Caution, no data in renal impairment
Golodirsen/Vyondys 53™
Goserelin/Zoladex®
Granisetron/Kytril®
Griseofulvin/Grifulvin®
Guaifenesin/Robitussin®
Guanabenz/Wytensin®
Guanfacine/Tenex®
Guselkumab/Tremfya®
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®
Human insulin inhalation powder/Afrezza®—Caution, patients with renal impairment may be at higher risk of hypoglycemia
Hyaluronate/Hylaform®, Juvederm®, Orthovisc®, Restylane®, Supartz™, Synvisc®
Hydralazine/Apresoline®
Hydrocodone/Zohydro® ER, Hysingla ER®—Caution, monitor closely for respiratory depression, sedation, and hypotension
Hydrocodone and acetaminophen/Lortab®, Norco®, Vicodin®, Zamicet®
Hydrocortisone/Cortef®, Solu-Cortef®
Hydromorphone/Dilaudid®
Hydroxocobalamin/Cyanokit®
Hydroxychloroquine/Plaquenil®
Hydroxyzine/Atarax®, Vistaril®
Hyoscyamine/Levsin®
Hyoscyamine, atropine, scopolamine, and phenobarbital/Donnatal®
Ibalizumab-uiyk/Trogarzo™
Ibritumomab/Zevalin®
Ibuprofen/Motrin®, Advil®—Caution, no data in advanced renal disease; not recommended
Ibrutinib/Imbruvica®
Ibutilide/Corvert®
Icatibant/Firazyr®
Icosapent ethyl/Vascepa®
Idarucizumab/Praxbind®
Idelalisib/Zydelig®
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®
Inotersen/Tegsedi®—Caution, generally not be initiated in patients with urinary protein-to-creatinine ratio ≥ 1000 mg/g; has not been studied in patients with stage 4 or 5 CKD
Inotuzumab ozogamicin/Besponsa™
Interferon alfa-2B/Intron® A
Insulin human/Humulin®, Novolin®—Caution, patients with renal impairment are at increased risk of hypoglycemia
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 I^{125}/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®
Isatuximab-irfc/Sarclisa®
Isavuconazonium/Cresemba®
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
Istradefylline/Nourianz™
Ivabradine/Corlanor®—Caution, no data are available for patients with CrCL <15 mL/min
Ivacaftor/Kalydeco®
Ivermectin/Stromectol®
Ivosidenib/Tibsovo®
Ixabepilone/Ixempra®
Ixekizumab/Taltz®—Caution, no formal trial of the effect of renal impairment on pharmacokinetics has been conducted

Ixazomib/Ninlaro®—Caution, reduce starting dose from 4 mg to 3 mg orally once a week on days 1, 8, and 15 of a 28-day cycle in patients with CrCL <30 mL/min
Japanese encephalitis virus vaccine/JE-Vax®
Ketamine/Ketalar®
Ketoconazole/Nizoral®
Labetalol/Trandate®
Lactitol/Pizensy®
Lactulose/Enulose®
Lamotrigine/Lamictal®—Caution, minimal data available in patients with renal impairment
Lanadelumab-flyo/Takhzyro™
Lansoprazole/Prevacid®
Lanthanum/Fosrenol®
Lapatinib/Tykerb®
Larotrectinib/Vitrakvi®
Lasmiditan/Reyvow™
Ledipasvir and sofosbuvir/Harvoni®
Lefamulin/Xenleta™
Leflunomide/Arava®—Caution in renal impairment
Letermovir/Prevymis™—In patients with CrCL <50 mL/min, accumulation of the intravenous vehicle, hydroxypropyl betadex, could occur; closely monitor SCr
Letrozole/Femara®—No dosage adjustment required if CrCL ≥10 mL/min
Leucovorin calcium
Leuprolide/Lupron®
Leuprolide and norethindrone/Lupaneta Pack
Levocarnitine/Carnitor®
Levodopa/Larodopa®
Levoleucovorin/Fusilev™
Levonorgestrel/Plan B®, Skyla®
Levorphanol/Levo-Dromoran®
Levothyroxine/Synthroid®
Lidocaine/Xylocaine®
Linaclotide/Linzess®
Linagliptin/Tradjenta™
Linezolid/Zyvox®
Liothyronine/Cytomel®
Liotrix/Thyrolar®
Lipid injectable emulsion/Clinolipid™, Intralipid®
Liraglutide/Victoza®, Saxenda®
Lisdexamfetamine/Vyvanse™
Lixisenatide/Adlyxin™
Lomitapide/Juxtapid®—Caution, patients with ESRD receiving hemodialysis should not exceed 40 mg/day
Loperamide/Imodium®
Lopinavir/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
Lorcaserin/Belviq®—Exposure of parent drug and metabolites is increased in renal impairment; use in patients with severe renal impairment (CrCL <30 mL/min) or end-stage renal disease is not recommended
Lorlatinib/Lorbrena®
Losartan/Cozaar®
Lovastatin/Mevacor®
Loxapine/Loxitane®, Adasuve®
Lubiprostone/Amitiza®—Caution, no data in renal impairment
Lumacaftor and ivacaftor/Orkambi®—Caution, not studied in renal impairment
Lumateperone/Caplyta™
Luspatercept-aamt/Reblozyl®
Lusutrombopag/Mulpleta®
Lutetium Lu 177 dotatate/Lutathera®
Macitentan/Opsumit®
Macimorelin/Macrilen™
Maprotiline/Ludiomil®
Measles/mumps/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®
Mepolizumab/Nucala®
Mesalamine/Asacol®, Delzicol®, 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®, Quillivant XR®, Concerta®, Metadate® ER
Methylprednisolone/Solu-Medrol®, Depo-Medrol®
Metolazone/Zaroxolyn®
Metoprolol/Lopressor®, Toprol-XL®
Metreleptin/Myalept®
Metronidazole/Flagyl®
Metyrosine/Demser®
Mexiletine/Mexitil®
Micafungin/Mycamine®
Midazolam/Versed®
Midostaurin/Rydapt®
Mifepristone/Mifeprex®, Korlym™—Caution, the maximum dose should not exceed 600 mg per day in renally impaired patients
Miltefosine/Impavido®—Caution, pharmacokinetics have not been studied in patients with renal impairment
Minocycline/Minocin®, Ximino™
Minoxidil/Loniten®
Mirtazapine/Remeron®—Caution, consider dose reduction in renal impairment; clearance is decreased 50% if CrCL <10 mL/min
Misoprostol/Cytotec®
Mitomycin
Mitotane/Lysodren®
Mitoxantrone/Novantrone®—Caution, no data in renal impairment

