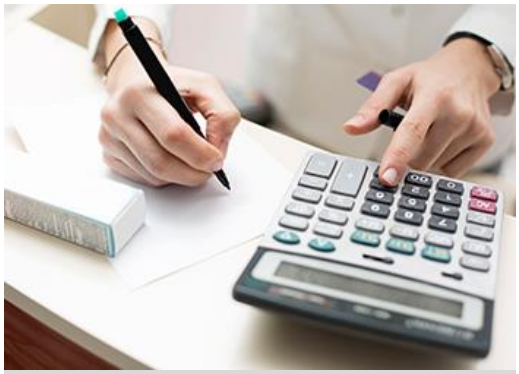
Antimicrobial Stewardship Strategy:

Therapeutic drug monitoring (with feedback)

Measurement and interpretation of serum drug concentrations to maximize efficacy and minimize toxicity.



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Priority Level: **A**

Difficulty Level: **2**

Program Stage:

- Early
- ✓ Intermediate
- Advanced

Antimicrobial Stewardship Outcomes:

- Clinical outcomes

For more information on these criteria and how they were developed, please see the Antimicrobial Stewardship Strategy Criteria Reference Guide.

Updated June 2016

Description

This is an overview and not intended to be an all-inclusive summary. As a general principle, patients must be monitored by the health care team after changes to therapy resulting from recommendations made by the antimicrobial stewardship team.

Optimizing antimicrobial use through therapeutic drug monitoring can maximize efficacy and minimize toxicity for individual patients.[1] It involves the measurement and interpretation of serum drug concentrations drawn at specific times relative to dose administration. The assessment of serum levels and subsequent dosing recommendations requires an understanding of a drug's pharmacokinetics; the timing of samples; the infection being treated; and the patient's clinical status, comorbidities and concomitant drug therapy. Pharmacists are best trained to perform this function.

The most extensive literature on and experience with anti-infective therapeutic drug monitoring involves aminoglycosides (e.g., gentamicin, tobramycin, amikacin) and vancomycin. There are definite associations between toxicity and aminoglycoside trough serum levels and between therapeutic efficacy and peak serum levels.[1] Patients on aminoglycoside therapy should have serum levels assessed and be monitored for adverse effects (e.g., renal and ototoxicity).

The monitoring of vancomycin trough levels is somewhat controversial, but may be considered in patients at higher risk of toxicity or therapeutic failure, with serious infections and/or with unpredictable pharmacokinetics.[2]

Many hospitals offer pharmacist consultation for patients on aminoglycosides and vancomycin, either automatically or by request; some use formalized programs. Such consultation ensures appropriate initial dosing; optimal timing of serum levels; timely and appropriate interpretation of levels and subsequent dosing recommendations; and adequate patient monitoring. Medical directives may be considered so that pharmacists can request serum levels and laboratory tests, and make dosing recommendations without a physician's approval. Documentation in the patient's chart is essential.

Software/calculator programs are available to assess aminoglycoside pharmacokinetics and calculate individualized dosing regimens. A number of vancomycin nomograms are also available to aid in initial and subsequent dosing.

Institutions that cannot measure levels onsite may experience delays in access to information (slow turn-around time), and this can negatively affect patient care. Efforts to minimize such barriers are necessary.

Therapeutic drug monitoring has typically been used for antimicrobials with a narrow therapeutic range, but increasing pharmacokinetic investigations in different patient groups (e.g., the critically ill, patients with extreme body size, patients with variable renal function) and rising antimicrobial resistance have led to a growing interest in monitoring other agents, such as beta-lactam antibiotics and select antifungal agents. However, the lack of availability of appropriate drug assays limits our ability to monitor many of these antimicrobials.

Advantages

- Important practice to reduce the risk of significant toxicity and adverse events.
- Maximizes pharmacokinetic and pharmacodynamic parameters to improve successful treatment of infection.
- Improves the use of laboratory resources (e.g., aminoglycoside/vancomycin levels).

Disadvantages

- Requires training to ensure adequate understanding of the antimicrobial's pharmacokinetics, interpretation of levels, patient monitoring and standardized pharmacist practice.
- Some institutions may encounter barriers to timely results (e.g., tests not performed onsite) and interpretation of levels (e.g., lack of knowledge/experience).

Requirements

- Trained personnel (to interpret results).
- Education on the importance of appropriate sampling time.
- Adequate and timely access to laboratory resources.
- Expertise to develop procedures and medical directives, if applicable.

Associated Metrics

- Proportion of patients with a therapeutic level.
- Average time to reach a therapeutic level.

- Number of patients with a 50 per cent increase in serum creatinine from baseline (before and after implementation of a therapeutic drug monitoring program and/or to reflect the effectiveness of a specific process).

References

1. Roberts JA, Norris R, Paterson DL, Martin JH. Therapeutic drug monitoring of antimicrobials. Br J Clin Pharmacol. 2012;73(1):27–36. Available from: http://onlinelibrary.wiley.com/doi/10.1111/j.1365-2125.2011.04080.x/full

2. Rybak M, Lomaestro B, Rotschafer JC, Moellering R Jr, Craig W, Billeter M, et al. Therapeutic monitoring of vancomycin in adult patients: a consensus review of the American Society of Health-System Pharmacists, the Infectious Diseases Society of America, and the Society of Infectious Diseases Pharmacists. Am J Health Syst Pharm. 2009;66(1):82–98. Erratum in: Am J Health Syst Pharm. 2009;66(10):887. Available from: http://www.ajhp.org/content/66/1/82.long

Additional Useful References

Select articles to provide supplemental information and insight into the strategy described and/or examples of how the strategy was applied; not a comprehensive reference list. URLs are provided when materials are freely available on the Internet.

- Bond CA, Raehl CL. Clinical and economic outcomes of pharmacist-managed aminoglycoside or vancomycin therapy. Am J Health Syst Pharm. 2005;62(15):1596–605.

Tools and Resources

- University of Kentucky Chandler Medical Center, Pharmacy Services. Clinical pharmacokinetics service and anticoagulation guidelines [Internet]. 35th ed. Lexington, KY: University of Kentucky Chandler Medical Center; 2013 [cited 2015 Sep 23]. Available from: http://www.hosp.uky.edu/pharmacy/CPS/PKmanual-disclaimer.html

  Guidelines for the dosing and monitoring of aminoglycosides (conventional and high dose, extended interval) and vancomycin.

- Scottish Antimicrobial Prescribing Group (SAPG). Gentamicin and vancomycin [Internet]. Glasgow: Scottish Medicines Consortium; date unknown [cited 2015 Sep 23]. Available from: http://www.scottishmedicines.org.uk/SAPG/Quality_Improvement/Gentamicin_and_Vancomycin

  Guidance documents for the use of vancomycin and gentamicin.
  Information and online calculators.

  Guidance for both intermittent (pulsed) and continuous infusion of vancomycin.
  Hartford and Greater Glasgow and Clyde nomograms, as well as administration and monitoring charts for gentamicin.

