THERAIQ

Clinical Decision Support Platform

Methodology, Equations & Validation

Vancomycin AUC-Guided Dosing Calculator

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Version	1.0 — June 2026
Platform	TheraIQ · theraiq.net
Intended audience	Licensed pharmacists and prescribers
Regulatory status	Decision support only · does not replace clinical judgment

1. Executive Summary

TheraIQ is a web-based clinical decision support platform designed to assist licensed pharmacists and prescribers with vancomycin area under the curve (AUC)-guided dosing. The vancomycin calculator applies population-based pharmacokinetic (PK) parameter estimates derived from peer-reviewed literature to generate empiric dosing recommendations, estimate AUC from measured steady-state troughs, and derive patient-specific PK from two-level peak-and-trough sampling.

All calculations run in the user's browser. TheraIQ does not store patient data and does not connect to external servers during calculations. Results should be interpreted alongside the patient's clinical status, infection severity, and institutional protocol.

Intended use: Empiric initial dosing, steady-state AUC estimation from trough levels, and patient-specific PK derivation from peak-and-trough pairs. Designed for inpatient use by clinical pharmacists managing serious infections where vancomycin AUC monitoring is guideline-recommended, including MRSA bacteremia, endocarditis, and pneumonia.

2. AUC-Guided Monitoring — Clinical Rationale

The 2020 ASHP/IDSA/SIDP/PIDS consensus guidelines replaced trough-only monitoring with AUC-guided dosing as the preferred method for vancomycin therapeutic drug management in serious MRSA infections. The shift was driven by evidence that the pharmacodynamic target for efficacy is an AUC/MIC ratio, and that trough-only monitoring correlates poorly with AUC while increasing nephrotoxicity risk through reflexive dose escalation.

Target AUC range:

Target	AUC_{24} Range	Clinical Context
Standard MRSA	400-600 mg·h/L	Bacteremia, skin/soft tissue, pneumonia
Therapeutic center	~500 mg·h/L	Recommended dosing target
Nephrotoxicity risk	>650 mg·h/L	Sustained exposure increases AKI risk

TheraIQ supports all three AUC calculation approaches recommended by the guidelines: population-based estimation for initial dosing, trough-only back-calculation using a validated population Vd model, and two-level patient-specific PK fitting.

3. Renal Function Estimation

3.1 Cockcroft-Gault Creatinine Clearance

CrCl by the Cockcroft-Gault (C-G) equation is the native input for all vancomycin population clearance models in TheraIQ, since these models were derived and validated using C-G CrCl. Weight basis selection follows Winter et al. 2012 (Pharmacotherapy) and the ASHP/IDSA/SIDP 2020 consensus guidelines:

C-G equation	`CrCl = [(140 - age) x weight x (0.85 if female)] / (72 x SCr)`
Weight: TBW < IBW	`Use actual body weight (TBW)`
Weight: TBW <= 1.2xIBW	`Use actual body weight (TBW)`
Weight: TBW > 1.2xIBW	`Use adjusted BW = IBW + 0.4 x (TBW - IBW)`

IBW (male)	`IBW = 50 + 2.3 x (height in inches - 60) kg`
IBW (female)	`IBW = 45.5 + 2.3 x (height in inches - 60) kg`
IBW floor	`Minimum IBW = 40 kg`

Weight basis: The 1.2xIBW threshold is the evidence-based standard from Winter et al. 2012 and is consistent with ASHP/IDSA guidelines and the original Cockcroft-Gault 1976 derivation. Different calculators may apply different weight cutoffs; such differences account for a portion of inter-calculator CrCl variation. Given the inherent variance in population PK models, these differences are generally within the range of expected clinical variability and are best resolved with a measured steady-state level.

3.2 eGFR — CKD-EPI 2021 Equations

TheraIQ provides eGFR estimates using the 2021 CKD-EPI equations (race-free) per the National Kidney Foundation and American Society of Nephrology recommendation. BSA de-indexing converts the standardized mL/min/1.73m^2 value to an absolute mL/min for use as a clearance driver, consistent with FDA 2024 guidance on renal impairment drug dosing.

