

Impact of a Target Drug Monitoring Program on the Usage of Clindamycin

Alfred S. Gin, Lauren A. Lipinski and Nicholas Honcharik

ABSTRACT

The use of parenteral clindamycin at the Health Sciences Centre had not been amendable to traditional cost containment strategies. Clindamycin was targeted through a Target Drug Monitoring (TDM) Program to improve its appropriate use. A retrospective audit was conducted to serve as a baseline. In the concurrent phase, the TDM pharmacist reviewed and assessed clindamycin cases based on approved criteria. Those cases which failed to meet the criteria were targeted in order to convert clindamycin to alternative agents.

The concurrent TDM program reviewed 339 cases of clindamycin over a 32-week period, of which 76 cases (22.4%) failed to meet the criteria and were targeted. Of the 76 recommendations, 48 (63.2%) were accepted. Cost-avoidance due to direct intervention was approximately \$16,000 annualized compared to \$28,000 estimated from the retrospective audit. Fiscal year-end antibiotic usage indicated a dramatic decline (32%) in clindamycin use. Net savings of \$37,600 were attributed to modification of physician prescribing.

The TDM program was successful in identifying areas of inappropriate clindamycin use and correcting them by direct interaction with the prescriber(s).

Key Words: *clindamycin, cost-avoidance, drug use evaluation*

Can J Hosp Pharm 1994;47: 53-58

RÉSUMÉ

L'utilisation de la clindamycine administrée par voie parentérale au Centre des sciences de la santé n'était pas conciliable avec les stratégies traditionnelles de limitation des coûts. On a ciblé la clindamycine dans le cadre d'un programme de monitoring de médicaments cibles (MMC) afin d'en favoriser l'utilisation appropriée. On a effectué une vérification rétrospective comme point de référence. Durant l'étape concurrente, le pharmacien MMC examinait et évaluait les cas de clindamycine en fonction de critères approuvés. Les cas qui ne répondaient pas aux critères ont été ciblés en fonction d'une conversion de la clindamycine à d'autres agents.

Le programme MMC concurrent a permis d'examiner 339 cas de clindamycine au cours d'une période de 32 semaines, y compris 76 cas (22,4%) qui, ne répondant pas aux critères, ont été ciblés; 48 des 76 recommandations (63,2%) ont été acceptées. L'évitement de coûts attribuable à l'estimation de 28 000 \$ tirée de la vérification rétrospective. L'utilisation d'antibiotiques en fin d'exercice a indiqué une baisse spectaculaire (32%) de l'utilisation de la clindamycine. Des économies nettes de 37 600 \$ ont été attribuées à la modification des habitudes de prescription.

Le programme MMC a permis de cerner des cas d'utilisation inappropriée de la clindamycine et d'apporter des corrections en communiquant directement avec le ou les prescripteurs.

Mots clés : *clindamycine, évaluation de l'utilisation des médicaments, évitement des coûts*

INTRODUCTION

Clindamycin is commonly used in the treatment of mixed aerobic and anaerobic infections. Since 1987, the average yearly expenditure on intravenous clindamycin at the Health Sciences Centre (HSC) was approximately \$150,000. Until recently, clindamycin was the

most expensive antimicrobial agent accounting for approximately 8-10% of the overall antimicrobial drug budget.

The HSC is a 985-bed tertiary care university affiliated teaching institution. The antimicrobial cost containment program at the HSC has utilized many of the strategies

reported in the literature¹⁻¹⁰. At our institution, clindamycin has been used for a number of indications including the treatment of intra abdominal, skin and soft tissue infections, and the empiric treatment of aspiration pneumonia. Even considering these indications, our utilization of clindamycin

Alfred S. Gin, Pharm.D., is a Clinical Pharmacist – Infectious Diseases, Department of Pharmaceutical Services, Health Sciences Centre (HSC) and Assistant Professor, Faculty of Pharmacy, University of Manitoba (U of M).

Lauren A. Lipinski, B.Sc.Pharm., is a Target Drug Monitoring Pharmacist, Department of Pharmaceutical Services, HSC.

Nicholas Honcharik, Pharm.D., is an Assistant Director – Clinical Pharmacy Services, Department of Pharmaceutical Services, HSC and Assistant Professor, Faculty of Pharmacy, U of M.