Modafinil/Provigil®—Safety not established in renal impairment
Mogamulizumab-kpkc/Poteligeo®
Molindone/Moban®
Montelukast/Singulair®
Moxetumomab pasudotox-tdfk/Lumoxiti™
Moxidectin/Moxidectin©
Moxifloxacin/Avelox®
Multivitamins/Hexavitamin
Muromonab-CD3/Orthoclone OKT3®
Migalastat/Galafold®
Mirabegron/Myrbetriq®—Caution, dose should not exceed 25 mg once daily in patients with severe renal impairment (GFR <30 mL/min); use in ESRD is not recommended
Nabilone/Cesamet™—Caution, no data in renal impairment
Nafarelin/Synarel®
Nafcillin/Unipen®
Nalbuphine/Nubain®—Caution in renal impairment; consider use of reduced doses
Naldemedine/Symproic®
Nalmefene/Revex®
Naloxone/Narcan®, Evzio®
Naltrexone/ReVia®
Natalizumab/Tysabri®
Nateglinide/Starlix®
Necitumumab/Portrazza®
Nefazodone/Serzone®
Nelarabine/Arranon®
Nelfinavir/Viracept®
Neratinib/Nerlynx®
Nesiritide/Natrecor®
Netupitant and palonosetron/Akynzeo®—Caution, the pharmacokinetics of neither netupitant nor palonosetron have been studied in ESRD; the manufacturer advises avoidance of use in patients with severe renal impairment and ESRD
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®, Nymalize®
Niraparib/Zejula®—Caution, the effect of severe renal impairment or ESRD/hemodialysis on niraparib pharmacokinetics is unknown
Nitedanib/Ofev®
Nisoldipine/Sular®
Nitazoxanide/Alinia®—Caution, no data in renal impairment
Nitroglycerin/Nitrostat®
Nitroprusside/Nitropress®
Nivolumab/Opdivo®
Norepinephrine/Levophed®
Norethindrone/Aygestin®
Nortriptyline/Pamelor®
Nusinersen/Spinraza®
Nystatin/Nilstat®, Mycostatin®
Obeticholic acid/Ocaliva®
Obiltoxaximab/Anthim®
Obinutuzumab/Gazyva®
Ocrelizumab/Ocrevus®
Octreotide/Sandostatin®
Ofatumumab/Arzerra™
Olanzapine/Zyprexa®
Olaratumab/Latruvo™
Olmesartan/Benicar®
Olsalazine/Dipentum®—Caution, monitor renal function
Omacetaxine/Synribo®
Omadacycline/Nuzyra®
Omalizumab/Xolair®
Ombitasvir, paritaprevir, ritonavir, and dasabuvir/Viekira Pak™
Omega-3-acid esters/Lovaza®, Omtryg™
Omeprazole/Prilosec®
Omeprazole/sodium bicarbonate/Zegerid®
Onabotulinumtoxin A/Botox®
Ondansetron/Zofran®
Opium tincture
Oritavancin/Orbactiv®—Caution, pharmacokinetics in severe renal impairment have not been evaluated
Orlistat/Xenical®, Alli™
Orphenadrine/Norflex™
Osilodrostat/Isturisa®
Osimertinib/Tagrisso®
Ospemifene/Osphena®
Oxaliplatin/Eloxatin®—Caution in renal impairment; safety not established
Oxandrolone/Oxandrin®
Oxazepam/Serax®
Oxybutynin/Ditropan®, Oxytrol®
Oxycodone/Roxicodone®, Oxecta™, OxyContin®
Oxymetholone/Anadrol®-50
Oxytocin/Pitocin®
Paclitaxel/Taxol®
Palbociclib/Ibrance®—Caution, pharmacokinetics have not been studied in patients requiring hemodialysis
Palifermin/Kepivance®
Palivizumab/Synagis®
Palonosetron/Aloxi®
Pancrelipase/Creon®, Zenpep®, Ultresa®, Viokase®, Pertzye®
Panitumumab/Vectibix®—Caution, no data in renal impairment
Panobinostat/Farydak®
Pantoprazole/Protonix®
Papaverine
Papillomavirus vaccine, human, recombinant/Gardasil®
Parathyroid hormone/Natpara®
Paregoric
Paricalcitol/Zemplar®
Paromomycin/Humatin®
Pasireotide/Signifor®
Patiromer/Veltassa®
Patisiran/Onpattro®
Pazopanib/Votrient™
Pegaptanib/Macugen®
Pegaspargase/Oncaspar®
Pegfilgrastim/Neulasta®
Peginesatide/Omontys®—Caution, not indicated in patients with chronic kidney disease not on dialysis
Peginterferon beta-1a/Plegridy™
Pegloticase/Krystexxa™
Pegvaliase-pqpz/Palynziq™
Pegvisomant/Somavert®—Caution, no data in renal impairment
Pembrolizumab/Keytruda®
Penbutolol/Levatol®
Penicillin G benzathine/Bicillin LA®
Penicillin G procaine/Wycillin®
Penicillin V potassium/Pen VK®
Pentamidine (inhaled)/Nebupent®

