



THIS OPTIMAL USAGE GUIDE IS PROVIDED FOR INFORMATION PURPOSES ONLY AND SHOULD NOT REPLACE THE JUDGMENT OF A PROFESSIONAL.

The scientific content of this guide was developed in collaboration with the Programme de gestion thérapeutique des médicaments (PGTM).

CONTEXT

In April of 2007, the American Heart Association (AHA) published updated guidelines for infective endocarditis prophylaxis. The AHA guidelines were significantly different from the previous versions, prophylaxis being now recommended for a much lower number of patients. More recently, the European Society of Cardiology (ESC) also issued new recommendations, which were different from those of the AHA. As for the National Institute for Health and Clinical Excellence (NICE), it does not recommend any prophylactic antibiotic therapy anymore. Although the three associations adopted different positions, they all agree that little data has been published on the matter, and that the available evidence still relies strongly on expert opinions; they also agree that prophylaxis should be restricted to fewer cases.

- ▶ **INESSS and the PGTM chose to use the AHA recommendations as their primary source since several Canadian associations endorse these recommendations, and current practice in Québec is based on them. This position represents a compromise between scientific evidence and current medical practice.**

GENERAL POINTS

- ▶ Infective endocarditis (IE): severe, potentially lethal illness, although relatively rare.
- ▶ The following contextual elements led the experts involved in the development of this document to modify the IE prophylaxis guidelines.
 - IE is more likely to occur following transient bacteremia induced by daily activities (frequent exposure such as dental care) than from bacteremia caused by a dental, genitourinary or gastrointestinal procedure.
 - IE is a rare complication of procedures. A significant number of patients must be treated to prevent one IE.
 - For a majority of patients, the first IE is often not linked to a procedure. Prophylaxis protects only a small portion of at-risk patients.
 - Prophylaxis prevents only a very small number of IEs, if any, in people who undergo dental, genitourinary or gastrointestinal procedures.
 - The risks associated with the adverse effects of antibiotics usually outweigh the benefits of IE prophylaxis.
 - A 2008 Cochrane review found that there was no evidence prophylactic antibiotic treatment was either effective or ineffective at preventing IEs in the at-risk population undergoing an invasive dental procedure.
 - Maintaining oral hygiene and health can reduce the bacteremia linked to daily activities and is more important than antibiotic treatment prophylaxis associated with dental procedures to reduce the risk of IE.
 - IE on a prosthetic valve is associated with a bad prognosis. In-hospital mortality of 20% to 40% has been reported.
 - The widespread use of antibiotics promotes the emergence of resistance. The role of IE antibiotic treatment prophylaxis in the global development of resistance is however unknown.

THEREFORE:

- ▶ **Only high-risk patient should be considered for prophylaxis. All moderate-risk patients are now excluded from the recommendations by all the organizations mentioned above.**
- ▶ **It should be noted that no pediatric study has assessed the effectiveness of antibiotic treatment prophylaxis on the incidence of endocarditis in children. Recommendations are based mostly on adult studies.**

PRINCIPLES OF PROPHYLACTIC TREATMENT

- ▶ The decision whether or not to offer antibiotic prophylaxis for endocarditis must be made on an individual basis, taking into account:

- THE HEART CONDITION
- SPECIAL CIRCUMSTANCES
- THE TYPE OF PROCEDURE OR INSTRUMENTS

HEART CONDITIONS

ASSOCIATED WITH ENDOCARDITIS FOR WHICH PROPHYLAXIS IS:

RECOMMENDED WHEN:

HIGH RISK OF ADVERSE OUTCOMES FOLLOWING THE DEVELOPMENT OF ENDOCARDITIS

- ▶ Prosthetic cardiac valve or prosthetic material used for cardiac valve repair
- ▶ Previous infective endocarditis
- ▶ **Congenital heart defects including:**
 - Unrepaired cyanotic congenital heart disease, including palliative shunts and conduits
 - Completely repaired congenital heart defect with prosthetic material, during the first six months after the procedure
 - Repaired congenital heart defect with residual defects, with prosthetic material in place
- ▶ Cardiac transplantation recipients who develop cardiac valvulopathy

NOT RECOMMENDED:

- Isolated atrial septal defect
- Surgical repair of atrial septal defect, ventricular septal defect, or patent ductus arteriosus (without residual lesions after six months)
- Previous coronary artery bypass
- Mitral valve prolapse without valvular regurgitation or thickened heart valve leaflets
- Functional or physiologic heart murmurs
- Previous Kawasaki disease without valvular dysfunction
- Previous rheumatic fever with or without valvular dysfunction
- Cardiac pacemakers (intravascular and epicardial) and implanted defibrillators
- Acquired valvular dysfunction (e.g., rheumatic heart disease)
- Hypertrophic cardiomyopathy
- Other underlying heart defects (other than the ones mentioned above)

NB: When in doubt, please refer to the documents cited at the end of this guide and consult with the patient's cardiologist.

SPECIAL CIRCUMSTANCES

- ▶ High-risk patients already receiving long-term antibiotic therapy
 - AHA recommendations remain the same as in 1997: select an antibiotic from a different class to minimize the risk of encountering resistance.
- ▶ High-risk patients who receive anticoagulants
 - IM injections of antibiotics should be avoided. In these circumstances, the oral route is preferable. IV administration should be reserved for cases where oral intake (capsule or oral suspension) is not possible.
- ▶ High-risk patients who undergo cardiac surgery
 - Preoperative dental evaluation is recommended in order to complete potential dental treatments before cardiac surgery. Such measures may lower the risk for late *Streptococcus viridans* endocarditis in patients with prosthetic cardiac valves.

