

The management of outpatient cellulitis at the Moncton hospital before and after the initiation of a clinical treatment pathway

Abstract

Introduction: Antimicrobial stewardship is a coordinated effort to improve the appropriate use of antimicrobials. Inappropriate antibiotic use is a major contributor of emerging antibiotic resistance. Broad-spectrum intravenous antibiotics are commonly used for moderate to severe skin and soft tissue infections when narrower-spectrum options would be adequate.

Objective: Objectives included characterizing the antibiotic prescribing for the management of uncomplicated cellulitis in an outpatient setting. In addition, a clinical treatment pathway (CTP) was developed and its use was evaluated.

Methods: The study was a retrospective chart review looking at antibiotic prescribing in The Moncton Hospital Emergency Department and included patients treated before and after the introduction of an outpatient management pathway for cellulitis. The pathway recommended once daily probenecid 1g followed by cefazolin 2g IV. Antibiotic usage, treatment failure rates, and adverse events were compared between the two groups.

Results: In the pre-intervention group; 3 patients received cefazolin, 50 received Ceftriaxone, and 1 received Levofloxacin. After the introduction of the clinical treatment pathway there was an absolute increase of 53.8% (n=35) in the use of cefazolin and absolute decrease of 53.7% (n=23) in the use of Ceftriaxone. Both results were statistically significant ($p<0.001$). In eligible patients, the treatment pathway was utilized 61.1% of the time.

Conclusion: The introduction of a clinical treatment pathway outlining the preferential use of once daily cefazolin plus probenecid for the treatment of outpatient cellulitis led to a significant increase in the use of cefazolin, and decrease use of Ceftriaxone, thus demonstrating a positive stewardship effect at a local level.

Keywords: cellulitis, antibiotic stewardship, skin & soft tissue infections, beta-hemolytic *Streptococci*, *Staphylococcus aureus*, antibiotic therapy

Definitions

Cefazolin: a first-generation cephalosporin antibiotic

Ceftriaxone: a third-generation cephalosporin antibiotic

Cellulitis: recent onset of soft-tissue erythema associated with signs of infection that include ≥ 1 of the following symptoms: pain, swelling, lymphangitis, and fever

CTP: clinical treatment pathway

IV: intravenous

Probenecid: a uricosuric medication that prevents the excretion of cefazolin in the urine

Broad spectrum therapy: an antibiotic that has a wide range of activity against disease-causing bacteria

Narrow spectrum therapy: an antibiotic that has a narrow range of activity against disease-causing bacteria

Primary outcomes: The type and duration of antibiotics used to treat outpatient cellulitis and adherence to the clinical order set

Volume 6 Issue 2 - 2018

S Andrew Dalziel,¹ Ahmed Ghaly,² Daniel Smyth,² Timothy MacLaggan,³ George Stoica⁴

¹Family Medicine, Dalhousie University, Canada

²Infectious Diseases/Internal Medicine, Horizon Health Network, Canada

³Clinical Resource Pharmacist, Infectious Disease, Horizon Health Network, Canada

⁴Chief Statistician, Horizon Health Network, Canada

Correspondence: Andrew Dalziel, Family Medicine, Dalhousie University, 135 MacBeath Ave, Suite 6400, Moncton, New Brunswick, Canada, Tel (902) 789-6575, Email andrew.dalziel@dal.ca

Received: March 01, 2018 | **Published:** April 18, 2018

Secondary outcomes: Treatment failure and rate of *C. difficile* infection within 30 days of treatment.

Introduction

The Infectious Diseases Society of America defines *antimicrobial stewardship* as a coordinated effort to improve and measure the appropriate use of antimicrobials by promoting the selection of the optimal antimicrobial drug regimen, dose, duration of therapy, and route of administration.¹ One of the recommendations they make is through the use of guidelines and clinical treatment pathways that involve evidence-based approaches to treating common infections. This aims to improve prescribing patterns while trying to avoid the unintended consequences such as antimicrobial resistance, adverse drug events, and cost.¹ Skin and soft tissue infections are a common reason for patients to seek medical care.² Cellulitis is generally defined as recent onset of soft-tissue erythema associated with signs of infection that include ≥ 1 of the following symptoms: pain, swelling, lymphangitis and fever.³ Many of these patients are systemically well and can be managed in an outpatient setting.