Pentobarbital/Nembutal®
Pentosan polysulfate/Elmiron®
Perampanel/Fycompa®—Caution, no data in severe renal impairment or hemodialysis, not recommended in these patients
Perflutren/Definity®
Perphenazine/Trilafon®
Pertuzumab/Perjeta™
Pexidartinib/Turalio™—Caution, in patients with CrCL 15–89 mL/min, dose should be reduced from the usual 400 mg orally twice daily to 400 mg in the morning and 200 mg in the evening
Phenelzine/Nardil®
Phenol
Phenoxybenzamine/Dibenzyline®
Phentermine/Ionamin®
Phentolamine/Regitine®
Phenylephrine/Neo-Synephrine®, Vazculep™
Phosphorated carbohydrate solution/Emetrol®
Physostigmine
Phytonadione (vitamin K1)/AquaMephyton®, Mephyton®
Pilocarpine/Salagen®
Pimavanserin/Nuplazid®
Pimozide/Orap®
Pindolol/Visken®
Pioglitazone/Actos®
Pirfenidone/Esbriet®—Caution, pharmacokinetics and safety have not been studied in subjects with ESRD requiring dialysis
Pitolisant/Wakix®—Caution, not recommended in ESRD
Plecanatide/Trulance®
Pneumococcal conjugate vaccine (13-valent)/Prevnar®
Pneumococcal polysaccharide vaccine/Pneumovax 23®
Polatuzumab vedotin-piiq/Polivy™
Polidocanol/Asclera®, Varithena®
Poliovirus vaccine (inactivated)/IPOL®
Polyethylene glycol 3350/Miralax®, MoviPrep®
Polyethylene glycol/electrolyte solution/Colyte®, Golytely®, Nulytely®, Suclear
Ponatinib/Iclusig®
Porfimer/Photofrin®
Posaconazole/Noxafil®
Potassium iodide/SSKI®
PrabotulinumtoxinA-xvfs/Jeuveau™
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®, Rayos®
Pretomanid—Caution, the effect of renal impairment on the safety, effectiveness, and pharmacokinetics of pretomanid is not known
Prilocaine/Citanest®
Primaquine
Procaine/Novocain®
Procarbazine/Matulane®
Prochlorperazine/Compazine®
Progesterone/Prometrium®
Pomalidomide/Pomalyst®—Caution, starting dose in patients with severe renal impairment requiring hemodialysis is 3 mg daily
Promethazine/Phenergan®
Propafenone/Rythmol®
Propantheline/Pro-Banthine®
Propofol/Diprivan®
Propranolol/Inderal®, Hemangeol®
Propylthiouracil
Protamine
Protriptyline/Vivactil®
Pseudoephedrine/Sudafed®
Psyllium/Metamucil®
Pyrantel pamoate/Combantrin™
Pyrazinamide
Pyrethrins/piperonyl butoxide/Rid®
Pyridoxine (vitamin B_6)
Pyrimethamine/Daraprim®
Quazepam/Doral®
Quetiapine/Seroquel®
Quinupristin and dalfopristin/Synercid®
Rabeprazole/AcipHex®
Rabies immune globulin/HyperRab®
Radium Ra 223/Xofigo®
Raloxifene/Evista®
Raltegravir/Isentress®
Ramelteon/Rozerem®
Ramucirumab/Cyramza®
Ranibizumab/Lucentis®
Rasagiline/Azilect®—Caution, no data in severe renal impairment
Rasburicase/Elitek®
Ravulizumab-cwvz/Ultomiris®
Raxibacumab
Regadenoson/Lexiscan®
Regorafenib/Stivarga®
Remdesivir (GS-5734)
Remifentanil/Ultiva®—Caution, in patients >65 years, decrease starting dose by 50%
Reslizumab/Cinqair®
Reteplase/Retavase®
$Rho_{(D)}$ immune globulin/RhoGam®
Ribavirin (inhaled)/Virazole®
Rilpivirine/Endurant™
Ribociclib/Kisqali®—Caution, starting dose is 200 mg orally once daily for patients with severe renal impairment
Riboflavin
Rifamycin/Aemcolo™
Rifapentine/Priftin®
Rifaximin/Xifaxan™
Rilpivirine/Edurant™
Riluzole/Rilutek®
Rimabotulinumtoxin B/Myobloc®
Rimegepant/Nurtec™ ODT—Caution, has not been studied in ESRD; the manufacturer recommends avoidance of use in these patients
Riociguat/Adempas®—Safety and efficacy have not been demonstrated in patients with creatinine clearance <15 mL/min or on dialysis and use is not recommended
Risankizumab-rzaa/Skyrizi®
Risperidone injection/Risperdal® Consta®
Ritonavir/Norvir®
Rituximab/Rituxan®—Caution, minimal data in renal impairment
Rivastigmine/Exelon®
Rizatriptan/Maxalt®
Rocuronium/Zemuron®
Roflumilast/Daliresp™
Rolapitant/Varubi®
Romidepsin/Istodax®
Romiplostim/Nplate™
Romosozumab-aqqg/Evenity™