Samples/Examples (updated June 2016)

- Example 1: Vancouver Coastal Health and Providence Health Care, BC - Vancomycin Empiric Dosing Guidelines
- Example 2: Markham Stouffville Hospital Corporation - Vancomycin Guidelines
- Example 3: Markham Stouffville Hospital Corporation - Aminoglycoside Dosing in Adults Policy and Guidelines
- Example 4: Markham Stouffville Hospital Corporation - Vancomycin Monitoring Record
- Example 5: Markham Stouffville Hospital Corporation - Aminoglycoside Monitoring Record
- Example 6: Sunnybrook Health Sciences Centre - Monitoring for Aminoglycoside Induced Ototoxicity
- Example 7: Sunnybrook Health Sciences Centre - Patient Information Sheet - Aminoglycoside Treatment

These documents have been generously shared by various health care institutions to help others develop and build their antimicrobial stewardship programs. We recommend crediting an institution when adopting a specific tool/form/pathway in its original form.

Examples that contain clinical or therapeutic recommendations may not necessarily be consistent with published guidelines, or be appropriate or directly applicable to other institutions. All examples should be considered in the context of the institution's population, setting and local antibiogram.

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Links with Other Strategies

- Dose optimization

Disclaimer

Citation

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For further information

Antimicrobial Stewardship Program, Infection Prevention and Control, Public Health Ontario.

Email: asp@oahpp.ca

Public Health Ontario acknowledges the financial support of the Ontario Government.

Example 1: Vancouver Coastal Health and Providence Health Care, BC - Vancomycin Empiric Dosing Guidelines

Vancouver Coastal Health
Promoting wellness. Ensuring care.

Providence Health Care
How you want to be treated.

Pharmacy
VANCOMYCIN EMPIRIC DOSING GUIDELINES
April 2016, 3rd edition

For more information, please contact Pharmacy
Or visit: www.vhpharmsci.com

KEY
1. Establish patient age, weight, and serum creatinine.

2. Using Table 1, identify initial loading dose and maintenance dose per interval according to patient weight and target pre-vancomycin level.

3. Using Table 2, determine target pre-vancomycin level based on clinical indication.

4. Using Tables 3 or 4, identify initial dosing interval according to target pre-vancomycin level, age, and serum creatinine.

5. Using Table 5, determine dialysis dosing.

TABLE 1 INITIAL DOSE PER INTERVAL

TOTAL BODY WEIGHT	LOADING DOSE (suggested maximum 2500 mg/dose)		MAINTENANCE DOSE
kg	Target pre-level 10-15 mg/L (20 mg/kg)	Target pre-level 15-20 mg/L (25 mg/kg)	(15 mg/kg)
40-50	1000 mg	1250 mg	750 mg
51-60	1250 mg	1500 mg	1000 mg
61-70	1250 mg	1750 mg	1000 mg
71-80	1500 mg	2000 mg	1250 mg
81-90	1750 mg	2250 mg	1250 mg
91-100	2000 mg	2500 mg	1500 mg

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Example 1: Vancouver Coastal Health and Providence Health Care, BC - Vancomycin Empiric Dosing Guidelines (continued)

TABLE 2 SUGGESTED TARGET PRE-VANCOMYCIN LEVELS BASED ON INDICATION

Pre-vancomycin Level 10-15 mg/L	Pre-vancomycin Level 15-20 mg/L
• Skin and soft tissue infection • Urinary tract infection (UTI) (if catheter-associated; rule out bacteremia)	• Catheter-associated bacteremia • Central nervous system infection • Deep-seated or sequestered infection (e.g. abscess) • Endocarditis • Osteomyelitis • MRSA bacteremia or pneumonia • MSSA bacteremia (penicillin allergic patient)

TABLE 3 FOR SKIN AND SOFT TISSUE INFECTION & UTI
LOW-TARGET 10-15 mg/L INITIAL DOSING INTERVAL (hours)

SCr (mcmol/L)	Age Group (years)					
	20-29	30-39	40-49	50-59	60-69^	70-79^
40-60	8	8	12	12	12	18
61-80	8	12	12	12	18	18
81-100	12	12	12	18	18	18
101-120	12	12	18	18	18	24
121-140	12	18	18	18	24	
141-160	18	24	24	24		
161-180	24	24				
181-200	24					
Above 200						
Dialysis	See TABLE 5 (back of card)					

TABLE 4 FOR ALL OTHER INDICATIONS (COMPLICATED INFECTIONS)
HIGH-TARGET 15-20 mg/L INITIAL DOSING INTERVAL (hours)

SCr (mcmol/L)	Age Group (years)						
	20-29	30-39	40-49	50-59	60-69^	70-79^	80-89^
40-60	6	6-8	8	8	8-12*	12	12
61-80	8	8	8-12*	12	12	12	12-18*
81-100	12	12	12	12	12-18*	18	18
101-120	12	12	12-18*	18	18	18	18
121-140	12	18	18	18	18	18-24*	
141-160	18	18	18	18-24*	24		
161-180	18-24*	24	24	24			
Above 180							
Dialysis	See TABLE 5 (back of card)						

^In elderly patients with low muscle mass, use clinical judgment as SCr may not reflect renal function accurately.
*If more aggressive therapy is desired, select more frequent dosing interval.

Shaded boxes: These patients have unstable and/or reduced renal function, and the nomogram may not be as predictive.
- For those with an interval stated, patients should receive a loading dose followed by 3 hour and pre-2nd dose serum levels to determine appropriate dosing.
- For those with no dosing interval stated, patients should receive a loading dose followed by 3 hour and 24 hour post-dose serum levels to determine subsequent dosing.
- A clinical pharmacist should be contacted for assistance with dosing and interpretation of levels.

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Example 1: Vancouver Coastal Health and Providence Health Care, BC - Vancomycin Empiric Dosing Guidelines (continued)

TABLE 5 DIALYSIS DOSING

	Hemodialysis (HD)	Continuous Ambulatory Peritoneal Dialysis (CAPD)
Loading Dose	25 mg/kg	Intraperitoneal (IP): 30 mg/kg **OR** Intravenous (IV): 20 mg/kg
Maintenance Dose	**weight < 70 kg:** 500 mg QHD **weight ≥ 70 kg:** 750 mg QHD	IP: 30 mg/kg every 5-7 days **OR** IV: 20 mg/kg every 4-7 days
When To Draw Level	Pre-second maintenance dose	3-4 days after first dose
Target Vancomycin Level	Pre-HD level: 15-20 mg/L	Trough level: 15-20 mg/L

THERAPEUTIC DRUG MONITORING

Vancomycin serum levels should be ordered in the following situations:

1. Pre-vancomycin level on 3rd or 4th dose (within 48 hours) if:
   - a higher level of 15-20 mg/L is desired **OR**
   - patient is at risk for accumulation (e.g. Q6-8H interval) **OR**
   - patient is receiving other nephrotoxic agents **OR**
   - serum creatinine is above normal, renal function is changing or uncertain **OR**
   - patient is obese (>125% IBW), pregnant, pediatric or hypermetabolic (e.g. burn patient, cystic fibrosis)

   Repeat at least weekly to ensure pre-vancomycin level is within desired therapeutic range

2. Pre-vancomycin level after 7 days of therapy (for prolonged course) if aiming for levels < 15 mg/L **AND** no other risk factors as per above