A retrospective chart review in one Canadian city with 5 urban Emergency Departments reported a principal diagnosis of cellulitis

in almost 4000 people in just one year. This represented 1.3% of all ED visits.² These infections are generally treated empirically as microbiologic culture is difficult and not practical to obtain.⁴ Although difficult to isolate a pathogen, the microbiology of uncomplicated cellulitis remains fairly well known with *Staphylococcus aureus* and beta-hemolytic *Streptococci* species being the most common causative organisms.⁵⁻⁷ Traditionally, moderate to severe cases of cellulitis require intravenous antibiotics. One of the first line treatments is cefazolin, a first-generation cephalosporin administered intravenously every 8 hours due to its short half-life.⁸ This provides relatively narrow spectrum, targeted therapy, against the most common bacteria responsible for cellulitis.⁸⁻¹⁰

The ability to manage moderate cellulitis in an outpatient setting using parenteral therapy was demonstrated in several trials investigating the effectiveness of a once daily injection of Ceftriaxone, a third-generation cephalosporin, compared to cefazolin that required dosing every 8 hours. Study authors found that once daily administration of Ceftriaxone was highly effective in treating skin and soft tissue infections because of its broad spectrum of activity and safety, as well as a huge cost saving measure allowing the option of outpatient treatment.¹¹⁻¹³ Although Ceftriaxone-dosing frequency makes it a convenient choice, it is unnecessarily broad in spectrum when compared to cefazolin. Recently there has been a worldwide emphasis on antibiotic resistance with the development of “superbugs” resistant to many common antibiotics.¹⁴ Other unintended consequences of antibiotic overuse include the depletion of normal gut bacteria, potentially leading to secondary infection with *Clostridium difficile*. This infection is associated with extensive use of broad spectrum cephalosporins such as Ceftriaxone.¹⁴ The impact of these infections on the health care system is massive with one review article estimating an annual cost for the management of *Clostridium difficile* infection in the United States to be approximately \$800 million.¹⁵

In an effort to reduce unnecessary use of broad spectrum antibiotics there has been a push to use once daily cefazolin with probenecid in treating outpatient cellulitis. Probenecid is a uricosuric agent that inhibits the renal clearance of cefazolin thereby prolonging its half-life.¹⁶ Studies have shown that in combination, cefazolin concentrations remained above the minimum inhibitory concentration for the twenty-four hour dosing interval.¹⁷⁻¹⁹ This leads to a reduction in the number and frequency of intravenous infusions and also leads to less resource utilization. There have been two randomized controlled trials to date that compared the efficacy of once daily cefazolin plus probenecid versus once daily Ceftriaxone in the management of outpatient cellulitis. Both authors concluded that once daily cefazolin plus probenecid was equally efficacious compared to Ceftriaxone.^{20,21} Many Emergency Departments in Canada have adopted this approach to managing outpatient cellulitis requiring intravenous antibiotics.² A separate retrospective study identified chronic venous disease as a risk factor for treatment failure with once daily cefazolin plus probenecid.²²

The objectives of this study were:

- a. To determine what antibiotics are currently being prescribed in the management of moderate to severe cellulitis that requires outpatient intravenous antibiotic therapy;

- b. To evaluate the success of a clinical treatment pathway (CTP) outlining optimal therapy, guided in the principles of antimicrobial stewardship.

Methods

Study design

This is a retrospective before and after intervention study. The goal was to identify at least 50 patients that received intravenous antibiotics both before and after the intervention. The before intervention analysis consisted of a retrospective chart review identifying patients that were discharged from the Emergency Department at The Moncton Hospital with a diagnosis of cellulitis which was considered severe enough to require the patient to return daily for intravenous antibiotics. A clinical treatment pathway for the outpatient management of cellulitis with intravenous antibiotics was produced and made available before the second half of data collection. The treatment pathway had defined usage criteria, exclusion criteria, and outlined management using once daily cefazolin plus probenecid (Appendix 1). The inclusion and exclusion criteria of the chart review aligned with the treatment pathway to assess its applicability. A standard data collection form was used to collect demographics, co-morbidities, antimicrobial treatment, inclusion/exclusion criteria, treatment failure, rates of *C. difficile* infection, and use of the CTP (Appendix 2). The chart review identified patients from September 2015 to February 2017. The CTP was made available in May 2016, along with hospital promotion and physician education. Prior to release of the CTP, feedback was obtained from the Departments of Family Medicine, Internal Medicine, Emergency Medicine, and Pharmacy.

Outcomes

Primary outcomes included:

- i. The choice and duration of intravenous antibiotic prescribed,
- ii. Adherence to the clinical treatment pathway in the post intervention group.

Secondary outcomes included:

- i. Treatment failure defined as admission to the hospital within 30 days for an infection at the same site or escalation of antibiotic therapy,
- ii. Infection with *C. difficile* within 30 days of treatment.

Data Analysis

All statistical analyses were performed using the R statistical software, version 3.2.5 ©GNU General Public License, 2016. A MANOVA test has been used for comparing demographics. A chi-square test was used to compare the amount of cefazolin and Ceftriaxone being prescribed, before versus after implementation of the CTP. A two-way ANOVA test was used to compare failure rates and *C. difficile* infection in patients receiving IV Ceftriaxone versus IV cefazolin. Research Ethics Board approval was granted through the Horizon Health Network.