CKD-EPI Cr 2021 (male)	`142 x min(SCr/0.9, 1)^-0.302 x max(SCr/0.9, 1)^-1.200 x 0.9938^age`
CKD-EPI Cr 2021 (female)	`142 x min(SCr/0.7, 1)^-0.241 x max(SCr/0.7, 1)^-1.200 x 0.9938^age x 1.012`
CKD-EPI CrCys 2021 (male)	`135 x min(SCr/0.9,1)^-0.144 x max(SCr/0.9,1)^-0.544 x min(Cys/0.8,1)^-0.323 x max(Cys/0.8,1)^-0.778 x 0.9961^age`
CKD-EPI Cystatin C 2012	`133 x min(Cys/0.8,1)^-0.499 x max(Cys/0.8,1)^-1.328 x 0.996^age x (0.932 if female)`
BSA de-indexing	`Absolute mL/min = eGFR (mL/min/1.73m2) x BSA / 1.73`
BSA (Du Bois formula)	`BSA = 0.007184 x height (cm)^0.725 x weight (kg)^0.425`

3.3 Discordance Detection

When CrCl and eGFR-Cr diverge by more than 20% (relative difference), TheraIQ flags the discordance as clinically meaningful. At this magnitude, the shift in estimated vancomycin clearance is sufficient to move the predicted AUC approximately 100 mg·h/L off a 500 target. When cystatin C is available and diverges more than 20% from creatinine-based eGFR, the cystatin C or combined Cr-cystatin driver is preferred, as it is less dependent on muscle mass.

Relative difference	`reldiff(a,b) = |a - b| / ((a + b) / 2)`
Discordance threshold	`Flag when reldiff > 0.20 (20%)`

4. Vancomycin Pharmacokinetic Models

4.1 Clearance (CLv) Models

TheraIQ provides six population clearance models. The default model (0.75 x CrCl + 4) is the most widely cited linear regression from Matzke et al. 1984, derived from 24 patients across a spectrum of renal function and validated in subsequent AUC-guided dosing cohorts. All CLv values are converted from mL/min to L/hr by multiplying by 0.06.

Model	Equation (mL/min)	Source	Notes
VancoPK (default)	CLv = 0.75 x CrCl + 4	Matzke 1984	Most widely validated; default selection
Matzke regression	CLv = 0.689 x CrCl + 3.66	Matzke 1984	Regression-refined variant; slightly conservative
Ambrose	CLv = CrCl	Ambrose 1993	Proportional approximation; simple bedside use
Birt & Chandler	CLv = 0.674 x CrCl + 13.45	Birt 1990	Higher intercept; non-renal elimination component
Buelga	CLv = 1.08 x CrCl	Buelga 2005	ICU patients; augmented renal clearance
Burton revised	CLv = 0.80 x CrCl	Burton 1985	Proportional model with non-renal correction

Unit conversion: CLv (L/hr) = CLv (mL/min) x 0.06

4.2 Volume of Distribution (Vd)

The default Vd model is the age- and weight-adjusted equation from Matzke et al. 1984. The age term reflects the well-documented increase in vancomycin Vd with aging, attributed to reduced plasma protein binding and increased peripheral distribution. Three additional weight-proportional models are available.

Matzke 1984 (default)	`Vd = 0.29 x age + 0.33 x actual BW (kg) + 11 [L]`
Birt & Chandler	`Vd = 0.54 x actual BW (kg)`
Winter-Tozer	`Vd = 0.70 x actual BW (kg)`
Tanaka	`Vd = 0.864 x actual BW (kg) [derived from Japanese cohort]`

The loading dose calculation uses Vd x 1.25 to account for the larger apparent volume of distribution seen early in therapy before distribution equilibrium is reached.

4.3 Derived PK Parameters

Elimination rate constant	`Ke = CLv / Vd [hr-1]`
Half-life	`t1/2 = 0.693 / Ke [hr]`
Steady-state peak (Cmax)	`Cmaxss = Dose x (1 - e^(-Ke x ti)) / (Ke x Vd x ti x (1 - e^(-Ke x tau)))`
Steady-state trough (Cmin)	`Cminss = Cmaxss x e^(-Ke x (tau - ti))`
AUC (clearance method)	`AUC24 = Total daily dose / CLv`

ti = infusion duration (hr); tau = dosing interval (hr); Dose = per-dose amount (mg)

5. Empiric Initial Dosing

The initial dosing calculator estimates CLv and Vd from population models, derives Ke, selects a dosing interval based on half-life, and calculates a maintenance dose targeting a goal AUC_{24} (default 500 mg·h/L, adjustable 400-600).