3. Pre-vancomycin level if patient is not responding to therapy

4. Pre- and 3 hour post-vancomycin level (target 20-40 mg/L) if calculation of precise kinetic parameters are necessary (e.g. in a case when a target pre-vancomycin level of 15-20 mg/L cannot be achieved while on prolonged therapy, or in an obese, pregnant or pediatric patient, especially when aggressive dosing is required)

Revised April 2016

Available online from:

http://vhpharmsci.com/PagePocket/index.html

Example 2: Markham Stouffville Hospital Corporation - Vancomycin Guidelines

INTERDISCIPLINARY MANUAL

AUTHOR:	Pharmacist	**FOLDER:**	Medication Guidelines & Protocols
APPROVED BY:	Drugs & Therapeutics Committee	**REVIEW FREQUENCY:**	3 years
ELECTRONIC RESPONSIBILITY:	Director of Pharmacy	**ORIGINAL APPROVAL DATE:**	03/11/05
POLICY HISTORY/ NUMBER CHANGES:		**REVIEWED/ REVISED DATE:**	29/01/09 25/05/13

290.914.916.190 VANCOMYCIN GUIDELINES

Expected Outcome:
Patients will receive Vancomycin for appropriate indications in a sufficient dose to achieve desired trough Vancomycin levels to promote efficacy and avoid development of resistance.

Appropriate Use:

- Treatment of serious infections suspected or documented to be caused by β-lactam resistant gram-positive microorganisms (e.g. ampicillin-resistant Enterococci, methicillin-resistant Staphylococcus aureus (MRSA) or coagulase-negative Staphylococcus)
- Treatment or surgical/procedure prophylaxis of gram-positive infections in patients with severe β-lactam allergy
- Empiric therapy for meningitis until culture and sensitivity results are available
- First-line oral treatment of severe or recurrent *Clostridium difficile* infection (CDI) or second-line therapy for non-severe cases in patients who have failed to tolerate or respond to oral metronidazole (for oral dosing guidelines for CDI, see Appendix B of policy # 040.912.040 *Clostridium Difficile Infection (CDI)* – Guidelines for the Diagnosis, Management and Treatment of Symptomatic Patients)

Example 2: Markham Stouffville Hospital Corporation - Vancomycin Guidelines (continued)

Situations in which Vancomycin use should be discouraged:

- Routine surgical prophylaxis other than patient with serious allergy to β-lactam antibiotics
- Empiric antimicrobial therapy for febrile neutropenic patient unless strong suspicion for β-lactam resistant gram-positive organism
- Treatment in response to a single blood culture positive for coagulase negative Staphylococcus if other blood cultures taken during same time frame are negative (contamination likely)
- Continued empiric use for presumed infections in patients whose cultures fail to show evidence of β-lactam resistant gram-positive microorganisms
- Eradication of MRSA colonization
- Treatment of infections caused by β-lactam sensitive gram-positive organisms
- Systemic or local prophylaxis for infection or colonization of indwelling central or peripheral intravascular catheters

IV Dosing Guidelines:

- Usual Dosage = 15-20 mg/kg q8-12h in patients with normal renal function
- With impaired renal function, the frequency is based on the estimate of creatinine clearance (CrCl). Use Cockcroft-Gault equation** to calculate estimated CrCl.
- Dose is based on actual body weight, even in the setting of obesity. Avoid doses larger than 2 g; instead consider shorter dosing interval
- Consider more aggressive dosing in serious, invasive infections where a trough level target of 15-20 mcg/mL is desired (see Monitoring section)
- In seriously ill patients, consider a **loading dose** of 25-30 mg/kg to facilitate rapid attainment of target trough concentrations. Infuse at a rate of 500 mg/h. Do NOT adjust loading dose for renal dysfunction.
- See the following tables for suggested dosing:

Table 1: Empiric Dosage

Actual Body Weight (kg)	Empiric Initial Dose (mg)
40-49	750
50-64	1000
65-74	1250
75-89	1500
90-114	1750
115-130	2000
Greater than 130	Consider alternate dosing strategy

Example 2: Markham Stouffville Hospital Corporation - Vancomycin Guidelines (continued)

Table 2: Empiric Dosing Interval Based on Creatinine Clearance

Creatinine Clearance (mL/min)	Empiric Initial Dosing Interval
Greater than or = 60	q12h
41-59	q24h
31-40	q36h
16-30	q48h
10-15	q72h
Less than 10 or hemodialysis	Order random level and repeat every 1 to 2 days. Repeat dose when level less than 20 mcg/mL.
CRRT	500 mg q24-48h. Adjust based on levels.

- Pharmacist may adjust the dose based on renal function and patient weight. See policy # 290.914.916.115 Pharmacist Medication Dosing Service.

Monitoring:

- Vancomycin therapeutic drug monitoring is used to determine individualized patient pharmacokinetics. The results may be used to guide dosing, enhance safety and efficacy, and to reduce the risk of resistance.
- Peak levels have not been shown to correlate well with toxicity or efficacy and adequate peak levels (20 – 80 mcg/mL) are achieved with recommended doses.
- Trough concentrations should always be maintained above 10 mcg/mL to avoid development of resistance.
- **Target trough range of 15-20 mcg/mL is recommended in select patients with**:
  - bacteremia, endocarditis, meningitis, hospital acquired pneumonia or osteomyelitis caused by S.aureus
- Trough levels greater than 20 mcg/mL *may* be associated with an increased risk of nephrotoxicity.
- Trough levels should be ordered in patients:
  - expected to remain on vancomycin for longer than 3 days
  - with rapidly changing renal function
  - receiving other nephrotoxic drugs (e.g. gentamicin, tobramycin, amphotericin)
  - receiving aggressive dosing
  - with severely altered volumes of distribution (e.g. burn patients, morbidly obese, compartment syndrome)
- Trough levels should be performed once weekly for patients requiring long term treatment (ie 4-6 weeks). Levels should be done more frequently in hemodynamically unstable patients or suspicion of subtherapeutic level.
- Anuric patients should have a random level drawn and repeated every 1 to 2 days until level is less than 20 mcg/mL. A repeat vancomycin dose is given at this time.
- Initial trough levels should be obtained no earlier than at steady state (before 4th dose in patients with normal renal function)

Example 2: Markham Stouffville Hospital Corporation - Vancomycin Guidelines (continued)

- Trough levels should be performed 30 minutes or less before scheduled dose. If peak levels are used to assess vancomycin pharmacokinetics, they should be done 1 hour after the end of the infusion.
- Serum creatinine, BUN should be checked at least twice weekly while on vancomycin or more frequently if renal function is unstable, on concomitant nephrotoxic agents or targeting higher trough concentrations. If signs of renal impairment develop, assess risk versus benefit of vancomycin therapy.
- Pharmacist may order vancomycin levels, serum creatinine and BUN as needed and adjust dose or interval according to above recommendations. See policy # 290.914.916.115 Pharmacist Medication Dosing Service. See the following table for suggested dose and interval adjustments.