Results

A total of 295 charts were reviewed during the study period. Of

these charts, 222 patients were diagnosed with cellulitis and treated with an antibiotic as an outpatient. Intravenous antibiotics were given to 113 (50.9%) of these patients, with 54 in the pre-CTP group and 59 in the post-CTP group, while the rest received oral antibiotics. The remaining patients did not meet diagnostic inclusion criteria or were admitted for treatment. Baseline characteristics of patients receiving IV antibiotics were not statistically different between the pre- and post-CTP groups (Table 1). The median ages were 54.5 versus 57. Co-morbidities were similar with diabetes mellitus present in 12% versus 15%, chronic kidney disease in 2% versus 3%, and immunosuppression in 2% versus 1%. One patient in the pre-group had a documented allergy to cefazolin while none in the post group did.

Table 1 Baseline demographics

Characteristic	Before intervention (N=54)	After intervention (N=59)
Median age—years	54.5	57
Male sex—no. (%)	31 (57.4)	32 (54.2)
Diabetes Mellitus—no. (%)	12 (22.2)	15 (26.3)
Chronic Kidney Disease—no. (%)	2 (3.7)	3 (5.1)
Immunosuppressed—no. (%)	2 (3.7)	1 (1.7)
Allergy to Cefazolin—no. (%)	1 (1.8)	0 (0)

Baseline characteristic of the patients included in the study. There were 54 patients in the before intervention group and 59 patients in the after intervention group. There was no significant difference between the two groups in any characteristic using a MANOVA test with $p=0.83$.

Primary Outcomes

In the pre-CTP arm, there were 54 patients that received IV antibiotics, consisting of cefazolin (3), ceftriaxone (50), clindamycin (2), and Levofloxacin (1). There were two patients in this arm that received double coverage with clindamycin, and Levofloxacin, respectively, in addition to their cephalosporin. The median duration of IV therapy in the pre-CTP group was 4 days (Table 2). In the post-CTP arm, there were 59 patients that received IV antibiotics, consisting of cefazolin (35), Ceftriaxone (23), and clindamycin (1). The median duration of IV therapy was 3.5 days (Table 2). There was a statistically significant increase in the use of cefazolin, 3 patients versus 35 patients ($p<0.001$), corresponding to a 53.8% absolute increase, after the introduction of the CTP. There was also a statistically significant decrease in the use of Ceftriaxone, 50 patients versus 23 patients ($p<0.001$), corresponding to 53.7% absolute decrease, after the introduction of the CTP (Figure 1).

In the post-CTP arm, there were 53 (out of 59) patients eligible for therapy with cefazolin based on the inclusion/exclusion criteria of the treatment pathway (Appendix 1). Of these 53 patients, 34 (64.1%) were started on the protocol. The protocol was only deviated from once where a patient was prescribed oral clindamycin during day 3 of cefazolin therapy due to “minimal improvement” as documented on the chart. The majority of follow up for patients on the CTP was completed in the Emergency Department (83.1% of patients) by either the Emergency Room Physician or Nurse Practitioner on duty. Various

other services provided follow up for the remaining patients: Infectious Disease (3.4%), other (10.2% consisting of Family Medicine, General Surgery, Dermatology, Gynecology, and Ophthalmology), while 3.4% of patients were not followed up.

Table 2 IV antibiotic usage

	Before intervention	After intervention	P-value
Number of patients	54	59	
Cefazolin	3	35	P<0.001
Ceftriaxone	50	23	P<0.001
Clindamycin	2*	1	P=0.831
Levofloxacin	1*	0	P=1.000
Median duration of therapy (days)	4	3.5	P=0.719

Choice of intravenous antibiotic prescribed before and after the introduction of a clinical treatment pathway outlining preferential use of once daily cefazolin plus probenecid. *There were two patients in the before intervention group that received double coverage; one patient received clindamycin and the other received Levofloxacin in addition to a cephalosporin.

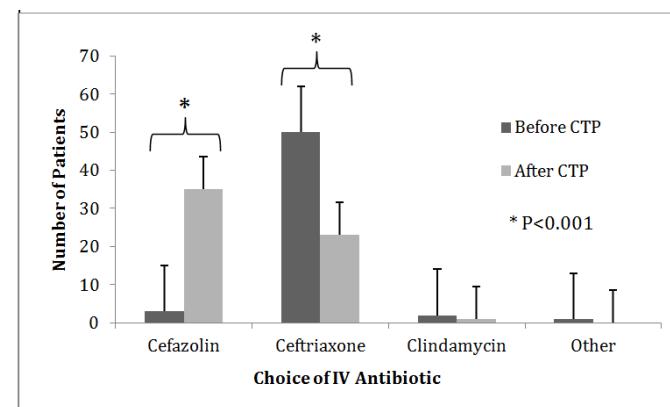


Figure 1 Intravenous antibiotic usage.

