

Cefazolin + Probenecid for Outpatient Treatment of Uncomplicated SSTIs[†]

BOTTOM LINE: Cefazolin plus probenecid is equally efficacious as broader spectrum alternatives for outpatient treatment of cellulitis, and is preferred.

- Cefazolin is preferred for treatment of uncomplicated skin and soft tissue infections (uSSTIs)[†] as it has excellent coverage of both β -hemolytic Streptococci and methicillin-sensitive *Staphylococcus aureus* (MSSA). It has a narrower spectrum of Gram negative activity, coverage which is not required in the treatment of uSSTIs, and it is less likely to cause *C. difficile* infection than broader spectrum antibiotics such as ceftriaxone and ertapenem.¹
- Probenecid reduces the renal tubular secretion and clearance of cefazolin thereby increasing the serum concentration and half-life of cefazolin. The use of probenecid therefore facilitates the use of IV cefazolin given once daily in outpatient IV clinics and/or emergency departments for the treatment of uncomplicated SSTIs[†].
- In clinical and pharmacokinetic trials, cefazolin 2g IV daily plus probenecid 1-2g PO daily has been shown to have similar efficacy and adverse effects as ceftriaxone 1-2g IV daily.²⁻⁴
- The recommended cefazolin + probenecid regimen for outpatient management of uncomplicated SSTIs[†] is:

	Adult Dose	Pediatric Dose	
Cefazolin* + Probenecid Give 30 min. prior to cefazolin and with food to minimize GI upset.	2g IV daily 1-2g** PO daily or 1g PO bid given 30 minutes prior to cefazolin and ~12 hours later, if unable to tolerate probenecid as a 2g daily dose.	33mg/kg IV daily (max 2g) 25mg/kg PO daily (rounded to nearest 125mg; max 1g)	*Switch to oral agent when resolution of systemic symptoms and no further progression of cellulitis. **Since probenecid's mechanism of action is dose-related, a 2g once daily dose results in higher and more sustained cefazolin levels than alternate probenecid dosages (e.g. 500mg qid, 1g daily), is well tolerated, and is recommended to ensure that therapeutic cefazolin concentrations are maintained for 24 hours. ³⁻⁵

[†] **Uncomplicated Skin & Soft Tissue Infections:** No evidence of complicated or polymicrobial skin and soft tissue infection such as: diabetic foot ulcer, necrotizing fasciitis, secondary infection of chronic skin disease, animal and human bites, decubitus ulcers, and trauma; or of osteomyelitis, septic arthritis or deep space infection, sepsis or septic shock.
Cefazolin plus probenecid should NOT be used for these complicated infections.

- Contraindications for the use of cefazolin + probenecid include:
 - cefazolin or probenecid allergy or intolerance
 - creatinine clearance less than 50 mL/min
 - acute gout attack or history of uric acid renal calculi
 - G6PD deficiency
 - children less than 2 years old
 - significant drug interactions between current medications and probenecid: high dose salicylates (ASA 81 mg PO daily is safe), ketorolac, lorazepam, nitrazepam, oseltamivir, methotrexate, mycophenolate.
- Treatment failure of cefazolin plus probenecid may be higher in patients with chronic venous insufficiency; use with caution.⁶

References

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