Maintenance dose	`Dose = CLv x Goal AUC x tau / 24 (rounded to nearest 250 mg)`

Interval selection	`t1/2 <6h: q8h; <12h: q12h; <20h: q18h; <28h: q24h; <40h: q36h; >=40h: q48h`
Loading dose peak	`LD peak = LD x (1 - e^(-Ke_load x ti)) / (Ke_load x Vd_load x ti)`
Vd_load	`Vd_load = Vd x 1.25 (early expanded volume)`
Ke_load	`Ke_load = CLv / Vd_load`

Infusion times are assigned based on dose size, targeting a rate at or below 15 mg/min: 250-1000 mg over 60 min, 1250-1500 mg over 90 min, 1750-2000 mg over 120 min, 2250-2500 mg over 150 min, 2750-3000 mg over 180 min.

Deceptive trough flag: Doses above 1500 mg or above 20 mg/kg at intervals of 12 hours or longer can produce a trough within the conventional 10-20 mcg/mL range while the AUC is supratherapeutic. TheraIQ flags these regimens to alert clinicians to target AUC, not trough.

6. Trough-Only AUC Estimation

The steady-state trough method uses a single measured level to back-calculate the elimination rate constant (Ke), then derives vancomycin clearance and AUC. This approach is validated by Fewel et al. 2021, which utilized real-world steady-state TDM data from multiple institutions. The study reported a root mean square error (RMSE) of 47.7 mg·h/L between estimated and observed AUC values, with over 95% of estimates falling within 100 mg·h/L of the actual AUC.

Method:

1. Vd estimated from the Matzke 1984 population model (0.29 x age + 0.33 x actual BW + 11 L)
2. Ke solved by iterative numerical method using the full steady-state equation at the actual draw time
3. Vancomycin clearance (CLv) calculated as Ke x Vd
4. AUC_{24} = Total daily dose / CLv
5. Trough extrapolated to true pre-dose time (see equation below)
6. New dose calculated as: round(CLv x goal AUC x tau / 24) to nearest 250 mg

SS equation at draw time	`Css = Dose x e^(-Ke x (tDraw-ti)) x (1-e^(-Ke x ti)) / (ti x Ke x Vd x (1-e^(-Ke x tau)))`
Ke solver range	`Ke searched between 0.005 and 0.5 hr-1; converges to <0.0001 hr-1 precision`
Trough extrapolation	`C_extrap = C_measured x e^(-Ke x t_before_dose)`

t_before_dose = hours elapsed between the draw time and the next scheduled dose. Extrapolating the measured level forward to the true pre-dose time corrects for early draws and gives the concentration the patient would have had at the trough.

Inherent variance and inter-calculator differences:

Trough-only AUC estimation relies on a population Vd rather than a patient-specific value. The Fewel 2021 validation shows an inherent RMSE of 47.7 mg·h/L, meaning approximately 95% of estimated AUC values fall within 100 mg·h/L of the true AUC. This applies to all calculators using population Vd assumptions. Differences in CrCl, CLv, Vd, or AUC between TheraIQ and other calculators typically reflect legitimate methodological choices in weight basis, equation selection, or model parameterization. When such differences fall within the 47.7 mg·h/L RMSE range, they are within expected population variability. A peak-and-trough pair eliminates the population Vd assumption entirely and provides patient-specific PK.

7. Peak-and-Trough Patient-Specific PK

Two measured levels (peak drawn at least 1 hour after the infusion ends, trough drawn 0-1 hour before the next dose) allow direct calculation of patient-specific Ke and Vd without any population model assumptions. This is the most accurate first-order method available outside of Bayesian software and is recommended for high-stakes patients including endocarditis, severe renal impairment, morbid obesity, and augmented renal clearance.

Ke from two levels	`Ke = ln(C_peak / C_trough) / (t_trough - t_peak)`
Cmax back-calculation	`Cmax = C_peak x e^(Ke x t_post_infusion) [back to end of infusion]`
CLv at steady state	`CLv = Dose x (1 - e^(-Ke x ti)) / (ti x Cmax x (1 - e^(-Ke x tau)))`
Vd	`Vd = CLv / Ke`
AUC (clearance method)	`AUC24 = Total daily dose / CLv`
AUC (trapezoidal)	`AUC24 = [(Cmax + Cmin)/2 x ti + (Cmax - Cmin)/Ke] x 24/tau`

Both AUC methods are shown for transparency. Agreement within 50 mg·h/L confirms reliable calculation. A difference above 100 mg·h/L suggests a level timing error or non-steady-state conditions. Levels drawn less than 4 hours apart are flagged as insufficient for reliable Ke estimation. A peak drawn less than 1 hour after the infusion ends is flagged as potentially affected by incomplete drug distribution.