Use of Cefazolin and Ceftriaxone before and after the introduction of a clinical treatment pathway outlining preferential use of once daily cefazolin plus probenecid for the treatment of moderate to severe cellulitis. There was a significant increase use of cefazolin and decrease use of Ceftriaxone (* $p<0.001$) after the introduction of the clinical treatment pathway. Error bars represent standard error within both groups.

Secondary outcomes

There was no statistically significant difference in rates of treatment failure defined as admission to hospital within 30 days with worsening or similar infection in that area or escalation in antibiotic therapy when comparing cefazolin versus Ceftriaxone (Table 3). There were no cases of diagnosis of *C. difficile* infection in either group within 30 days of antibiotic therapy (Table 3).

Discussion

The microbiology of skin and soft tissue infections remains primarily beta-hemolytic *Streptococci* and *Staphylococcus aureus*. Historically patients were admitted to the hospital for frequent

intravenous infusions of antibiotics when treating moderate to severe cellulitis until the use of once daily administration of Ceftriaxone, a broad spectrum third-generation cephalosporin, was favored.¹¹⁻¹³ This therapy allowed outpatient treatment without the need to hospitalize patients but with the growing emergence of antibiotic resistance it is desirable to use more targeted, narrow spectrum therapy. In recent years there has been a push to use once daily cefazolin with probenecid for the management of outpatient cellulitis. Cefazolin provides excellent coverage for the usual pathogens without the unintended drawbacks of broad spectrum coverage.²³ When given with probenecid, a uricosuric agent that prevents its renal elimination thereby prolonging its half-life, it allows for once daily dosing instead of traditional dosing every eight hours, facilitating convenient outpatient therapy.¹⁸⁻²⁰ The purpose of this study was to characterize current patterns in antibiotic prescribing for the treatment of cellulitis at the Moncton Hospital, and also to assess the effectiveness of a clinical treatment pathway outlining optimal treatment of these infections. We hypothesized that the majority of patients being treated at The Moncton Hospital were receiving unnecessarily broad spectrum antibiotics and that with the introduction of a clinical treatment pathway outlining therapy with once daily cefazolin; we would see a shift in this prescribing pattern.

Table 3 Secondary outcomes

Outcome Measure	Cefazolin* (N=38)	Ceftriaxone* (N=73)	P-value
Treatment Failure			
Admission–no. (%)	5 (13.1)	10 (13.6)	P=0.781
Change of therapy–no. (%)	7 (18.4)	11 (15.0)	P=0.831
C. difficile infection–no. (%)	0 (0)	0 (0)	P=1.000

Secondary outcome measures comparing patients who received cefazolin versus Ceftriaxone. Both groups include patients from before and after the introduction of the treatment pathway. Admission was defined as admission to hospital within 30 days of initial diagnosis, for cellulitis or another infection at that same site. Change of therapy indicated an escalation or change in intravenous antibiotic therapy within 30 days of diagnosis. *C. difficile* infection was defined as occurring within 30 days of receiving antibiotics as evidence from microbiology results in the electronic medical record.

The results demonstrated that the majority of patients (92.6%) received Ceftriaxone while only a small minority (5.6%) of patients received cefazolin before the introduction of the CTP. This confirmed the overwhelming preference for Ceftriaxone in this population of patients treated for cellulitis. We suspect this is primarily due to once daily dosing of Ceftriaxone versus dosing every eight hours with cefazolin. After the introduction of the CTP, cefazolin was used in 59.3% of patients while Ceftriaxone use fell to 39.0%. This represented a significant increase in the use of cefazolin and a significant decrease in the use of Ceftriaxone. We attributed this in part to the use of the clinical treatment pathway. Looking at treatment outcomes, there was no significant difference in rates of treatment failure comparing cefazolin versus Ceftriaxone. This aligns with prior research indicating their similar efficacy in treating cellulitis.^{20,21} Although Ceftriaxone is associated with an increased risk of secondary *C. difficile* infection²⁴ we did not see a difference in this outcome compared to cefazolin. This is perhaps due to the overall low numbers included in the study. When comparing costs, the hospital price of Ceftriaxone and cefazolin were similar therefore no

cost saving measures were recorded after the CTP. It should be noted that there are extremely low rates of MRSA colonization in Moncton, NB, which is reflected by the low use of MRSA active antimicrobials during the study. A limitation of this study was that it was retrospective in nature. There was no randomization of antibiotic therapy and could therefore introduce selection bias on the part of the treating clinician based on how severe they determined the infection to be. Small study numbers may have been insufficient to detect differences in efficacy and adverse events. Data collection also relied upon review of paper and electronic charting which is prone to error or omission.