Table 3: Dosage Adjustments Based on Trough Levels

Trough less than 10 mcg/mL	**Trough 10-13 mcg/mL**	**Trough 13.1-20 mcg/mL**	**Trough 20.1-40 mg/mL**	**Trough greater than 40 mcg/mL**
If dose already given, order peak level (1 hour after end of infusion) and determine patient's pharmacokinetics . While level pending, **either** increase dose by 250-500 mg **OR** decrease dosing interval.	Keep same dose and interval. If targeting trough of 15-20 mcg/mL, then increase dose by 25-50% and keep same dosing interval or if at max dose for weight, decrease interval	Keep same dose and interval.	Decrease dose by proportion **OR** increase dosing interval.	Hold vancomycin. Order 2 random levels separated by 24 hrs and determine patient's pharmacokinetics .

Adverse Effects:

Red person syndrome

Histamine mediated reaction characterized by erythematous flushing, tingling and pruritis involving face, neck and upper torso most often occurring during vancomycin infusion. Associated hypotension may also occur. Management should include extending the duration of infusion to 90-120 minutes with or without premedication with an antihistamine. This does not preclude further use of vancomycin.

Nephrotoxicity

Nephrotoxicity due to vancomycin monotherapy is uncommon and often reversible. Vancomycin induced nephrotoxicity is defined as an increase in

Example 2: Markham Stouffville Hospital Corporation - Vancomycin Guidelines (continued)

serum creatinine concentration of 45 µmol/L or 50% increase from baseline (whichever is greater) in at least 2-3 consecutive measurements after several days of vancomycin therapy in the absence of an alternate explanation. The incidence of nephrotoxicity increases when vancomycin is combined with aminoglycosides or other nephrotoxic drugs; or when the duration of therapy is prolonged (greater than 21 days).

Ototoxicity

Severe ototoxicity induced by vancomycin is rare. Case reports are confounded by concurrent use of other ototoxic agents and early reports (1950-60s) felt to be related to impurities in the formulation. The occurrence of ototoxicity does not appear to correlate with excessive peak or trough vancomycin concentrations. Recommendations are to discontinue vancomycin if patient loses ability to hear high frequency sounds or tinnitus occurs.

Other

Thrombophlebitis and/or pain, tingling at injection site, neutropenia, thrombocytopenia, rash, hypersensitivity and very rare reports of cardiac arrest related to rapid IV injection

Administration:

- Less than or = 500 mg in 100 mL NS or D5W
- Greater than 500 to 1250 mg in 250 mL NS or D5W
- Greater than 1250 mg in 500 mL NS or D5W
- Infuse doses less than or equal to 1000 mg over at least 1 hour, 1100-1500 mg over 90 minutes and greater than 1500 mg over 2 hours
- Adjust doses in increments of 250 mg

** Cockcroft-Gault equation:

$$\text{Creatinine clearance (CrCl)} = \frac{(140-\text{age}) \times \text{weight (kg)}}{\text{Serum creatinine } (\mu\text{mol/L})} \quad \text{multiply by 1.2 if male}$$

References:

1. CDC. Recommendations for preventing the spread of vancomycin resistance recommendations of the hospital infection control practices advisory committee; Sept. 22, 1995.
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3. Intravenous Drug Therapy Manual. Ottawa General Hospital. 2005
4. Anderson P. Handbook of Clinical Drug Data, ninth edition, 1999; p 191-2.
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Example 2: Markham Stouffville Hospital Corporation - Vancomycin Guidelines (continued)

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9. Tunkel A, et al. Practice Guidelines for the Management of Bacterial Meningitis. Clin Infect Dis 2004; 39: 1267-1284.
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11. Jeffres MN, et al. Predictors of mortality for methicillin-resistant Staphylococcus aureus health-care-associated- pneumonia: Specific evaluation of vancomycin pharmacokinetic indices. Chest 2006; 130:947-55.
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ENDORSEMENT(S):
Antibiotic Stewardship Subcommittee
Drugs & Therapeutics Committee

PREVIOUS REVIEWED/REVISED DATE(S):
29/01/09

Example 3: Markham Stouffville Hospital Corporation - Aminoglycoside Dosing in Adults Policy and Guidelines

INTERDISCIPLINARY MANUAL

AUTHOR:	Director of Pharmacy	**FOLDER:**	Medication Guidelines & Protocols
APPROVED BY:	Drugs and Therapeutics Committee	**REVIEW FREQUENCY:**	3 years
RESPONSIBILITY:	Director of Pharmacy	**ORIGINAL APPROVAL DATE:**	03/11/2005
POLICY HISTORY/ NUMBER CHANGES:		**REVISED/ REVIEWED DATE:**	12/09/2013

290.914.916.025 AMINOGLYCOSIDE DOSING IN ADULTS

POLICY:

High dose "once daily" aminoglycoside regimen or Conventional Multiple daily dosing regimen will be used for aminoglycoside dosing in adults. The pharmacist will determine the appropriate regimen based on baseline clinical data, creatinine clearance and assessment parameters, see policy # 290.914.916.115 Pharmacist Medication Dosing Service.

GUIDELINES:

1. **COLLECTION OF BASELINE CLINICAL DATA:**

a) **Obtain the following baseline clinical data:**

- differential diagnosis, site and severity of infection
- height (Ht), weight (Wt), ideal body weight (IBW), lean body weight (LBW), and dosing body weight (DBW)
- age, sex
- serum creatinine (SCr), BUN, urinary output
- WBC and differential
- temperature
- concurrent disease states or conditions which may affect the pharmacokinetics of aminoglycosides, e.g. cystic fibrosis, burns, obesity, ascites

Example 3: Markham Stouffville Hospital Corporation - Aminoglycoside Dosing in Adults Policy and Guidelines (continued)

2. DETERMINATION OF DOSING BODY WEIGHT AND CREATININE CLEARANCE:

a) Determination of DBW

Select the most appropriate value for the DBW. This value is determined by considering the patient's actual weight (ABW), IBW, LBW, or estimation of ABW. Use the equations below or Micromedex to calculate IBW and DBW.

Female: IBW = 45.5 kg + (2.3 X inches over 5')
LBW = 1.07 X Wt(kg) - 148 X (Wt(kg)2)/ (Ht(cm)2)

Male: IBW = 50 kg + (2.3 X inches over 5')
LBW = 1.10 X Wt(kg) - 128 X (Wt(kg)2)/ (Ht(cm)2)

- If ABW greater than IBW (but not more than 30% over IBW), use DBW = IBW
- If ABW geater than IBW (more than 30% over IBW), use DBW = IBW + 0.4 (ABW - IBW)
- If ABW less than IBW, use ABW or LBW, as appropriate

b) Calculation of Creatinine Clearance:

Calculate creatinine clearance (CrCl) using the Crockcroft-Gault equation below or Micromedex.

Note: Conversion factor for serum creatinine: mg/Dl = umol/L 88.4

Males: $Clcr = \frac{IBW\ (kg) \times (140-age) \times 1.2}{Scr\ (umol/L)}$ (mL/min)

Females: 0.85 X Clcr (for males - as above)

3. ASSESSMENT - DETERMINATION OF HIGH DOSE OR MULTIPLE DAILY DOSING:

Assess patient for appropriateness for either the high dose ('once daily') aminoglycoside dosing regimen or the conventional multiple daily dose regimen. Patients are initiated on the high dose regimen unless one of the following exclusion criteria is met:

- Pregnancy
- Neonatal or paediatric age
- Endocarditis (except strep viridans endocarditis)
- Ascites, burns
- Cystic fibrosis
- Dialysis

- CrCl less than 20 mL/min
- Surgical prophylaxis
- Post-partum less than 7 days
- Use with caution in patients greater than 60 years old
- Amputation

Patients who meet one or more of the above criteria must have therapy initiated with the conventional multiple daily dosing regimen with monitoring of pre and post aminoglycoside levels.