Ropinirole/Requip®
Ropvivacaine/Naropin®
Rosiglitazone/Avandia®
Rucaparib/Rubraca®—Caution, the pharmacokinetic characteristics of rucaparib in patients with CrCL <30 mL/min or patients on dialysis are unknown
Rufinamide/Banzel™
Sacrosidase/Sucraid®
Sacubitril and valsartan/Entresto®—Caution, for patients with GFR <30 mL/min, starting dose is 24/26 mg orally twice daily with up titration every 2–4 weeks as tolerated to a maximum of 97/103 mg orally twice daily
Safinamide/Xadago®
Sapropterin/Kuvan®
Saquinavir/Invirase®
Sarecycline/Seysara®
Sargramostim/Leukine®
Sarilumab/Kevzara®
Scopolamine/Transderm Scōp®
Sebelipase alfa/Kanuma®
Secnidazole/Solosec®
Secobarbital/Seconal®
Secukinumab/Cosentyx®
Selegiline/Eldepryl®
Selinexor/Xpovio™
Selenium (homeopathic)/Male Libido™
Selexipag/Uptavi®
Semaglutide/Ozempic®
Sertraline/Zoloft®
Sevelamer/Renagel®
Sevoflurane/Ultane®
Sildenafil/Revatio®, Viagra®—Caution, if CrCL <30 mL/min, consider starting dose at Viagra 25 mg
Siltuximab/Sylvant®
Simethicone/Mylicon®
Simvastatin/Zocor®
Siponimod/Mayzent®
Sipuleucel-T/Provenge®
Sirolimus/Rapamune®
Sodium bicarbonate/Alka Seltzer® Heartburn and Acid Indigestion Relief
Sodium citrate/citric acid/Bicitra®
Sodium nitrate—Substantially excreted by the kidney; the risk of toxic reactions may be greater in patients with impaired renal function
Sodium oxybate/Xyrem®
Sodium picosulfate, magnesium oxide, and citric acid/Prepopik®
Sodium polystyrene sulfonate/Kayexalate®
Sodium tetradecyl sulfate/Sotradecol®
Sodium thiosulfate—Substantially excreted by the kidney; the risk of toxic reactions may be greater in patients with impaired renal function
Sodium zirconium cyclosilicate/Lokelma™
Sofosbuvir/Sovaldi®—Caution, safety and efficacy have not been established in patients with severe renal impairment (GFR <30 mL/min/1.73 m^2) or ESRD requiring hemodialysis
Sofosbuvir and velpatasvir/Epclusa®
Sofosbuvir, velpatasvir, and voxilaprevir/Vosevi®
Somatropin/Humatrope®
Sonidegib/Odomzo®
Sorbitol
Stiripentol/Diacomit®
Succimer/Chemet®—Caution in renal impairment
Succinylcholine/Anectine®
Sucralfate/Carafate®
Sucroferric oxyhydroxide/Velphoro®
Sufentanil/Sufenta®
Sulfadiazine
Sulfasalazine/Azulfidine®—Caution, 37% cleared renally
Sulfur hexafluoride lipid-type A microspheres/Lumason®
Sulindac/Clinoril®—Caution, not recommended in advanced renal disease
Sumatriptan/Imitrex®, Onzetra®, Sumavel®, Zembrace™ SymTouch™
Suvorexant/Belsomra®
Tacrine/Cognex®
Tacrolimus/Prograf®, Envarsus XR®—Caution, careful monitoring indicated in renal dysfunction
Tafenoquine/Krintafel©
Tagraxofusp-erzs/Elzonris™
Talazoparib/Talzenna®—Caution, the recommended dose for patients with CrCL 15–29 mL/min is 0.5 mg orally once daily; pharmacokinetics have not been studied in patients requiring hemodialysis
Tamoxifen/Nolvadex®
Tasimelteon/Hetlioz®
Telaprevir/Incivek™
Taliglucerase alfa/Elelyso®
Tazemetostat/Tazverik™
Tecovirimat/TPOXX®
Tedizolid/Sivextro®
Teduglutide/Gattex®—Caution, in patients with GFR <60 mL/min, the recommended dose should be halved to 0.025 mg/kg subcutaneously once daily
Tafamidis meglumine/Vyndamax™; Vyndaqel®
Telmisartan/Micardis®
Telotristat/Xermelo™
Temazepam/Restoril™
Temozolomide/Temodar®—Caution in severely impaired renal function (CrCL <36 mL/min); no data in hemodialysis
Temsirolimus/Torisel®
Tenapanor/Ibsrela™
Tenecteplase/TNKase®
Teniposide/Vumon®
Teprotumumab-trbw/Tepezza™
Terazosin/Hytrin®
Teriflunomide/Aubagio®
Teriparatide/Forteo®
Tesamorelin/Egrifta™—Caution, safety not established in renal impairment
Testosterone/Delatestryl®, Depo®-Testosterone®, Aveed®, Jatenzo®, Testopel®
Tetanus immune globulin/HyperTet™
Tetrabenazine/Xenazine®
Tetracaine/Pontocaine®
Tezacaftor and ivacaftor/Symdeko®—Caution is recommended in patients with severe renal impairment or end-stage renal disease
Thalidomide/Thalomid®
Theophylline/Elixophyllin®, Uniphyl®
Thiabendazole/Mintezol®—Caution in renal impairment
Thiamine (vitamin B_1)