Conclusion

There is a growing trend of antimicrobial resistance worldwide due to overuse of broad-spectrum antibiotics. The concept of antimicrobial stewardship was developed to help combat this problem, promoting optimal antimicrobial therapy and monitoring. This study supported the introduction of a clinical treatment pathway outlining the treatment of outpatient cellulitis with the use of once daily cefazolin plus probenecid as a narrower alternative to once daily Ceftriaxone. The study also demonstrated a measurable change in prescribing patterns when the CTP was introduced leading to more use of cefazolin and less use of Ceftriaxone in managing outpatient cellulitis.

Acknowledgement

I would like to thank Dr. Ahmed Ghaly, Dr. Daniel Smyth, and Timothy MacLaggan for their guidance, support, and manuscript revision in this study. I would also like to thank Dr. George Stoica for statistical analysis.

Conflict of interest

The authors report no conflict of interest.

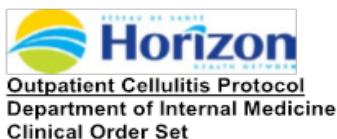
References

1. Dellit TH, Owens RC, Mc Gowan JE, et al. Infectious Diseases Society of America, Society for Healthcare Epidemiology of America guidelines for developing an institutional program to enhance antimicrobial stewardship. *Clin Infect Dis.* 2007;44(2):159–177.
2. Dong SL, Kelly KD, Oland RC, et al. ED management of cellulitis: A review of five urban centers. *Am J Emerg Med.* 2001;19(7):535–540.
3. Leder K, Turnidge JD, Grayson ML. Home-based treatment of cellulitis with twice-daily cefazolin. *Med J Aust.* 1998;169(10):519–522.
4. Sachs MK. The optimum use of needle aspiration in the bacteriologic diagnosis of cellulitis in adults. *Arch Intern Med.* 1990;150(9):1907–1912.
5. Hook EW, Hooton TM, Horton CA, et al. Microbiologic evaluation of cutaneous cellulitis in adults. *Arch Intern Med.* 1986;146(2):295–297.
6. Schwartz R, Das-Young LR, Ramirez-Ronda C, et al. Current and future management of serious skin and skin-structure infections. *Am J Med.* 1996;100(6):90S–95S.
7. Vinh DC, Embil JM. Rapidly progressive soft tissue infections. *Lancet Infect Dis.* 2005;5(8):501–513.
8. Stevens DL, Bisno AL, Chambers HF, et al. Practice guidelines for the diagnosis and management of skin and soft tissue infections: 2014 update by the infectious diseases society of america. *Clin Infect Dis.* 2014;59(2):e10–52.
9. Goldstein N, Topiel M, Ehrlich A, et al. A comparative study of ceftriaxone vs cefazolin in the treatment of cellulitis. *Curr Ther Res.* 1984;36:653.

10. Chirurgi VA, Edelstein H, Oster SE, et al. Randomized comparison trial of teicoplanin i.v., teicoplanin i.m., and cefazolin therapy for skin and soft tissue infections caused by gram-positive bacteria. *South Med J.* 1994;87(9):875–880.
11. Bradsher RW, Snow RM. Ceftriaxone treatment of skin and soft tissue infections in a once daily regimen. *Am J Med.* 1984;77(4C):63–67.
12. Gordin FM, Wofsy CB, Mills J. Once-daily ceftriaxone for skin and soft tissue infections. *Antimicrob Agents Chemother.* 1985;27(4):648–649.
13. Tice AD. Once-daily ceftriaxone outpatient therapy in adults with infections. *Cancer Chemotherapy.* 1991;37(Suppl 3):7–10.
14. Davies J, Davies D. Origins and evolution of antibiotic resistance. *Microbiol Mol Biol Rev.* 2010;74(3):417–433.
15. Bouza E. Consequences of clostridium difficile infection: Understanding the healthcare burden. *Clin Microbiol Infect.* 2012;18(Suppl 6):5–12.
16. Cox VC, Zed PJ. Once-daily cefazolin and probenecid for skin and soft tissue infections. *Ann Pharmacother.* 2004;38(3):458–463.
17. Brown G, Zemcov SJ, Clarke AM. Effect of probenecid on cefazolin serum concentrations. *J Antimicrob Chemother.* 1993;31(6):1009–1011.
18. Andes D, Craig WA. Pharmacokinetics and pharmacodynamics of outpatient intravenous antimicrobial therapy. *Infect Dis Clin North Am.* 1998;12(4):849–860.
19. Spina SP, Dillon EC. Effect of chronic probenecid therapy on cefazolin serum concentrations. *Ann Pharmacother.* 2003;37(5):621–624.
20. Brown G, Chamberlain R, Goulding J, et al. Ceftriaxone versus cefazolin with probenecid for severe skin and soft tissue infections. *J Emerg Med.* 1996;14(5):547–551.
21. Grayson ML, Mc Donald M, Gibson K, et al. Once-daily intravenous cefazolin plus oral probenecid is equivalent to once-daily intravenous ceftriaxone plus oral placebo for the treatment of moderate-to-severe cellulitis in adults. *Clin Infect Dis.* 2002;34(11):1440–1448.
22. Bader MS, Twells L, Hawboldt J. Risk factors of cellulitis treatment failure with once-daily intravenous cefazolin plus oral probenecid. *South Med J.* 2011;104(12):789–793.
23. Macy E, Contreras R. Adverse reactions associated with oral and parenteral use of cephalosporins: A retrospective population-based analysis. *J Allergy Clin Immunol.* 2015;135(3):745–752.
24. Owens RC, Donskey CJ, Gaynes RP, et al. Antimicrobial-associated risk factors for clostridium difficile infection. *Clin Infect Dis.* 2008;46(Suppl 1):S19–S31.