4. HIGH DOSE "ONCE DAILY" AMINOGLYCOSIDE REGIMEN:

RATIONALE AND BACKGROUND:
Pharmacokinetic Properties of Aminoglycosides:

Concentration-dependent killing:
It has been demonstrated that achievement of high peak serum concentration of aminoglycosides relative to the minimum inhibitory concentration of the microorganism is the major determinant of the clinical response to aminoglycosides. This is best achieved with high dose regimens, which result in high peak concentrations of drug.

Post antibiotic effect:
Post antibiotic effect is defined as a period of time after complete removal of the antibiotic from the body during which there is no growth of the target organism. Use of high dose aminoglycosides may result in a period of up to 12 hours of antibiotic effect during which there is no detectable serum concentration of the drug. This property of the aminoglycoside allows for daily dosing without compromising therapeutic efficacy. The higher the concentration of drug, the longer the duration of the post antibiotic effect.

Toxicity:
A major determinant of aminoglycoside induced renal toxicity and ototoxicity is the accumulation of these agents within the renal cortex and perilymph of the inner ear. The accumulation follows saturable kinetics so even though the peak serum drug concentration is higher with high dose aminoglycosides, the kidney does not accumulate more drug. Conversely, it allows for back diffusion of the drug from the kidney and inner ear to flow back out, reducing drug exposure and limiting toxicity.

Clinical Efficacy:
Many studies have been published comparing high dose aminoglycoside regimens (once daily) to conventional multiple daily dosing regimens. In all these studies, high dose aminoglycosides were as effective, and not more toxic, than multiple daily dosing of the drug.

Example 3: Markham Stouffville Hospital Corporation - Aminoglycoside Dosing in Adults Policy and Guidelines (continued)

DOSING GUIDELINES:

Dose:

Gentamicin and Tobramycin

- 5 mg/kg DBW (use increments of 20 mg)
- 3 mg/kg DBW (Gentamicin only, for strep viridans endocarditis)

Amikacin

- 15 mg/kg DBW (use increments of 25 mg)

Interval:

Creatinine Clearance	
mL/min	Dosing Interval
greater than 60	Q24h
40 – 59	Q36h
20 – 39	Q48h
less than 20	Use conventional multiple daily dosing

Administration:

- Dilute in 100 mL D5W or NS and infuse over 30 minutes

Monitoring:

1. DO NOT DRAW ROUTINE PEAK AND TROUGH LEVELS.
   Exceptions:
   - significant changes in renal function
   - infections involving highly resistant organisms

Desired Trough and Peak Levels

	Trough	Peak
Gentamicin*/Tobramycin	Less than 0.5 mg/L	20 mg/L
Amikacin	Less than 2.5 mg/L	60 mg/L

a. Draw ONE trough level 30 min before the second to fourth dose
   If level is greater than desired trough extend the dosing interval by 12 hours and repeat level (or use conventional dosing and monitoring methods).

   OR

b. Draw a trough level 30 min before and a peak level 30 min after the second to fourth dose. If peak or trough levels are outside of desired range adjust further doses using pharmacokinetic principles (see section on Dosage Adjustment Form Serum Drug Levels).

Note: Amikacin blood samples are sent out of the hospital for processing so a delay in reporting is to be expected.

2. Repeat trough levels if therapy is greater than 7 days and reassess weekly thereafter and with any significant changes in renal function.
3. Monitor serum creatinine pre dose and then 3 x a week.
4. **Do not use high dose aminoglycosides for greater than 14 days** due to an increased risk of nephrotoxicity/ototoxicity. Consider alternative therapy.
5. Baseline audiology should be performed for patients on long-term treatment.

* There are no specific guidelines for drug concentration monitoring of gentamicin 3 mg/kg q24h for streptococci endocarditis. A target trough of less than 0.5 mg/L, as with other dosing regimens, is reasonable.

Orders and Documentation:

1. Pharmacist will order the dose, route and frequency.
2. Indicate time for the next dose and order trough level.
3. Pharmacist will document on the electronic record.

References:

1. Carmi B, Abraham D, et al. Pharmacokinetic Dosing of Aminoglycosides: A Controlled Trial. Am J Med 2003;114:194-198.
2. Antibiotic Guidelines, 2010. Div of Infectious Disease, Columbia University Medical Center. From http://www.id.hs.columbia.edu/clinical_dosing.html.
3. Guidelines for Antimicrobial Use, University Health Network, 2007 p.133-138
4. Freeman CD, Nicolau DP, Belliveau PP, Nightingale CH. Once-daily dosing of aminoglycosides: review and recommendations for clinical practice. J Antimicrob Chemother 1997;39,677-686.
5. Baily TC, Little JR, Littenberg B et al. A meta-analysis of extended-interval dosing verses multiple daily dosing of aminoglycosides. Clin Infect Dis 1997:24(5):786-95
6. Sunnybrook Health Science Centre Formulary, September 1996 p.295-302

5. CONVENTIONAL MULTIPLE DAILY DOSING REGIMEN:

a) Initial Calculation of Dose and Interval:

Method I:

Computer software – Selinger Kinetics or Abbott Kinetics

Example 3: Markham Stouffville Hospital Corporation - Aminoglycoside Dosing in Adults Policy and Guidelines (continued)

Method II:

Dose: General Guidelines

Drug	Dose
Gentamicin Tobramycin Netilmicin	1 – 2 mg/kg/dose (based on DBW)
Amikacin	5 – 7.5 mg/kg/dose (based on DBW)

Select dose based on the severity and site of infection according to the following:

Indication/Site of Infection	Gentamicin/ Tobramycin	Amikacin
Synergy (gentamicin)	1 mg/kg	
UTI	1 mg/kg	5 mg/kg
Gram neg sepsis, other serious infections	1.5-2 mg/kg	7.5 mg/kg
pneumonia	2 mg/kg	7.5 mg/kg

Interval

Choice of the dosing interval is based on the patient's renal function. The patient's urinary output should be considered in addition to the serum creatinine concentration.

Select the appropriate dosing interval as follows:

CrCl (mL/min)	Dosing Interval
Greater than 70	q8h
40-69	q12h
15-39	q24h
Less than 15	Give a dose and draw levels in 24 hours to determine dosing interval

When selecting the interval, additional consideration should be given to patients with factors, which may alter creatinine production. (i.e. muscle wasting, severe muscle atrophy/dystrophy, hyperthyroidism, paralysis, chronic glucocorticoid therapy, aging, hepatic diseases, trauma, surgery, sepsis).

Method III:

Dose: = DBW (kg) X Vd (L/kg) X Cpd (mg/L)

Cpd = desired peak concentration
Vd = volume of distribution (estimated considering hydrational status)

Hydration Status	Vd (L/kg)
Normal	0.20 - 0.25
Dehydrated	0.15
Overhydrated	0.3

Interval:

Interval should be selected based on the criteria given in Method II above.