Address reprint requests to: Dr. Gin at the Department of Pharmaceutical Services, Health Sciences Centre, 820 Sherbrook Street, Winnipeg, Manitoba R3A 1R9. This project was awarded the 1992/93 Sandoz Award for pharmacoeconomics.

seemed excessive and attempts to modify the prescribing of clindamycin by education (e.g., newsletters, antimicrobial guidelines) were of limited or no benefit. Despite the widespread availability of antimicrobial guidelines, susceptibility information, and cost and efficacy data of alternative agents, the use of intravenous clindamycin continued to be higher than desired in our institution. More effective means of modifying the prescribing of parenteral clindamycin were sought.

Based on the results and successes of previous studies, it was anticipated that a TDM approach could favourably alter the use of this antibiotic.¹¹⁻¹⁸ This article describes the impact of our TDM program on the usage of clindamycin.

METHODS

Criteria Development

Criteria for TDM intervention with clindamycin were developed by the TDM pharmacist and the Infectious Diseases clinical pharmacist. Approval of the criteria (Appendix A) was obtained from the Antibiotic Subcommittee of the Pharmacy and Therapeutics Committee and the Section of Infectious Diseases. Criteria for the use of clindamycin in aspiration pneumonia were not approved until late January 1992 due to ongoing discussions with the Section of Infectious Diseases.

Retrospective Review

A retrospective audit of clindamycin use was conducted from June 2 to June 29, 1991 to obtain baseline information. All adult parenteral clindamycin orders during this period were identified by the TDM pharmacist. Patient charts were reviewed and information pertaining to indication(s),

concomitant antibiotics, history of present illness, concomitant illness, clinical and microbiologic data, and dose and duration of antimicrobial therapy were documented. Clindamycin courses were evaluated based on approved criteria and available clinical and microbiologic information. Cases which did not meet the approved criteria were considered inappropriate and were reviewed to assess what alternative antimicrobial agents could have been used in place of clindamycin. Cases of aspiration pneumonia were documented but not assessed.

Concurrent TDM

The concurrent clindamycin TDM program began on September 9, 1991 and ended April 12, 1992. Targeting of clindamycin for aspiration pneumonia cases was incorporated within the TDM program on February 17, 1992. The TDM pharmacist screened all adult prescriptions for new intravenous clindamycin orders each morning Monday to Friday. Patient charts were reviewed and evaluated, as above, according to established criteria and available clinical and laboratory information.

In cases where it was determined that other agents could be used in place of clindamycin, the prescriber was contacted directly to convert the patient to alternative therapies based on available data, indication, and clinical status of the patient. During the discussion with the prescriber, information was presented regarding the similarities and differences of and between clindamycin and alternative agents including efficacy, *in vitro* data and cost differences. The outcome of this discussion was documented. The Infectious Diseases clinical pharmacist and an Infectious Diseases physician served as resource contacts. Dur-

ing the study period, case assessments were summarized every four weeks to assess trends in drug use and program effectiveness.

The cost of clindamycin therapy during the retrospective and concurrent audit period was determined by the acquisition cost of the total number of grams of clindamycin administered per treatment course for all patient cases. Estimated cost-avoidance (retrospective audit) was determined by subtracting the cost of alternative agents from the cost of clindamycin had they been used in place of clindamycin for the entire treatment course. Cost-avoidance in the concurrent TDM was determined by subtracting the cost of the actual therapy used from the calculated cost of clindamycin for the same length of therapy.

RESULTS

Retrospective Review

A total of 55 intravenous clindamycin courses were retrospectively reviewed by the TDM pharmacist between June 2 and June 29, 1991 (Table I). Of the 55 cases, 18 (32.7%) were considered appropriate, 20 cases (36.4%) were considered inappropriate based on available information, and 17 (30.9%) cases received clindamycin for aspiration pneumonia. The most common reasons for inappropriate use (Table II) included: a) the empiric use of clindamycin for suspected or documented anaerobic infections or indications other than those described; b) availability of other therapeutic antimicrobial options; c) culture and sensitivity results; and d) therapeutic overlap with other antimicrobials (e.g., combination of cloxacillin and clindamycin for a methicillin-sensitive *S. aureus* infection). Based on the 20 inappropriate cases, po-

Table I: Summary of Clindamycin Utilization

	Retrospective Audit	Concurrent TDM
Total Cases Reviewed	55	339
Appropriate Cases	18 (32.7%)	205 (60.5%)
Inappropriate	20 (36.4%)	76 (22.4%)
a) recommendations accepted	—	48
b) recommendations rejected	—	17
c) surgical prophylaxis*	—	11
Aspiration Pneumonia	17 (30.9%)	58 (17.1%)**
Potential Cost-Avoidance	\$2,141	—
Actual Cost-Avoidance	—	\$9,722