Appendix

Appendix I



APPROVED FOR USE IN
ER/CLINIC C, ZONE-1
MONCTON ONLY

No Known Allergies <input type="checkbox"/>																
Allergies:																
Describe Reaction:																
INSTRUCTIONS 1. The following orders will be carried out only on the authority of a physician/nurse practitioner . 2. A bullet preceding an order indicates the order is standard and should always be implemented. 3. A check box preceding an order indicates the order is optional and must be checked off to be implemented. 4. Applicable boxes to the right of an order must be checked off and initialed by the person implementing the order. 5. All dates must be written mm/dd/yy. All times must be on the 24 hour clock hr/min.																
General Principles This clinical order set can be used for the treatment of outpatients with uncomplicated cellulitis requiring IV antimicrobial therapy. If cellulitis is mild to moderate in nature and unlikely to require parenteral antibiotics then patient should be treated with oral cefodroxil or cephalexin as per the NB Provincial Health Authorities Anti-Infective Stewardship Committee's Antimicrobial Therapy for Skin and Soft Tissue Guideline . Please review inclusion and exclusion criteria below. If criteria met, please fill orders for Days 1 to 3. Day 4 and follow-up orders to be completed by Infectious Disease (ID) Physician or other primary care physician. If day 4 falls on a weekend or holiday the patient should be continued on probenecid/cefaZolin until a weekday when the patient can be assessed by an ID physician or primary care physician																
Criteria <table><tr><td>– Clinical evidence of cellulitis characterised by recent onset of soft-tissue erythema associated with signs of infection that included greater than 1 of the following symptoms: pain, swelling, lymphangitis and fever</td><td>– No evidence of foreign body or prosthetic material underlying cellulitis (i.e. prosthetic joint, vascular graft)</td></tr><tr><td>– Hemodynamically stable and no evidence of sepsis</td><td>– No contraindications to probenecid: allergy to probenecid, acute gout, methotrexate use, history of renal stones estimated Creatinine Clearance less than 30 mL/min (see page 2)</td></tr><tr><td>– Not associated with contiguous osteomyelitis</td><td>– AST, ALT, Alk Phos less than 2 times upper limit of normal (if known)</td></tr><tr><td>– No immune deficiency or immune compromise other than diabetes</td><td>– No history of allergy to ceFAZolin (Immediate hypersensitivity to penicillin described as anaphylaxis, bronchospasm, angioedema, hypotension, urticaria or pruritus is <u>NOT</u> a contraindication)</td></tr><tr><td>– No evidence of necrotizing infection (or pain out of proportion of clinical findings)</td><td></td></tr><tr><td>– Diabetic foot ulcer less than 2 weeks duration</td><td></td></tr></table>					– Clinical evidence of cellulitis characterised by recent onset of soft-tissue erythema associated with signs of infection that included greater than 1 of the following symptoms: pain, swelling, lymphangitis and fever	– No evidence of foreign body or prosthetic material underlying cellulitis (i.e. prosthetic joint, vascular graft)	– Hemodynamically stable and no evidence of sepsis	– No contraindications to probenecid: allergy to probenecid, acute gout, methotrexate use, history of renal stones estimated Creatinine Clearance less than 30 mL/min (see page 2)	– Not associated with contiguous osteomyelitis	– AST, ALT, Alk Phos less than 2 times upper limit of normal (if known)	– No immune deficiency or immune compromise other than diabetes	– No history of allergy to ceFAZolin (Immediate hypersensitivity to penicillin described as anaphylaxis, bronchospasm, angioedema, hypotension, urticaria or pruritus is <u>NOT</u> a contraindication)	– No evidence of necrotizing infection (or pain out of proportion of clinical findings)		– Diabetic foot ulcer less than 2 weeks duration	
– Clinical evidence of cellulitis characterised by recent onset of soft-tissue erythema associated with signs of infection that included greater than 1 of the following symptoms: pain, swelling, lymphangitis and fever	– No evidence of foreign body or prosthetic material underlying cellulitis (i.e. prosthetic joint, vascular graft)															
– Hemodynamically stable and no evidence of sepsis	– No contraindications to probenecid: allergy to probenecid, acute gout, methotrexate use, history of renal stones estimated Creatinine Clearance less than 30 mL/min (see page 2)															
– Not associated with contiguous osteomyelitis	– AST, ALT, Alk Phos less than 2 times upper limit of normal (if known)															
– No immune deficiency or immune compromise other than diabetes	– No history of allergy to ceFAZolin (Immediate hypersensitivity to penicillin described as anaphylaxis, bronchospasm, angioedema, hypotension, urticaria or pruritus is <u>NOT</u> a contraindication)															
– No evidence of necrotizing infection (or pain out of proportion of clinical findings)																
– Diabetic foot ulcer less than 2 weeks duration																
Day 1 – Initial Consultation • CBC, serum creatinine (arranged by referring physician) probenecid 1 g PO x 1 dose AND ceFAZolin 2 g IV x 1 dose <u>30 to 60 minutes after receiving probenecid</u> Other: _____ • Follow-up to be completed by: Primary Care Physician OR Emergency Department OR Infectious Diseases Service (dictated, called)																
Days 2 – 3 (or more if day 4 falls on a weekend or holiday) probenecid 1 g PO once daily AND ceFAZolin 2 g IV once daily <u>30 to 60 minutes after receiving probenecid x _____ days</u> } in Clinic C OR ED Other: _____																