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®
Tildrakizumab-asmn/Ilumya™
Tilmanocept/Lymphoseek®
Timolol/Blocadren®
Tinidazole/Tindamax®
Tipranavir/Aptivus®
Tocilizumab/Actemra®
Tofacitinib/Xeljanz®, Xeljanz XR®—Caution, in severe renal impairment and patients on chronic hemodialysis, dosage should be limited to 5 mg once daily in rheumatoid and psoriatic arthritis and 5 mg once or twice daily in ulcerative colitis
Tolazamide/Tolinase®
Tolbutamide/Orinase®
Tolcapone/Tasmar®—Caution in severe renal impairment (CrCL <25 mL/min)
Tolvaptan/Samsca™
Toremifene/Fareston®
Torsemide/Demadex®
Trabectedin/Yondelis®—Caution, pharmacokinetics have not been studied in patients with CrCL <30 mL/min
Trametinib/Mekinist®
Tranylcypromine/Parnate®
Trastuzumab/Herceptin®
Trazodone/Desyrel®
Treprostinil/Remodulin®, Orenitram®
Tretinoin/Vesanoid®—Caution, no data in renal impairment
Triamcinolone/Kenalog®, Aristospan®
Triazolam/Halcion®
Triclabendazole/Egaten®
Trientine/Syprine®
Trifluoperazine/Stelazine®
Trihexyphenidyl/Artane®
Trimethobenzamide/Tigan®
Trimipramine/Surmontil®
Triprolidine/pseudoephedrine/Actifed®
Triptorelin/Trelstar®—Caution, rate of elimination is diminished in renal impairment
Typhoid vaccine/Vivotif®
Upadacitinib/Rinvoq™
Uridine triacetate/Xuriden®
Urofollitropin/Bravelle®
Ursodiol/Actigall®, Urso®
Ustekinumab/Stelara®—Caution, minimal data in renal impairment
Valbenazine/Ingrezza®—Caution, despite minimal elimination in urine, not recommended in patients with CrCL <30 mL/min
Valproic acid/Depacon®, Depakene®
Valsartan/Diovan®
Vancomycin (oral)/Vancocin®
Vardenafil/Levitra®
Varicella virus vaccine/Varivax®
Varicella-zoster immune globulin/VariZIG™
Vasopressin/Pitressin®, Vasostrict®
Vecuronium/Norcuron®
Vedolizumab/Entyvio®
Vemurafenib/Zelboraf™
Venetoclax/Venclexta®—Caution, a recommended dose has not been determined for patients with CrCL <30 mL/min
Verapamil/Calan®, Isoptin®—Caution in renal impairment
Verteporfin/Visudyne®
Vestronidase alfa-vjbk/Mepsevii™
Vilazodone/Viibryd™
Vinblastine/Velban®
Vincristine/Oncovin®, Marqibo®
Vinorelbine/Navelbine®
Vismodegib/Erivedge®
Vitamin A/Aquasol A®
Vitamin E/Aquasol E®
Vorapaxar/Zontivity®
Vorinostat/Zolinza®
Vortioxetine/Trintellix®
Voxelotor/Oxbryta™
Warfarin/Coumadin®
Yohimbine/Yocon®
Zafirlukast/Accolate®
Zaleplon/Sonata®
Zanamivir/Relenza®
Zanubrutinib/Brukinsa™
Zileuton/Zyflo®
Zinc sulfate/Zincate®
Ziprasidone/Geodon®
Ziv-aflibercept/Zaltrap®
Zolmitriptan/Zomig®
Zolpidem/Ambien®, Intermezzo®
Zoster vaccine/Zostavax®