* interventions occurred after drug administered

** aspiration pneumonia was not targeted until February, 1992

Table II: Rationale for Clindamycin TDM Intervention

Inappropriate Uses	Number of Cases(%)	
	Retrospective Audit	Concurrent TDM
Empiric use of clindamycin in suspected or documented anaerobic infections	6 (30%)	33 (43%)
Therapeutic overlap with other antimicrobial agents	4 (20%)	15 (20%)
Culture and Sensitivity Results	4 (20%)	10 (13%)
Other therapeutic antimicrobial options available*	5 (25%)	8 (11%)
Aspiration Pneumonia	—	6 (8%)**
Miscellaneous	1 (5%)	4 (5%)
Total Cases	20	76

* antibiotics such as cefazolin, cloxacillin

** based on cases targeted after January 1992

tential cost avoidance was estimated to be \$2,141 or \$27,838 annualized if alternative agents had been used instead of clindamycin.

Concurrent TDM Program

A total of 339 patient cases receiving intravenous clindamycin were identified and evaluated by the TDM pharmacist between September 9, 1991 to April 12, 1992 (Table I). Of the 339 cases, 205 cases (60.5%) were considered appropriate, 76 (22.4%) cases were considered inappropriate and targeted for intervention, and 58 cases (17.1%) of aspiration pneumonia (prior to February 1992) were documented but not assessed. Of the 205 appropriate cases, 79 cases (38.5%) were considered appro-

priate based on a history of penicillin allergy. The remaining 126 (61.5%) patient cases were not allergic to penicillin and were considered appropriate based on available patient data. There were 76 cases that were deemed inappropriate. Of these, 11 cases involved the use of clindamycin for surgical prophylaxis and the acceptance rate could not be determined as assessment occurred following clindamycin administration.

The most common reasons for intervention (Table II) by the TDM pharmacist were for: a) the empiric use of clindamycin for suspected or documented anaerobic infections other than those specified by criteria; b) therapeutic overlap with another antimicrobial agent; c) culture and sensitiv-

ity results supporting the use of other therapies; d) the availability of other therapeutic antimicrobial options; and, e) the inappropriate use of clindamycin for aspiration pneumonia (based on cases evaluated after January 1992 when criteria were approved). Of the 48 recommendations accepted, clindamycin was changed to metronidazole in 23 cases (47.9%), cloxacillin in nine cases (18.7%), discontinued in 14 cases (29.2%), converted to oral clindamycin in one case (2.1%), and in the remaining case, cefoxitin (therapeutic overlap) was discontinued (2.1%). In the 11 cases of surgical prophylaxis, prescribers in nine cases indicated they would consider using alternative agents in the future.

Cost-avoidance based on the recommendations accepted, was determined to be \$9,722 or \$15,798 annualized.

DISCUSSION

Although parenteral clindamycin has been available since the early 1970s, very little has been published regarding its rational use. The most commonly reported approach has been to modify the dose of parenteral clindamycin from 600 mg every six hours to 600 mg every eight hours^{14,19,20} but that approach does not necessarily increase appropriate use but rather simply reduces the amount used. In another approach, Greene and associates described a program involving the distribution of a newsletter and the attendance of clinical pharmacists at patient care rounds resulting in a substantial decrease clindamycin usage.²¹

The clindamycin TDM program was developed with the support of the Antibiotic Subcommittee and the Section of Infectious Diseases. This process required considerable discussion to establish the

role of parenteral clindamycin within our institution. In general, agreement on the criteria was established quickly with the exception of the use of clindamycin in aspiration pneumonia. Until recently, it was widely believed by clinicians in our institution that clindamycin was the agent of choice for aspiration pneumonia based on work by Levison et al²². This study suggested clindamycin was superior to penicillin in the treatment of lung abscesses or necrotizing pneumonia. We noted in our institution that in the cases where clindamycin was administered for presumed "aspiration" pneumonia, the majority of patients often presented without evidence of radiologic or microbiologic findings of a lung abscess or necrotizing pneumonia secondary to anaerobic organisms. As a result, our Infectious Diseases physicians agreed that parenteral clindamycin was not necessary. Beta-lactam monotherapy was considered sufficient unless patients presented with definitive findings of an anaerobic infection. This discussion occurred over several months; hence, the delay in the targeting of clindamycin for this indication. The use of clindamycin in aspiration pneumonia was targeted only after the approval of these guidelines.