Method IV:
This method should be used for patients whose renal function is very poor or unknown.

Dose:
Use method II or III to determine dose.

Interval:

No interval should be ordered at this time. The interval should be determined based on the results of a post and random level. Refer to "Dosage Adjustments from Serum Drug Levels".

b) Timing of Serum Drug Levels:

Intravenous Administration: Aminoglycosides are to be administered over 30 minutes. Pre levels should be taken 0 - 15 minutes before the dose. Post levels should be taken 30 minutes after the end of the infusion.

Intramuscular Administration: Pre levels should be taken 0 – 15 minutes before the IM injection. Post levels should be taken 1 hr after the injection.

Aminoglycoside pre and post levels should be taken around the third dose of a dosage regimen (e.g. 3rd 80 mg dose from a regimen of 100 mg loading dose, followed by 80 mg q8h) for q6 - q12h dosing intervals, or around the second dose for intervals greater than q12h. Pre and post levels should be done following the initiation of therapy or a change in dosage regimen. It may be necessary to draw levels at other specified times for patients with variable renal function

c) Desired Serum Drug Levels:
The following are the desired serum concentrations for aminoglycosides:

Example 3: Markham Stouffville Hospital Corporation - Aminoglycoside Dosing in Adults Policy and Guidelines (continued)

Indication/Site of Infection	Gentamicin/Tobramycin		Amikacin	
	Trough (mg/L)	Peak (mg/L)	Trough (mg/L)	Peak (mg/L)
Synergy (gentamicin)	Less than 1	3-4 mg/L		
UTI	0.8 – 2 mg/L	4-5 mg/L	5 – 10 mg/L	20-25 mg/L
Gram neg sepsis, other serious infections		6-7 mg/L		25-30 mg/L
pneumonia		7-8 mg/L		25-30 mg/L

d) Dosage Adjustments from Serum Drug Levels:
Four methods may be used to make DOSAGE and INTERVAL adjustments.

Method I:
Computer software - Selinger or Abbott Kinetics

Method II:

Interval:
a) Determine half-life based on rough estimate or equation as follows:

$$t1/2 = \frac{0.693}{k-}$$

k = elimination rate constant

= slope of ln concentration VS time curve

b) Calculate the number of t1/2's between the desired pre and post.
ie. desired post = 7.5 mg/L
desired pre = 1 mg/L
7.5 ---------> 3.75 ----------> 1.875 ---------> 0.95 (~1)
1 t1/2 2 t1/2 3 t1/2

Three t1/2's are required for the dosing interval. If the t1/2 = 3.5 hours, 3 X 3.5 hours = 10.5 hours. Choose the closest standard interval (q12h in this case).

Dose:
Adjust dose based on proportional difference between pre and post levels.
i.e. observed pre = 2.5 mg/L desired pre = 1 mg/L
observed post = 5 mg/L desired post = 7 mg/L
difference = 2.5 mg/L difference = 6 mg/L

60 mg dose -----> difference = 2.5 mg/L
X mg dose -----> difference = 6 mg/L
∴new dose = 144 mg, round off to 140 mg for new dose

Check validity of new dose by calculating the mg/kg/dose. This new dose will likely be within the 1 - 2.5mg/kg range.

Method III:

Use Pharmacokinetic Formulas:

$$Vd = \frac{R(1 - e^{-(kt)})}{k\ Cmax - Cmin\ e^{-(kt)}}$$

$$T = -\frac{2.303}{K} \log \frac{(Cmin)}{(Cmax)} + t$$

$$R = Cmax, desired \times k \times Vd \times \frac{(1 - e^{-(kT)})}{(1 - e^{-(kt)})}$$

Check:

$$Cmax = \frac{R\ (1 - e^{-(kt)})}{kVd\ (1 - e^{-(kT)})}$$

$$Cmin = Cmax\ e^{-(k(T-t))}$$

Vd = volume of distribution

k = elimination rate constant

t = time for infusion

T = dosing interval

Method IV:

To use this method, two or three drug levels should be taken following the first dose. One level must be a post, and the others are random levels taken at appropriate times following administration.

Dose:
Adjust dose as outlined in method II (observed pre = 0)

Interval:
Determine the t1/2 from the measured serum drug levels, and select the appropriate interval using the approach outlined in method II.

Monitoring:

The following parameters should be monitored:

- Temperature - monitor daily
- Weight
- BUN, SCr - monitor 2 to 3 times per week (more frequent monitoring may be necessary for patients with unstable renal function
- 24 hour urine for CrCl - to be monitored when SCr is not an accurate indication of renal function
- Urinary output (I/O)
- Hydration status
- Culture and sensitivity reports - monitor daily
- Concomitant antibiotics - monitor daily

Example 3: Markham Stouffville Hospital Corporation - Aminoglycoside Dosing in Adults Policy and Guidelines (continued)

Orders and Documentation:

1. Pharmacist will order the dose, route, and frequency.
2. State the time the next dose is due.
3. Specifically order pre, post, or random levels. An order for "gentamicin" levels is not acceptable.
4. State the dose the levels are to be taken around or before, e.g. pre and post gentamicin levels around 1400h dose, or gentamicin pre level before 2200h dose.

Example 4: Markham Stouffville Hospital Corporation - Vancomycin Monitoring Record

Vancomycin Monitoring Record

Patient Name:	Age: ____ Sex: _____ Unit: _____	
Unique #:	Other Antibiotics:	
Diagnosis: **Target level (mcg/mL)** □ 10-15 □15-20		
Allergies:	MD:	Pharmacist:
Ht: _____ Wt: _____ IBW: _____ Baseline CrCl: _____mL/min	Doses Given: _____mg @ _____h _____ (date) _____mg @ _____h _____ (date)	
Orders written _____ (date) 1) Vancomycin_____ mg IV q _____hr (= _____ mg/kg) 1st dose: _____hr _____(date) 2) Bloodwork _____ _____		

MICROBIOLOGY

Date	Site	Results	Sensitivities

Date	Site	Results	Sensitivities

LAB MONITORING

Date	Scr (µmol/L)	Urea (µmol/L)	Clcr (mL/min)	WBC	Neuts (%)	Tmax (°C)	ESR	C-Reactive Protein

LEVELS

Date/ Time (Levels)	Current Regimen	Trough level Time	Level	New Regimen	(mg/kg/ dose)	Comments	Initial

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Example 4: Markham Stouffville Hospital Corporation - Vancomycin Monitoring Record (continued)

IV Vancomycin Dosing Guidelines:

- Usual Dosage = 15-20 mg/kg (**actual body weight**) q8-12h in patients with normal renal function. Adjust frequency based on estimated CrCl
- Avoid doses larger than 2 g; instead consider shorter dosing interval
- Consider more aggressive dosing in serious, invasive infections where a trough level target of 15-20 mcg/mL is desired (see Monitoring section)
- In seriously ill patients, consider a **loading dose** of 25-30 mg/kg to facilitate rapid attainment of target trough concentrations. Infuse at a rate of 500 mg/h. Do NOT adjust loading dose for renal dysfunction.****Pharmacist to please add note to emar and order re: administration rate for loading dose.**
- See the following tables for suggested dosing:

Table 1: Empiric Dosage

Actual Body Weight (kg)	Empiric Initial Dose (mg)
40-49	750
50-64	1000
65-74	1250
75-89	1500
90-114	1750
115-130	2000
Greater than 130	Consider alternate dosing strategy

Table 2: Empiric Dosing Interval Based on Creatinine Clearance

Creatinine Clearance (mL/min)	Empiric Initial Dosing Interval
Greater than or = 60	q12h
41-59	q24h
31-40	q36h
16-30	q48h
10-15	q72h

Vancomycin Monitoring Guidelines:

- **Trough concentrations should always be maintained above 10 mcg/mL to avoid development of resistance.**
- **Target trough range of 15-20 mcg/mL is recommended in select patients with** bacteremia, endocarditis, meningitis, hospital acquired pneumonia or osteomyelitis caused by S.aureus
- Trough levels should be ordered in patients:
  - expected to remain on vancomycin for longer than 3 days
  - with rapidly changing renal function
  - receiving other nephrotoxic drugs (e.g. gentamicin, tobramycin, amphotericin, acyclovir)
  - receiving aggressive dosing
  - with severely altered volumes of distribution (e.g. burn patients, morbidly obese, compartment syndrome)
- Trough levels should be performed once weekly for patients requiring long term treatment (i.e. 4-6 weeks). Levels should be done more frequently in hemodynamically unstable patients or suspicion of sub therapeutic level.
- Anuric patients should have a random level drawn and repeated every 1 to 2 days until level is less than 20 mcg/mL. A repeat vancomycin dose is given at this time.
- Initial trough levels should be obtained no earlier than at steady state (before 4th dose in patients with normal renal function)

Example 4: Markham Stouffville Hospital Corporation - Vancomycin Monitoring Record (continued)

Vancomycin Monitoring cont'd: **PATIENT:** _____ **UNIT:** _____

Lab Monitoring:

Date	Scr (µmol/L)	Urea (µmol/L)	Clcr (mL/min)	WBC	Neuts (%)	Temp (°C)	ESR	C-Reactive Protein

Levels:

Date@time	Current Regimen	Trough level Time	Level	New Regimen (mg/kg/dose)	Comments/Initial

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Example 5: Markham Stouffville Hospital Corporation - Aminoglycoside Monitoring Record

AMINOGLYCOSIDE MONITORING RECORD

1. PATIENT INFORMATION
NAME: | AGE: _____ SEX:_____UNIT: _____

DIAGNOSIS: | OTHER ANTIBIOTICS:

ALLERGIES:

MD: | PHARMACIST:

2. HT:_____ WT:_____

Female: IBW = 45.5 kg + (2.3 X inches over 5')
LBW = 1.07 X Wt(kg) - 148 X (Wt(kg)2)/ (Ht(cm)2)

Male: IBW = 50 kg + (2.3 X inches over 5')
LBW = 1.10 X Wt(kg) - 128 X (Wt(kg)2)/ (Ht(cm)2)

If ABW greater than IBW (but not more than 30% over IBW), use DBW = IBW
If ABW greater than IBW (more than 30% over IBW), use DBW = IBW + 0.4 (ABW - IBW)
If ABW less than IBW, use ABW or LBW, as appropriate

IBW:_____ DBW:_____ LBW:_____

3.
DATE:_____
Sr CREATIN_____umol/L
CLEARANCE: _____ mL/min

4. REGIMEN ORDERED:
Gentamicin / Tobramycin / Amikacin _____mg IV q _____h = _____(mg/kg)

Doses Given: 1st: _____mg @ _____h 2nd: _____mg @ _____h 3rd: _____mg @ _____h

5. ASSESSMENT:
Contraindications to High Dose Extended Interval Dosing

- Pregnancy
- Neonatal – Pediatric (less than 18 yr)
- Enterococal Endocarditis
- Ascites, burns
- Cystic Fibrosis
- Dialysis
- CrCl less than 20 mL/min
- Surgical Prophylaxis (ie x 24 - 48 hr)
- Post Partum less than 7 days
- Use with caution in patients over 60 years old

6. DOSE AND FREQUENCY:
a) High Dose Extended Interval Dosing
Gentamicin/Tobramycin: 5 mg/kg
Gentamicin for synergy: 3 mg/kg
Amikacin: 15 mg/kg

DBW: _____ x _____mg/kg = _____mg
(Increments of 20 mg for Gent/Tobra, 25 mg for Amikacin)

Interval
Clearance:
□ over 60 mL/min q 24 h
□ 40 – 59 mL/min q 36 h
□ 20 – 39 mL/min q 48 h
□ <less than 20 – use conventional multiple daily dosing

b) Conventional Multiple Daily Dosing

Indication/Site of Infection	Gentamicin/ Tobramycin	Amikacin
Synergy (gentamicin)	1 mg/kg	
UTI	1 mg/kg	5 mg/kg
Gram neg sepsis, other serious infections	1.5-2 mg/kg	
pneumonia	2 mg/kg	

DBW: _____ x _____mg/kg = _____mg
(Increments of 20 mg for Gent/Tobra, 25 mg for Amikacin)

Interval
Clearance:
□ over 70 mL/ min q 8 h
□ 40-69 mL/min q 12 h
□ 15-39 mL/min q 24 h
□ less than 15 Give a dose and draw levels in 24 hours to determine dosing interval

7. ORDER WRITTEN:
Gentamicin / Tobramycin / Amikacin _____ mg q ___h First Dose @ _____ h on _____Date

Levels @ _____h on _____Date Blood Work: _____

Date Discontinued:

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Example 5: Markham Stouffville Hospital Corporation - Aminoglycoside Monitoring Record (continued)

8. DESIRED LEVELS:

a) High Dose Extended Interval Dosing

DO NOT DRAW ROUTINE PEAK AND TROUGH LEVELS. Exceptions:

- Significant existing renal dysfunction or significant changes in renal function
- Infections involving highly resistant organisms
- Patients receiving therapy for more than 7 days, and therapy is likely to continue.