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Acamprosate – Selected References

Antonelli M, Ferrulli A, Sestito L, et al. Alcohol addiction: the safety of available approved treatment options. Expert Opin Drug Saf. 2018;17:169–77.

Brasser SM, McCaul ME, Houtsmuller EJ. Alcohol effects during acamprosate treatment: a dose-response study in humans. Alcohol Clin Exp Res. 2004;28:1074–83.

Campral® tablet, delayed release [package insert]. St Louis, MO: Forrest Pharmaceuticals Inc; 2016.

Hammarberg A, Beck O, Eksborg S, et al. Acamprosate determinations in plasma and cerebrospinal fluid after multiple dosing measured by liquid chromatography-mass spectroscopy: a pharmacokinetic study in healthy volunteers. Ther Drug Monit. 2010;32:489–96.

Johnson BA, O'Malley SS, Ciraulo DA, et al. Dose-ranging kinetics and behavioral pharmacology of naltrexone and acamprosate, both alone and combined, in alcohol-dependent subjects. J Clin Psychopharmacol. 2003;23:281–93.

Jonas DE, Amick HR, Feltner C, et al. Pharmacotherapy for adults with alcohol use disorders in outpatient settings: a systematic review and meta-analysis. JAMA. 2014;311:1889–900.

Kalk NJ, Lingford-Hughes AR. The clinical pharmacology of acamprosate. Br J Clin Pharmacol. 2012;77:315–23.

Kranzler HR, Soyka M. Diagnosis and pharmacotherapy of alcohol use disorder. JAMA. 2018;320:815–24.

Mason BJ, Goodman AM, Dixon RM, et al. A pharmacokinetic and pharmacodynamic drug interaction study of acamprosate and naltrexone. Neuropsychopharmacology. 2002;27:596–606.

Namkoong K, Lee B-O, Lee P-G, Choi M-J, Lee E. Acamprosate in Korean alcohol-dependent patients: a multi-centre, randomized, double-blind, placebo-controlled study. Alcohol. 2003;38:135–41.