There was a high degree of acceptance of the recommendations with 48 of 65 recommendations (73.5%) accepted (excluding the 11 cases of surgical prophylaxis). Reasons for rejection of interventions were: a) patients were improving on the current regimen; and b) personal preference of the prescriber. The cases of surgical prophylaxis were excluded since interventions occurred after the patients had received clindamycin. As a result, there was no measurable outcome in terms of either

acceptance or rejection of the recommendation.

Cost-avoidance secondary to TDM intervention was \$9,722 or \$15,798 annualized. This was somewhat less than the cost-avoidance figure estimated from the retrospective audit (\$27,838 annualized). This may be explained by an acceptance rate of 73.5% in the concurrent phase versus the calculated acceptance rate of 100% during the retrospective phase and an overall decline in clindamycin usage at our institution. Fiscal year (April to March) usage figures (Figure 1) indicated a dramatic decline in the use of clindamycin by 32% or \$41,000 accompanied by a concomitant 66% or \$3,400 increase in the use of metronidazole. This represented a net saving of \$37,600 in acquisition costs. These figures demonstrate a substantial change in the prescribing of parenteral clindamycin which is unprecedented for clindamycin in our institution. It is interesting to speculate that the house staff, because of the clindamycin TDM, may have altered their prescribing patterns. It is likely that the cost-avoidance may have been greater if the TDM program was initiated earlier in the fiscal year and if the criteria for the use of clindamycin in aspiration pneumonia had been available sooner.

One issue that should always be addressed in a program such as this is the use of alternate therapies. Indeed cost-avoidance could be more than offset by the use of alternate more expensive medication but we did not observe this. Conversion to metronidazole occurred in 47.9% of the recommendations accepted. There was no therapeutic shifting to other antimicrobials such as cefoxitin or imipenem. An increase in the overall degree of appropriate use from 32.7% to 60.5% and the decrease

in the overall degree of inappropriate use from 36.4% to 22.4% compared to the retrospective audit also suggests the effectiveness of the program. A comparison of appropriate and inappropriate cases over eight four-week periods suggests an apparent trend towards increased appropriate use reaching 80% at the end of the TDM period (Figure 2). The increase in inappropriate use in the last eight weeks of TDM is attributed to the targeting of aspiration pneumonia during this time period.

The most common reason for TDM intervention was the empiric use of clindamycin for the treatment of suspected or documented anaerobic infections other than those identified by the criteria. We were however, surprised that the second most common reason for intervention was therapeutic overlap with other antimicrobials such as cefoxitin, penicillin or cloxacillin.

We suspected that the effectiveness of an education program would not be sustained due to the large numbers and frequent turnover of house staff. This was confirmed by a post TDM audit which indicated a decline in appropriate use. The most common reasons for inappropriate use in the followup audit were similar to those during the TDM. The lack of long-term effect of an education program has been previously described in literature^{23,24}. Hence, there remained a need for a specific, ongoing TDM approach. As a result, we are in the process of re-implementing the clindamycin TDM program.

The success of the TDM program can be attributed to the degree of preparedness of the TDM pharmacist with respect to criteria development; knowledge base and case evaluation; the support re-

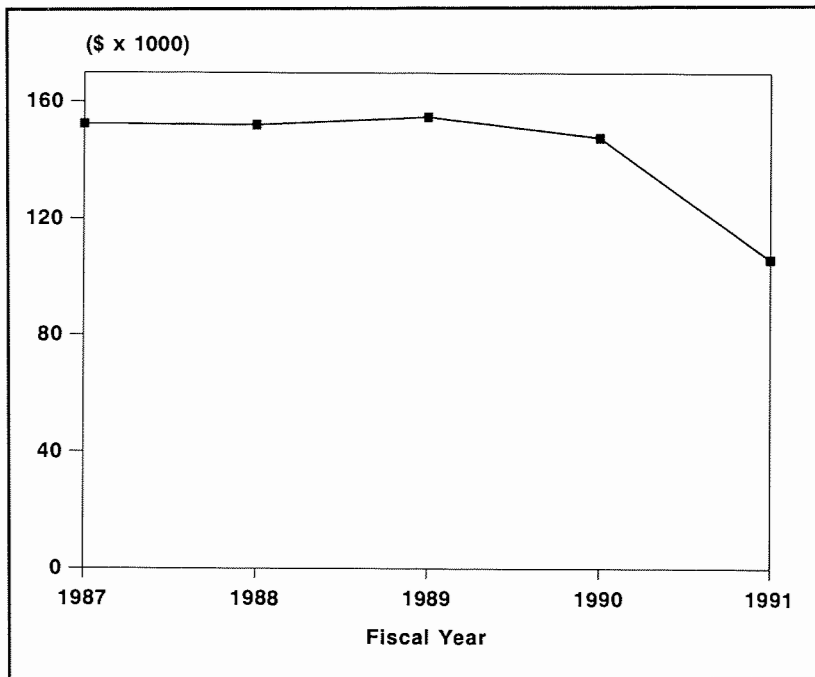


Figure 1: Annual parenteral clindamycin expenditures.