Options:

a) draw trough level prior to 2-4th dose and extend dosing interval by 12 hours if level greater than desired

b) draw trough and peak level around 2-4th dose and adjust dose/interval using pharmacokinetic principals

	Trough	Peak
Gentamicin/Tobramycin	Under 0.5 mg/L	20 mg/L
Amikacin	Under 2.5 mg/L	60 mg/L

b) Conventional Multiple Daily Dosing

Indication/Site of Infection	Gentamicin/Tobramycin (mg/L)		Amikacin (mg/L)	
	Trough	Peak	Trough	Peak
Synergy (gent)	Under 1	3-4		
UTI	0.8–2	4-5	5–10	20-25
Gram neg sepsis, other serious infections		6-7		25-30
pneumonia		7-8		25-30

Date/Time (levels)	Current Regimen	Pre (mg/L) Level	Pre (mg/L) Time	Post (mg/L) Level	Post (mg/L) Time	t1/2 (hr)	New Regimen Ordered	mg/kg/dose (DBW)	Comments	Phmst Int'l	QA

Date	SCr umol/L	Urea (umol/L)	ClCr (mL/min)	WBC	Neuts (%)	Temp (° C)	Hydration Status/ Other Comments	Microbiology (Specimen, Culture, Sensitivity)
								NOTES

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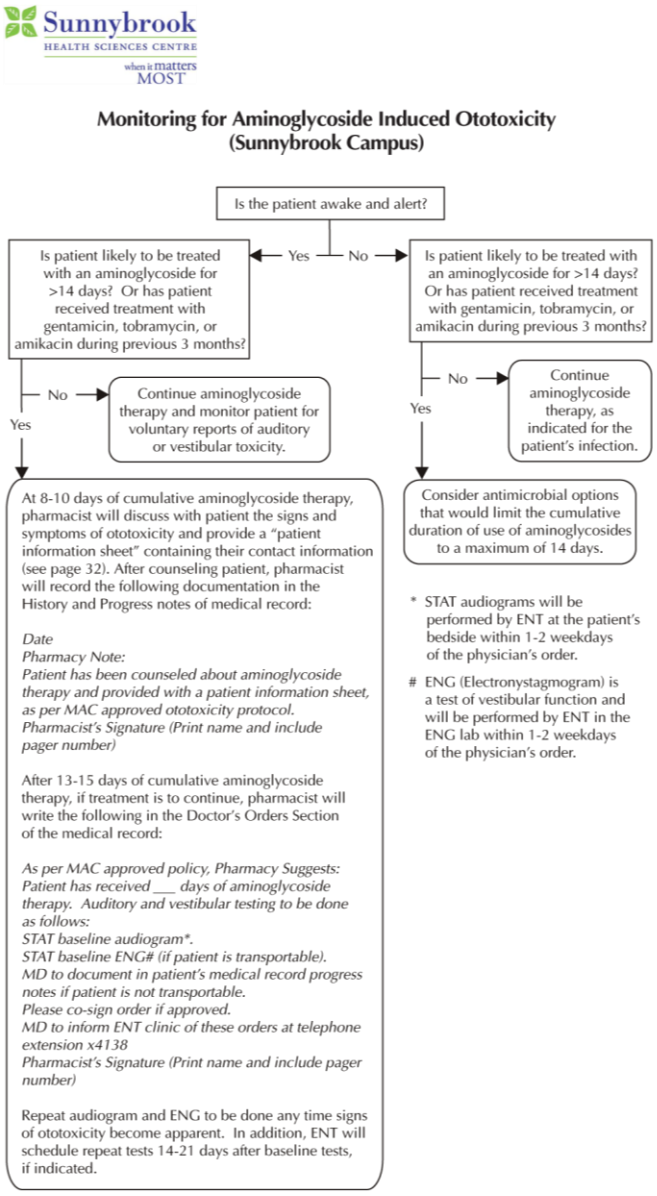
Example 6: Sunnybrook Health Sciences Centre - Monitoring for Aminoglycoside Induced Ototoxicity



Sunnybrook
HEALTH SCIENCES CENTRE
when it matters
MOST

Monitoring for Aminoglycoside Induced Ototoxicity
(Sunnybrook Campus)

Is the patient awake and alert?

Yes — Is patient likely to be treated with an aminoglycoside for >14 days? Or has patient received treatment with gentamicin, tobramycin, or amikacin during previous 3 months?

No — Is patient likely to be treated with an aminoglycoside for >14 days? Or has patient received treatment with gentamicin, tobramycin, or amikacin during previous 3 months?

No → Continue aminoglycoside therapy and monitor patient for voluntary reports of auditory or vestibular toxicity.

Yes → At 8-10 days of cumulative aminoglycoside therapy, pharmacist will discuss with patient the signs and symptoms of ototoxicity and provide a "patient information sheet" containing their contact information (see page 32). After counseling patient, pharmacist will record the following documentation in the History and Progress notes of medical record:

Date
Pharmacy Note:
Patient has been counseled about aminoglycoside therapy and provided with a patient information sheet, as per MAC approved ototoxicity protocol.
Pharmacist's Signature (Print name and include pager number)

After 13-15 days of cumulative aminoglycoside therapy, if treatment is to continue, pharmacist will write the following in the Doctor's Orders Section of the medical record:

As per MAC approved policy, Pharmacy Suggests:
Patient has received ___ days of aminoglycoside therapy. Auditory and vestibular testing to be done as follows:
STAT baseline audiogram.*
STAT baseline ENG# (if patient is transportable).
MD to document in patient's medical record progress notes if patient is not transportable.
Please co-sign order if approved.
MD to inform ENT clinic of these orders at telephone extension x4138
Pharmacist's Signature (Print name and include pager number)

Repeat audiogram and ENG to be done any time signs of ototoxicity become apparent. In addition, ENT will schedule repeat tests 14-21 days after baseline tests, if indicated.

No → Continue aminoglycoside therapy, as indicated for the patient's infection.

Yes → Consider antimicrobial options that would limit the cumulative duration of use of aminoglycosides to a maximum of 14 days.

* STAT audiograms will be performed by ENT at the patient's bedside within 1-2 weekdays of the physician's order.

ENG (Electronystagmogram) is a test of vestibular function and will be performed by ENT in the ENG lab within 1-2 weekdays of the physician's order.

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Example 7: Sunnybrook Health Sciences Centre - Patient Information Sheet- Aminoglycoside Treatment

PATIENT INFORMATION SHEET
AMINOGLYCOSIDE TREATMENT

You have been prescribed an antibiotic which is called an aminoglycoside. Aminoglycoside antibiotics include drugs such as gentamicin, tobramycin, and amikacin. Aminoglycosides have been available for the treatment of bacterial infections for over 30 years and are highly effective agents. Your doctor has prescribed an aminoglycoside for you because they consider it to be the best option to treat the infection you have, at this time.

Unfortunately, like most medications, there are potential side effects that may occur when aminoglycosides are used. Aminoglycosides may cause reversible kidney damage in 5-10% of patients receiving more than 5 days of treatment with the aminoglycoside. They may also cause irreversible hearing loss or imbalance and dizziness in less than 3% of patients receiving more than 10-14 days of therapy.

- To minimize the risk of kidney damage, your care-givers are monitoring your kidney function weekly, with the use of blood tests.
- To minimize the risk of hearing loss, you should report any symptoms of ringing in the ears, feeling of fullness in the ears, earache, or hearing loss to your care-givers immediately, so that your aminoglycoside therapy can be re-evaluated.
- To minimize the risk of problems with your balance, you should report any symptoms of dizziness, unsteady walking, or loss of balance to your care-givers immediately, so that your aminoglycoside therapy can be re-evaluated.
- If it is necessary to treat your infection for more than 14 days, you will undergo a hearing function test and a test to evaluate your balance. These tests will be done about 2 weeks after aminoglycoside therapy began. A second test will be done 2-3 weeks after the first test. Additional testing will also be done at any time that you report symptoms of hearing or balance problems.

If you have any additional questions about your aminoglycoside therapy, please ask your nurse to arrange for either your pharmacist or physician to come and speak with you about your aminoglycoside therapy.

Pharmacist Name: _____

Contact Number: _____

Date Counseled: _____

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