Plosker GL. Acamprosate: a review of its use in alcohol dependence. Drugs. 2015;75:1255–68.

Reus VI, Fochtmann LJ, Bukstein O, et al. The American Psychiatric Association Practice Guideline for the pharmacological treatment of patients with alcohol use disorder. Am J Psychiatry. 2018;175:86–90.

Rhee Y-S, Park S, Lee T-W, et al. Investigation of the relationship between in vitro and in vivo release behaviors of acamprosate from enteric-coated tablets. Arch Pharm Res. 2008;31:798–804.

Saivin S, Hulot T, Chabac S, Potgieter A, Durbin P, Houin G. Clinical pharmacokinetics of acamprosate. Clin Pharmacokinet. 1998;35:331–45.

Scott LJ, Figgitt DP, Keam SJ, Waugh J. Acamprosate: a review of its use in maintenance of abstinence in patients with alcohol dependence. CNS Drugs. 2005;19:445–64.

Soyka M, Müller CA. Pharmacology of alcoholism: an update on approved and off-label medications. Expert Opin Pharmacother. 2017;18:1187–99.

Umhau JC, Momenan R, Schwandt ML, et al. Effect of acamprosate on magnetic resonance spectroscopy measures of central glutamate in detoxified alcohol-dependent individuals: a randomized controlled experimental medicine study. Arch Gen Psychiatry. 2010;67:1069–77.

Weinstein A, Feldtkeller B, Feeney A, Lingford-Hughes A, Nutt DJ. A pilot study on the effects of treatment with acamprosate on craving for alcohol in alcohol dependent patients. Addict Biol. 2003;8:229–32.

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 3 times daily	
Typical maximum dose:	1998 mg/day	
Proportion eliminated unchanged in urine:	~90%	
Adjustment for Kidney Disease		
FDA-approved product labeling:	*CrCL > 50 mL/min*	*666 mg orally 3 times daily*
	CrCL 30–50 mL/min	*333 mg orally 3 times daily*
	CrCL < 30 mL/min	*Contraindicated*
Alternative adjustment:	*Data not available*	

Acarbose – Selected References

Abe M, Okada K, Soma M. Antidiabetic agents in patients with chronic kidney disease and end-stage renal disease on dialysis: metabolism and clinical practice. Curr Drug Metab. 2011;12:57–69.

Ahr HJ, Boberg M, Krause HP, et al. Pharmacokinetics of acarbose. Part I: Absorption, concentration in plasma, metabolism and excretion after single administration of [^{14}C] acarbose to rats, dogs and man. Arzneimittelforschung. 1989;39:1254–60.

Aronoff GA, Bennett WM, Berns JS, et al. Drug Prescribing in Renal Failure: Dosing Guidelines for Adults and Children. 5th ed. Philadelphia, PA: American College of Physicians; 2007.

Balfour JA, McTavish D. Acarbose: an update of its pharmacology and therapeutic use in diabetes mellitus. Drugs. 1993;46:1025–54.

Chao CT, Wang J, Huang JW, Chien KL. Acarbose use and liver injury in diabetic patients with severe renal insufficiency and hepatic diseases: a propensity score-matched cohort study. Front Pharmacol. 2018;9:860.

Chen YH, Tarng DC, Chen HS. Renal outcomes of pioglitazone compared with acarbose in diabetic patients: a randomized controlled study. PLoS One. 2016;11:e0165750.

Gagne JJ, Polinski JM, Jiang W, et al. Outcomes associated with generic drugs approved using product-specific determinations of therapeutic equivalence. Drugs. 2017;77:427–33.

Harrower AD. Pharmacokinetics of antihyperglycaemic agents in patients with renal insufficiency. Clin Pharmacokinet. 1996;31:111–9.

Lee S, Chung JY, Hong KS, et al. Pharmacodynamic comparison of two formulations of acarbose 100-mg tablets. J Clin Pharm Ther. 2012;37:553–7.

Olyaei AJ, Bennett WM. Drug dosing in elderly patients with chronic kidney disease. Clin Geriatr Med. 2009;25:459–527.

Precose® tablet [package insert]. Whipany, NJ: Bayer HealthCare Pharmaceuticals Inc; 2015.

Salvatore T, Giugliamo D. Pharmacokinetic-pharmacodynamic relationships of acarbose. Clin Pharmacokinet. 1996;30:94–106.

Zhang M, Yang J, Tao L, Li L, Ma P, Fawcett JP. Acarbose bioequivalence: exploration of new pharmacodynamic parameters. AAPS J. 2012;14:345–51.