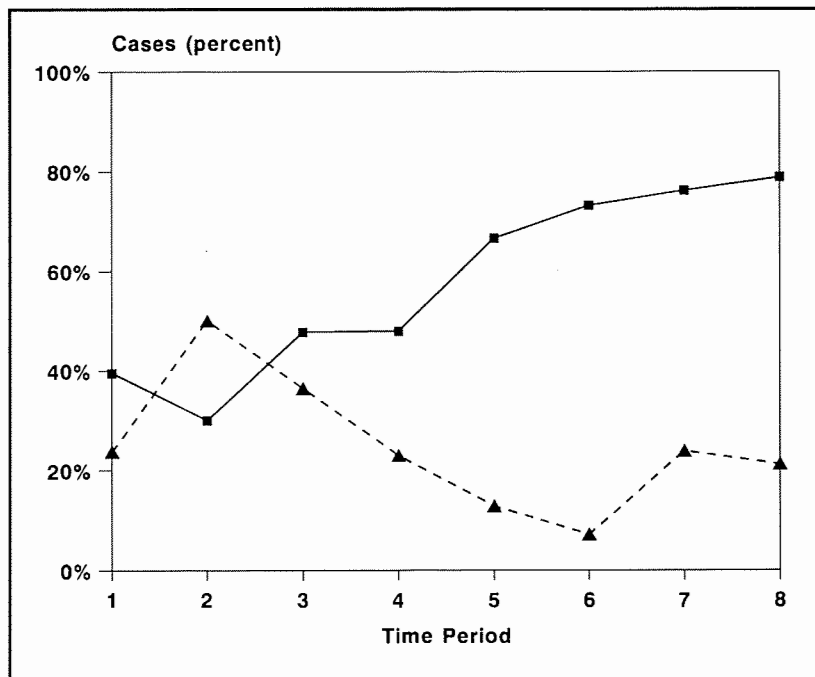


Figure 2: Comparison of appropriate (—■—) and inappropriate (—▲—) during clindamycin TDM over eight – 4 week periods.

ceived from hospital administration and the Section of Infectious Diseases; and the “one-on-one” interaction with the house staff which contributed to the high degree of acceptance. As with other

TDM programs described in the literature, we believe that this aspect was critical to the success of this program.

In conclusion, a clindamycin TDM program resulted in a reduc-

tion in the use of clindamycin at our hospital. With strong support from hospital administration and medical staff, a TDM program can promote rational drug therapy within an institution and avoid excessive costs. ☒

REFERENCES

1. Todd WM, Keith TD, Foster MT. Development and implementation of a comprehensive, criteria-based drug-use program. *Am J Hosp Pharm* 1987;44:529-35.
2. Hess DA, Mahoney CD, Johnson PN, et al. Integration of clinical and administrative strategies to reduce expenditures for antimicrobial agents. *Am J Hosp Pharm* 1990;47:585-91.
3. Quintiliani R, Nightingale CH, Crowe HM, et al. Strategic antibiotic decision-making at the formulary level. *Rev Infect Dis* 1991;13(suppl 9):S770-7.
4. Goff D, Thorton J. Pharmacy-laboratory interactions: a unique method to control antibiotic costs. *Hosp Pharm* 1989;24:26-9.
5. Moleski RJ, Andriole VT. Role of the infectious disease specialist in containing costs of antibiotics in the hospital. *Rev Infect Dis* 1986;8:488-93.
6. American Society of Hospital Pharmacists. Guidelines on the pharmacist's role in drug-use evaluation. *Am J Hosp Pharm* 1988;45:385-6.
7. Himmelberg CJ, Pleasants RA, Wever DJ, et al. Use of antimicrobial drugs in adults before and after removal of a restriction policy. *Am J Hosp Pharm* 1991;48:1220-7.
8. Gupta S, Bachand RL, Jewesson PJ. Impact of a two-stage intervention program on cefazolin usage at a major teaching hospital. *Hosp Formul* 1989;24:41-6.
9. Hirschman SZ, Meyers BR, Bradbury K, et al. Use of antimicrobial agents in a university teaching hospital. *Arch Intern Med* 1988;148:2001-7.
10. Marr JJ, Moffet HL, Kunin CM. Guidelines for improving the use of antimicrobial agents in hospital: a statement by the infectious diseases society of America. *J Infect Dis* 1988;157:869-76.