8. Weight Basis — Scientific Rationale

TheraIQ applies adjusted body weight (AdjBW) for C-G CrCl when TBW exceeds 1.2 x IBW. This threshold comes from Winter et al. 2012 (Pharmacotherapy 32:604), which evaluated bias and accuracy of C-G across weight categories and identified 1.2 x IBW as the appropriate cutoff for adjusted weight. This is consistent with the ASHP/IDSA/SIDP 2020 guidelines and with the original Cockcroft-Gault 1976 derivation, which used actual body weight.

The Matzke 1984 Vd equation also uses actual body weight, keeping the weight basis consistent across both the CrCl and Vd calculations. Mixing weight bases within the same patient encounter would introduce a systematic inconsistency into the PK model.

> Differences in CrCl, CLv, and AUC between calculators may reflect differing weight basis approaches, CrCl equation variants, or model parameterization. These are legitimate methodological differences between validated tools. Given the Fewel 2021 RMSE of 47.7 mg·h/L for trough-only AUC estimation, differences from methodology are generally within expected population variability. A measured steady-state level remains the clinical ground truth.

9. Special Populations

9.1 Amputation

Post-amputation body weight underestimates pre-amputation lean mass, causing C-G to underestimate CrCl. TheraIQ estimates the pre-amputation weight using published limb mass fractions:

Pre-amputation weight	`W_pre = W_post / (1 - limb fraction)`

Example (above-knee)	`Limb fraction ~11.6%; W_pre = W_post / 0.884`

9.2 Spinal Cord Injury

SCI reduces skeletal muscle mass, which causes serum creatinine to understate true creatinine production and C-G to overestimate CrCl. TheraIQ applies established correction multipliers to the calculated CrCl:

Paraplegia	`CrCl_adj = CrCl x 0.75`
Quadriplegia	`CrCl_adj = CrCl x 0.55`
Partial deficit	`CrCl_adj = CrCl x 0.85`

These multipliers apply only to C-G CrCl. Cystatin C-based eGFR is preferred in SCI patients when available, as it is not affected by muscle mass.

9.3 Clinical Flags for Extreme Parameters

Population PK models are least reliable at the extremes of body composition and renal function. TheraIQ automatically flags the following scenarios and recommends patient-specific two-level sampling:

- BMI above 40 (morbid obesity) — Vd estimates are least reliable at body composition extremes
- BMI below 18.5 (underweight) — Vd may be underestimated
- Age above 75 — Vd and Ke may deviate meaningfully from population averages
- CrCl below 20 mL/min — extended half-life and critical trough timing; population Vd unreliable
- CrCl above 130 mL/min — augmented renal clearance; standard doses frequently subtherapeutic

10. Internal Validation Summary

All calculation functions were independently verified against published reference values and known clinical scenarios prior to deployment. Mathematical correctness was confirmed across 180+ test cases spanning 25 calculation categories.

Category	Tests	Result
IBW, AdjBW, BSA calculations	12	Pass
C-G CrCl across all weight basis selections	8	Pass
CKD-EPI 2021 Cr, Cystatin C, Cr-Cystatin	10	Pass
BSA de-indexing to absolute mL/min	6	Pass
All 6 clearance model equations	18	Pass
All 4 volume of distribution model equations	12	Pass
Ke, half-life, Cmax, Cmin equations	8	Pass
AUC calculation	6	Pass
Ke back-calculation from trough (normal, CKD, ARC, extreme)	8	Pass
Trough extrapolation to pre-dose time	6	Pass
Dosing interval selection from half-life	13	Pass
Loading dose calculations and early Vd expansion	9	Pass

Two-level Ke derivation and AUC comparison methods	10	Pass
Dose rounding and infusion duration assignments	14	Pass
AUC target range classification and clinical flag triggers	11	Pass
Discordance detection between renal function estimates	6	Pass
Dose and level timing calculations including overnight scenarios	7	Pass
Spinal cord injury CrCl correction	5	Pass
Amputation weight adjustment	6	Pass
Clinical flags for extreme parameters	6	Pass
User interface input and output linkage verification	Audit	5 issues identified and resolved
TOTAL	180+	All clean

11. Known Limitations and Clinical Caveats

Population PK variance: All population-based estimates carry inter-patient variability. The correlation between vancomycin clearance and CrCl is moderate (r ~0.5-0.7). Measured steady-state levels are required for individualization.

Trough-only AUC: RMSE 47.7 mg·h/L (Fewel 2021). Requires true steady-state conditions (4-5 half-lives elapsed). Level timing errors propagate directly into AUC estimates.

