

Outpatient Cellulitis Pathway

February 2020

High Dose Oral Flucloxacillin Plus Probenecid

IV cefazolin once daily plus probenecid? — there is a better way!

Once daily IV cefazolin with oral probenecid has been used to treat moderately severe cellulitis in order to avoid hospital admission.

Last year over 400 people were treated on the community cellulitis pathway in SDHB. This consumed 750 hours of district nursing time, 225 ED attendances, 60 hours of pharmacy time, at an overall estimated cost of \$175,000.

However a recent RCT demonstrated **oral therapy** with cefalexin was **equally effective** as IV cefazolin, with no difference in admission rates.¹

High dose oral flucloxacillin or cefalexin (e.g. 1g QID) with oral probenecid has been shown to be as good or even better than the IV cefazolin pathway.²

Probenecid: Important Points

- Probenecid's half-life is 6 – 8 hours, so prescribe with each dose of flucloxacillin or cefalexin i.e. probenecid 500mg QID.
- Must **NOT** be prescribed if taking **methotrexate**, as toxic accumulation of methotrexate can occur.
- Should **NOT** be prescribed if the patient participates in competitive sports and undergoes urine testing. Probenecid is a masking agent of performance enhancing drugs and is prohibited by WADA.
- Avoid if recent attack of gout or CrCL <30 mL/min
- For patients on multiple medications – check the NZF interaction checker.



Probenecid – turbocharge the flucloxacillin!

The *peak* drug levels of penicillins and cephalosporins are irrelevant. The key parameter is the amount of time the drug level is above the minimum inhibitory concentration of the bacteria (time > MIC).

Probenecid delays renal elimination of many beta-lactam drugs, particularly cefalexin, cefazolin, flucloxacillin, and amoxicillin. This greatly improves the half life and time > MIC.

High dose oral flucloxacillin given with probenecid can achieve **similar drug levels to IV therapy**.²



HOT OFF THE PRESS:

Flucloxacillin can be taken with food!

A recent study³ conducted in New Zealand has shown that ingestion of flucloxacillin **with food** has minimal impact on flucloxacillin levels, **reduces nausea** and improves compliance.

Key Benefits:

- Patient convenience
- Time & cost saving
- Equally effective

Outpatient Treatment of Moderately Severe Cellulitis:

Preferred: Flucloxacillin 1g PO QID **PLUS** Probenecid 500mg PO QID x 7 days (with food)

If allergic to penicillin: Cefalexin 1g PO QID **PLUS** Probenecid 500mg PO QID x 7 days (with food)

If severe penicillin or cephalosporin allergy: Clindamycin 600mg PO TDS x 7 days (with or without food)

Pitfalls in Cellulitis Treatment

- Inadequate trial of oral therapy before hospital referral – insufficient dose and inadequate time.
- Do not expect improvement for **at least** the first 3 days. Cellulitis *looks* worse before it gets better – this does not reflect treatment failure.
- Streaky erythema spreading up the inside of the thigh is likely associated lymphangitis - not spreading of the cellulitis.
- Inadequate elevation of the limb. The limb should be elevated above the level of the heart, as much as possible in the first 72 hours.
- Confusing varicose eczema and venous stasis with cellulitis. Consider concurrent treatment with a topical steroid and emollient.

Consider admission if:

Cellulitis of face, hand, or over a joint

Severe pain

Systemic toxicity: tachycardia, tachypnoea, hypotension, high fever, acute confusion

Comorbidities e.g. poorly controlled diabetes, renal failure, peripheral vascular disease, frailty and advanced age.

Immunosuppression

Non-response to adequate trial of high dose oral antibiotic

Morbid obesity

Fluctuant wound requiring drainage

Cellulitis or Mimic?

- Cellulitis is acutely tender to palpation, associated with tissue oedema, and develops over a few days.
- If it's not particularly tender, tissue oedema is absent, or it has been present for more than a few days - it's unlikely to be cellulitis.
- Elevate leg for 2 minutes – does the redness fade or disappear? This suggests dependent rubor.
- Itchy, scaling, or hyperpigmented with dilated leg veins? These features suggests chronic venous insufficiency and varicose eczema
- The **Cellulitis Score**⁴ below may assist diagnosis:

Cellulitis Score

Acute onset over ≤ 3 days	1 point
Erythema	1 point
Fever >38°C	1 point
History of recent skin break / trauma	1 point
Tender to light touch	1 point
Unilateral, one limb only	1 point
Leukocytosis WCC > 10	1 point

Score ≥4 has 95% specificity and 100% sensitivity for cellulitis. If score <4 then unlikely to be cellulitis.

References:

- (1) Dalen D *et al.* Emerg Med J. 2018 Aug;35(8):492-498
- (2) Everts R *et al.* J Infection 2019 (*In press*)
- (3) Gardiner SJ *et al.* PLoS One. 2018 Jul 12;13(7):e0199370
- (4) Ezaldein H *et al.* Cutis 2018;102:E8-E12

Authors:

Dr Brendan Arnold *Infectious Disease Physician;*
 Dr Amy Leuthauser *Emergency Physician;*
 Dr Aidan Murry *Emergency Physician;*
 Joyce Lim *Antimicrobial Pharmacist*
 Diane Redding *Antimicrobial Pharmacist*