11. Strong DK, Dupuis LL, Domaratzki JL. Pharmacist intervention in prescribing of cefuroxime for pediatric patients. *Am J Hosp Pharm* 1990;47:1330-3.
12. Berman JR, Zaran FK, Rybak MS. Pharmacy-based antimicrobial-monitoring service. *Am J Hosp Pharm* 1992;49:1701-6.
13. Briceland LL, Nightingale CH, Quintiliani R, et al. Antibiotic streamlining from combination therapy to monotherapy utilizing an interdisciplinary approach. *Arch Intern Med* 1988;148:2019-22.
14. Coleman RW, Rodondi LC, Kaubisch S, et al. Cost-effectiveness of prospective and continuous parenteral antibiotic control: experience at the Palo Alto veterans affairs medical center from 1987 to 1989. *Am J Med* 1991;90:439-44.
15. Murray MD, Kohler RB, Main JW. Effect of a targeted antibiotic advisory consult program on hospital costs. *Hosp Formul* 1988;23:518-30.
16. O'Hanley P, Rodondi L, Coleman R. Efficacy and cost-effectiveness of antibiotic monitoring at a veterans administration hospital. *Chemotherapy* 1991;37(suppl 3):22-5.
17. Puckett F, Baars R, Seay K. Antibiotic use review using the "target drug" method. *Hosp Formul* 1987;22:489-91.
18. Fletcher CV, Giese RM, Rodman JH. Pharmacist interventions to improve prescribing of vancomycin and tobramycin. *Am J Hosp Pharm* 1986;43:2198-201.
19. Avorn J, Soumerai SB, Taylor W, et al. Reduction of incorrect antibiotic dosing through a structured education order form. *Arch Intern Med* 1988;148:1720-4.
20. Buchwald D, Soumerai SB, Vandervanter N, et al. Effect of hospital wide change in clindamycin dosing schedule on clinical outcome. *Rev Infect Dis* 1989;11:619-24.
21. Greene SA, Record KE, Rapp RP, et al. Pharmacy initiatives to reduce clindamycin use. *Am J Hosp Pharm* 1986;43:1210-3.
22. Levison ME, Mangura CT, Lorber B, et al. Clindamycin compared with penicillin for the treatment of anaerobic lung abscess. *Ann Intern Med* 1983;98:466-71.
23. Schroeder SA, Myers LP, McPhee SJ, et al. The failure of physician education as a cost containment strategy. *JAMA* 1984;252:225-30.
24. Denig P, Haaijer-Ruskamp FM, Zijsling DH. Impact of a drug bulletin on the knowledge, perception of drug utility, and prescribing behavior of physicians. *Ann Pharmacother DICP* 1990;24:87-93.

Appendix A: Criteria for Clindamycin Use

Situations where clindamycin may be considered appropriate;

1. Treatment of documented or highly suspected gram positive (e.g. *S. aureus* or Streptococcal) infections in patients allergic to penicillins or cephalosporins.
2. Empiric treatment of selected infections presumed to involve *S. aureus*, Streptococcal sp. and anaerobes (e.g., head and neck infections and diabetic foot infections) pending cultures and susceptibilities.
3. Treatment of actinomycosis in a patient allergic to penicillin/cephalosporins.
4. Treatment of known or suspected pleuropulmonary infections where response to penicillin has been sub optimal.
- 5.* Treatment of lung abscess or necrotizing pneumonia caused by susceptible organisms.
 - a) Radiologic and / or microbiologic evidence of an anaerobic bronchopulmonary infection (i.e. lung abscess, cavitation, necrotizing pneumonia or empyema).
 - b) History of evidence of gross feculent aspiration at time of admission.

Note: In absence of these condition, beta-lactam antibiotics should be used for the treatment of aspiration pneumonia.
6. Agent for surgical prophylaxis in penicillin / cephalosporin allergic patients requiring gram positive antimicrobial coverage.

* criteria for aspiration pneumonia approved January 1992