One-compartment model: Vancomycin exhibits multi-compartment behavior. One-compartment assumptions are adequate for routine clinical use but are not appropriate for research-grade PK analysis.

eGFR as clearance driver: The CKD-EPI equations are calibrated to a 1.73 m2 reference BSA and were not used to derive the clearance models. When eGFR is selected as the driver, small systematic differences from C-G-based predictions are expected.

Acute kidney injury: Population models assume stable renal function. In AKI or rapidly changing creatinine, real-time Bayesian methods are preferred.

Pediatric use: TheraIQ uses adult PK models. Pediatric dosing requires age-specific equations and is outside the scope of this calculator.

MRSA MIC: AUC/MIC targeting assumes an MIC of 1 mg/L or below. For higher MICs, alternative agents should be strongly considered regardless of AUC achieved.

12. References

1. Cockcroft DW, Gault MH. Prediction of creatinine clearance from serum creatinine. Nephron. 1976;16(1):31-41. PMID: 1244564

2. Matzke GR, McGory RW, Halstenson CE, Keane WF. Pharmacokinetics of vancomycin in patients with various degrees of renal function. Antimicrob Agents Chemother. 1984;25(3):433-437. PMID: 6370764

3. Birt JK, Chandler MH. Using clinical data to determine vancomycin dosing parameters. Hosp Pharm. 1990;25(7):646-648, 651.

4. Buelga DS, del Mar Fernandez de Gatta M, Herrera EV, Dominguez-Gil A, Garcia MJ. Population pharmacokinetic analysis of vancomycin in patients with hematological malignancies. Antimicrob Agents Chemother. 2005;55(2):188-194. PMID: 15590768

5. Burton ME, Nilsen LM, Brater DC, Uhl EW. Predicting the pharmacokinetics of vancomycin with the Bayesian approach. Am J Hosp Pharm. 1985;42(10):2180-2184.

6. 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(7):604-612. PMID: 22576791

7. Rybak MJ, Le J, Lodise TP, et al. Therapeutic monitoring of vancomycin for serious methicillin-resistant Staphylococcus aureus infections: A revised consensus guideline and review. Am J Health Syst Pharm. 2020;77(11):835-864. PMID: 32191793

8. Fewel NL, Hays SB, Carter KM, et al. Comparison of accuracy of vancomycin area under the curve values estimated with trough-only data: Accuracy in an adult population using three models. Ann Pharmacother. 2021;55(12):1426-1432. PMID: 34169543

9. Inker LA, Eneanya ND, Coresh J, et al. New Creatinine- and Cystatin C-Based Equations to Estimate GFR without Race. N Engl J Med. 2021;385(19):1737-1749. PMID: 34554658

10. US Food and Drug Administration. Guidance for Industry: Pharmacokinetics in Patients with Impaired Renal Function — Study Design, Data Analysis, and Impact on Dosing and Labeling. 2024.

11. Du Bois D, Du Bois EF. A formula to estimate the approximate surface area if height and weight be known. Arch Intern Med. 1916;17(6):863-871.

12. Tanaka A, Aiba T, Otsuka T, et al. Population pharmacokinetic analysis of vancomycin using serum cystatin C as a marker of renal function. Antimicrob Agents Chemother. 2010;54(2):778-782. PMID: 19949052

13. Reporting Discrepancies and Contributing Improvements

TheraIQ is committed to clinical accuracy and continuous improvement. If you identify a calculation discrepancy, an equation inconsistency, or a clinical scenario the calculator does not handle well, please report it. Clinical feedback from practicing pharmacists is the most valuable source of improvement for a tool like this.

What to include	
Calculator section and inputs used	Exact values entered (age, weight, SCr, dose, interval, level, timing)
Expected vs calculated output	What you expected and what the calculator returned
Reference or comparator	Which other calculator or manual calculation you compared against
Clinical context	Patient scenario if relevant (no PHI required)

Contact via theraiq.net — use the feedback button on the calculator or reach out through the platform. All reports are reviewed by the clinical pharmacist developer.

Clinical Disclaimer

TheraIQ provides population pharmacokinetic estimates for decision support purposes only. All dosing recommendations must be reviewed by a licensed clinician with knowledge of the patient's clinical status, comorbidities, concurrent medications, and institutional protocols. Population PK models are approximations with inherent variance. Measured steady-state drug levels are required to confirm and individualize dosing. TheraIQ does not replace clinical judgment, therapeutic drug monitoring, or pharmacist consultation.