Fax to Pharmacy Services

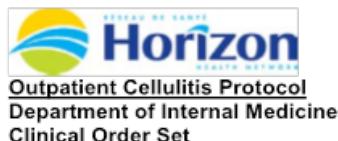
Prescriber's signature: _____ Date: _____ Time: _____

IM-450

Approved: May 5, 2016

Page 1 of 3

Note: This is a **controlled** document. Any documents in paper form is not controlled and should **ALWAYS** be checked against the electronic version prior to use.



APPROVED FOR USE IN
ER/CLINIC C, ZONE-1
MONCTON ONLY

No Known Allergies

Allergies:

Describe Reaction:

INSTRUCTIONS

1. The following orders will be carried out **only** on the **authority of a physician/nurse practitioner**.
2. A bullet preceding an order indicates the order is standard and should always be implemented.
3. A check box preceding an order indicates the order is optional and must be checked off to be implemented.
4. Applicable boxes to the right of an order must be checked off and initialed by the person implementing the order.
5. All dates must be written mm/dd/yy. All times must be on the 24 hour clock hr/min.

Action by:	
OE	
MAR	
Care Plan	

Day 4 – Re-Assessment (to be completed by ID physician OR primary care physician OR emergency department Physician/Nurse Practitioner)

- If Day 4 falls on a weekend or holiday the patient should be continued on probenecid/ceFAZolin until a weekday when they can be assessed by an ID physician or primary care physician
- Most patients can be converted to oral therapy by day 4 – Criteria for IV to PO conversion are afebrile and no further progression in erythema or pain. If appropriate for oral therapy fill outpatient Rx on page 3

CBC, serum creatinine if previous results not within the normal range

probenecid 1 g PO once daily **AND**

ceFAZolin 2 g IV once daily 30 to 60 minutes after receiving probenecid x days } in **Clinic C OR ED**

Other: _____

Return to _____ in _____ days for reassessment

See outpatient Rx

Follow-up Assessments (Day 5 +)

Cockcroft-Gault equation for estimated creatinine clearance (mL/min):

CrCl (females) = $(140 - \text{age}) \times \text{weight (kg)}^*$
serum creatinine (mcg/L)

CrCl (males) = CrCl (females) x 1.2

*For weight, use ideal body weight *unless* actual body weight is greater than 20% of ideal body weight, in which case use dosing body weight.

Ideal body weight (IBW):

IBW (females) = $45.5 \text{ kg} + 0.92 \times (\text{height in cm} - 150 \text{ cm})$ **OR** $45.5 \text{ kg} + 2.3 \times (\text{height in inches} - 60 \text{ inches})$

IBW (males) = $50 \text{ kg} + 0.92 \times (\text{height in cm} - 150 \text{ cm})$ **OR** $50 \text{ kg} + 2.3 \times (\text{height in inches} - 60 \text{ inches})$

Dosing weight (kg) = IBW + 0.4 x (actual body weight – IBW)

Fax to Pharmacy Services

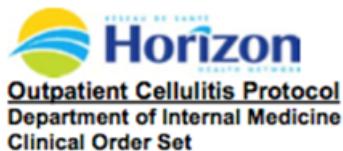
Prescriber's signature: _____ Date: _____ Time: _____

IM-450

Approved: May 5, 2016

Page 2 of 3

Note: This is a **controlled** document. Any documents in paper form is not controlled and should **ALWAYS** be checked against the electronic version prior to use.