SUMMARY OF RECOMMENDATIONS ON ANTIBIOTIC PROPHYLAXIS FOR ENDOCARDITIS,
 DEPENDING ON THE **TYPES OF PROCEDURES OR INSTRUMENTS USED**,
 IN PATIENTS WHO SUFFER FROM A HEART CONDITION ASSOCIATED WITH A **HIGH RISK** OF ADVERSE OUTCOMES

TYPE OF PROCEDURE	PROPHYLAXIS RECOMMENDED	PROPHYLAXIS NOT RECOMMENDED
Cardiac or vascular	<ul style="list-style-type: none"> ▶ For cardiac surgeries: <ul style="list-style-type: none"> ▪ Use a first-generation cephalosporin (<i>Class I, level of evidence A</i>) ▪ In hospitals with a high prevalence of methicillin-resistant <i>Staphylococcus aureus</i> (MRSA), consider vancomycin (<i>Class IIb, level of evidence C</i>) ▪ In case of prolonged procedures, antibiotic administration should be extended to maintain serum concentrations intraoperatively, and continued for no more than 48 hours postoperatively¹ (<i>Class IIa, level of evidence B</i>) 	
Respiratory tract	<ul style="list-style-type: none"> ▶ For procedures involving: <ul style="list-style-type: none"> • Incision or biopsy of the respiratory mucosa, such as tonsillectomy and adenoidectomy (<i>Class IIa, level of evidence C</i>) <p>NB: The antibiotic regimen administered should contain an agent active against <i>viridans</i> group <i>streptococci</i> for patients who undergo an invasive respiratory tract procedure to treat an established infection, such as drainage of an abscess or empyema.</p>	For bronchoscopy, unless the procedure involves incision of the respiratory tract mucosa.
Dental	<ul style="list-style-type: none"> ▶ For procedures involving: <ul style="list-style-type: none"> • Manipulation of gingival tissue or the periapical region of teeth (including forms of professional teeth cleaning) • Perforation of the oral mucosa (extractions, etc.) (<i>Class IIa, level of evidence C</i>) 	For anesthetic injections through noninfected tissue, the taking of dental radiographs, placement of prosthodontic or orthodontic appliances, shedding of deciduous teeth and bleeding following trauma to the lips and oral mucosa.
Infected cutaneous or musculoskeletal tissues	<p style="text-align: center;">NO PROPHYLAXIS (<i>Class IIb, level of evidence C</i>)</p> <p>NB: It is reasonable to treat the infected site with an antibiotic regimen that is active against <i>staphylococci</i> and β-hemolytic <i>streptococci</i>, such as penicillin or a cephalosporin. Vancomycin or clindamycin may be considered for patients with contraindications to the recommended regimen or who are carriers of MRSA.</p>	Even in the presence of high-risk heart conditions
Genitourinary tract	<p style="text-align: center;">NO PROPHYLAXIS (<i>Class III, level of evidence B</i>)</p> <p>NB: Antibiotic therapy to eradicate <i>Enterococcus</i> spp. urinary colonization is reasonable before cystoscopy or other urinary tract manipulations.</p>	Even in the presence of high-risk heart conditions
Gastrointestinal tract	<p style="text-align: center;">NO PROPHYLAXIS (<i>Class III, level of evidence B</i>)</p>	Even in the presence of high-risk heart conditions

1. The recommended duration of 48 hours is based on historical data. The experts consulted recommend antibiotic coverage **FOR A MAXIMUM DURATION OF 24 HRS.**

PROPHYLACTIC TREATMENT

DRUG REGIMENS RECOMMENDED BY THE AHA FOR INFECTIVE ENDOCARDITIS PROPHYLACTIC TREATMENT

SITUATION	SINGLE DOSE 30 TO 60 MINUTES BEFORE THE PROCEDURE		
	ANTIBIOTIC ¹	ADULT ²	PEDIATRICS ³
Oral route	Amoxicillin	2 g	50 mg/kg
Allergy to penicillin⁴ and oral route available	Cephalexin (generic for Keflex™) or Cefadroxil (Duricef™)	2 g 2 g	50 mg/kg 50 mg/kg ⁵
	OR Clindamycin (Dalacin™)	600 mg	20 mg/kg
	OR Azithromycin (Zithromax™) or Clarithromycin (Biaxin™)	500 mg 500 mg	15 mg/kg 15 mg/kg
	Oral route not available	Ampicillin OR Cefazolin (generic for Ancef™) or Ceftriaxone (Rocephin™)	2 g IV or IM 1 g IV or IM 1 g IV or IM
Allergy to penicillin⁴ and oral route not available	Cefazolin (generic for Ancef™) or Ceftriaxone (Rocephin™) OR Clindamycin (Dalacin™)	1 g IV or IM 1 g IV or IM 600 mg IV or IM	50 mg/kg IV or IM 50 mg/kg IV or IM 20 mg/kg IV or IM

1. Only one trademark listed, although several manufacturers can offer the drugs under different brand names. Various generic versions are also available.
2. IM injections should not be administered to patients taking anticoagulants.
3. The maximum pediatric dose should not exceed the adult dose.
4. Cephalosporins should not be used in patients with a type 1 allergy to penicillin.
5. Cefadroxil is not offered in Canada in suspension form.

CONCLUSION AND IMPLICATIONS

From now on, the number of patients to receive prophylaxis will be considerably lower. This change will require a discussion between the health care professional and the patient.

- ▶ In order to further identify real risks and to inform the next guideline modifications, it is suggested to:
 - promote the assessment of the effectiveness of IE prophylaxis through a clinical trial protocol;
 - monitor and document cases of endocarditis following a procedure.
- ▶ The evolution of guidelines should be monitored to remain apprised of the latest trends in the IE prophylactic treatment.

MAIN REFERENCES

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