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 in urine:	35%	
Adjustment for Kidney Disease		
FDA-approved product labeling:	*SCr > 2.0 mg/dL:*	*Plasma concentrations of (acarbose) in renally impaired volunteers were proportionally increased relative to the degree of renal dysfunction. Long-term 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 ≥ 60 mL/min*	*50 mg orally three times daily with meals*
	GFR 15–59 mL/min	*Minimal data to support safety are available. Preferably avoid unless no suitable alternative exists; if indeed necessary, begin with low doses and monitor carefully*
	GFR < 15 mL/min	*Minimal data to support safety are available. Preferably avoid unless no suitable alternative exists; if indeed necessary, begin with low doses and monitor carefully*
	Hemodialysis	*Minimal data to support safety are 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*

Acebutolol – Selected References

Acebutolol hydrochloride capsule [package insert]. Morgantown: Mylan Pharmaceuticals Inc; 2012.

Aronoff GA, Bennett WM, Berns JS, et al. Drug Prescribing in Renal Failure: Dosing Guidelines for Adults and Children. 5th ed. Philadelphia, PA: American College of Physicians; 2007.

Bailey DG. Fruit juice inhibition of uptake transport: a new type of food-drug interaction. Br J Clin Pharmacol. 2010;70:645–55.

Baker JG, Hall IP, Hill SJ. Agonist actions of "β-blockers" provide evidence for two agonist activation sites or conformations of the human β1-adrenoceptor. Mol Pharmacol. 2003;63:1312–21.

Begg E, Munn S, Bailey RR. Acebutolol in the treatment of patients with hypertension and renal functional impairment. N Z Med J. 1979;89:293–5.

Cuthbert MF, Collins RF. Plasma levels and β-adrenoceptor blockade with acebutolol, practolol and propranolol in man. Br J Clin Pharmacol. 1975;2:49–55.

Daly MJ, Flook JJ, Levy GP. The selectivity of β-adrenoceptor antagonists on cardiovascular and bronchodilator responses to isoprenaline in the anaesthetized dog. Br J Pharmacol. 1975;53:173–81.

Gabriel R. Acebutolol in the management of hypertension in patients with renal disease. Br J Clin Pract. 1979;33:259–62.

Kaye CM, Dufton JF. Preliminary observations on the elimination of acebutolol in severe chronic renal failure [letter]. Br J Clin Pharmacol. 1976;3:198–9.

Kirch W, Köhler H, Berggren G, Braun W. The influence of renal function on plasma levels and urinary excretion of acebutolol and its main N-acetyl metabolite. Clin Nephrol. 1982;18:88–94.

Lilja JJ, Raaska K, Neuvonen PJ. Effects of grapefruit juice on the pharmacokinetics of acebutolol. Br J Clin Pharmacol. 2005:60:659–63.

Martin MA, Phillips FC, Tucker GT, Smith AJ. Acebutolol in hypertension: relationships between drug concentration and effects. Eur J Clin Pharmacol. 1978;14:383–90.

McIntyre CW, Owen PJ. Prescribing drugs in kidney disease. In: Brenner BM. Brenner & Rector's The Kidney. 8th ed. Philadelphia, PA: Saunders Elsevier; 2008:1930–55.

Meffin PJ, Winkle RA, Peters FA, Harrison DC, Harapat SR, Yee Y-G. Dose-dependent acebutolol disposition after oral administration. Clin Pharmacol Ther. 1978;24:542–7.

Munn S, Bailey RR, Begg E, Ebert R, Ferry DG. Plasma and urine concentrations of acebutolol and its acetyl metabolite in patients with renal impairment. N Z Med J. 1980;91:289–91.

Olyaei AJ, Bennett WM. Drug dosing in elderly patients with chronic kidney disease. Clin Geriatr Med. 2009;25:459–527.

Roux A, Aubert P, Buedon J, Flouvat B. Pharmacokinetics of acebutolol in patients with all grades of renal failure. Eur J Clin Pharmacol. 1980;17:339–48.

Singh BN, Thoden WR, Wahl J. Acebutolol: a review of its pharmacology, pharmacokinetics, clinical uses, and adverse effects. Pharmacotherapy. 1986;6:45–63.

Smith RS, Warren DJ, Renwick AG, George CF. Acebutolol pharmacokinetics in renal failure. Br J Clin Pharmacol. 1983;16:253–8.

Weir MA, Dixon SN, Fleet JL, et al. β-Blocker dialyzability and mortality in older patients receiving hemodialysis. J Am Soc Nephrol. 2015;26:987–96.

Winkle RA, Meffin PJ, Ricks WB, Harrison DC. Acebutolol metabolite plasma concentration during chronic oral therapy. Br J Clin Pharmacol. 1977;4:519–22.