APPROVED FOR USE IN
ER/CLINIC C, AREA-1
MONCTON ONLY

Rx Outpatient Uncomplicated Cellulitis

Community Pharmacy: _____

Community Pharmacy Fax Number: _____

Antimicrobial Therapy:

ceFAZolin 2 g IV once daily (30 to 60 minutes after receiving prebenecid 1 g PO) x _____ days (probenecid supplied by hospital; supply ceFAZolin as dry vials)

cefadroxil _____ mg PO _____ x _____ days (usual total duration of antibiotic therapy is 7 - 10 days)

Other: _____ x _____ days

No Refills

If the prescription is to be faxed then the following statements are correct:

- This prescription represents the original of the prescription drug order
- The pharmacy addressee noted above is the only intended recipient and there are no others

Fax to Pharmacy Services

Prescriber's signature: _____ Date: _____ Time: _____

IM-450

Approved: May 5, 2016

Page 3 of 3

Amended: November 7, 2016

Note: This is a controlled document. Any documents in paper form is not controlled and should **ALWAYS** be checked against the electronic version prior to use.

Printed On: 11/09/2016

Appendix 2

Clinical Information		Patient Enrolment Form	
Cellulitis Antimicrobial Prescribing Research Project		Date Assessed: _____ Study ID: _____	
Background Information			
Initials: _____	Age: _____	Gender:	<input type="checkbox"/> M <input type="checkbox"/> F
Unique #: MO _____	Attending Service: <input type="checkbox"/> FP <input type="checkbox"/> Surg. <input type="checkbox"/> IM <input type="checkbox"/> EM <input type="checkbox"/> Other _____		
Medical Co-morbidities:			
Diabetes: <input type="checkbox"/> Yes <input type="checkbox"/> No HgbA1c _____	Chronic Renal Failure: <input type="checkbox"/> Yes <input type="checkbox"/> No		CrCl _____
Immunosuppression: <input type="checkbox"/> Yes <input type="checkbox"/> No	Others: _____		
If yes, Why: _____			
Allergies			
Medication(s)	Reaction		
Diagnosis of Cellulitis:		<input type="checkbox"/> Yes <input type="checkbox"/> No	
Documented Clinical Symptoms:		<input type="checkbox"/> Soft-tissue erythema	<input type="checkbox"/> Pain <input type="checkbox"/> Swelling <input type="checkbox"/> Lymphangitis <input type="checkbox"/> Fever
Inclusion Criteria:		<input type="checkbox"/> Cellulitis <input type="checkbox"/> Outpatient treatment	<input type="checkbox"/> Requiring intravenous antibiotics

<u>Exclusion Criteria:</u>	Diabetic foot infection greater than 2 weeks duration	<input type="checkbox"/> Yes <input type="checkbox"/> No	Evidence of foreign body or prosthetic material underlying cellulitis (ie prosthetic joint vascular graft)	<input type="checkbox"/> Yes <input type="checkbox"/> No
	<u>Hemodynamically unstable or sepsis</u>	<input type="checkbox"/> Yes <input type="checkbox"/> No	Estimated creatinine clearance <30mL/min	<input type="checkbox"/> Yes <input type="checkbox"/> No
	Associated with contiguous osteomyelitis	<input type="checkbox"/> Yes <input type="checkbox"/> No	AST, ALT, Alk Phos > 2 times upper limit of normal (if known)	<input type="checkbox"/> Yes <input type="checkbox"/> No
	Immune deficiency	<input type="checkbox"/> Yes <input type="checkbox"/> No	Allergy to cefazolin (or immediate hypersensitivity to penicillin)	<input type="checkbox"/> Yes <input type="checkbox"/> No
	Evidence of necrotizing infection	<input type="checkbox"/> Yes <input type="checkbox"/> No	Allergy to probenecid	<input type="checkbox"/> Yes <input type="checkbox"/> No

Antibiotic Therapy								
Day	Type	Dose	Route	Frequency	Type	Dose	Route	Frequency
1								
2								
3								
4								
5								
6								
7								
8								
9								
10								
11								
12								
13								
14								
15								
16								
17								
18								
19								
20								

Outcomes	
(Documented only if given IV antibiotics)	
<u>Admission to hospital within 30 days for cellulitis or other infection in similar area:</u>	<input type="checkbox"/> Yes <input type="checkbox"/> No
<u>Escalation or change of IV therapy within 30 days:</u>	<input type="checkbox"/> Yes <input type="checkbox"/> No
<u>Use of clinical order set:</u>	<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> N/A (met exclusion criteria) <input type="checkbox"/> No (but used cefazolin plus probenecid as treatment)
If yes, was there deviation from the order set?	<input type="checkbox"/> Yes <input type="checkbox"/> No Explain:
<u>Follow up by:</u>	<input type="checkbox"/> FP <input type="checkbox"/> ED <input type="checkbox"/> ID <input type="checkbox"/> None <input type="checkbox"/> Other _____
<u>Diagnosis of C. difficile within 30 days:</u>	<input type="checkbox"/> Yes <input type="checkbox"/> No