

If pre-existing peripheral vascular disease is likely to hinder the healing process a vascular surgeon should assess the patient's suitability for a bypass or stenting procedure.

## Conclusion

All foot infections in the diabetic patient need to be taken seriously. Small surface lesions may conceal significant deeper pathology requiring surgical intervention or aggressive antibiotic therapy. When in doubt about the severity of an infection, or if diabetic (Charcot's) arthropathy is suspected, seek an immediate second opinion from an orthopaedic surgeon or diabetes foot service. If this is not available then the patient should be admitted to hospital for observation and further investigations.

## References

1. Jeffcoate WJ, Harding KG. Diabetic foot ulcers. *Lancet* 2003;361:1545-51.  
<http://image.thelancet.com/extras/02art6190web.pdf> [cited 2007 Jan 15]
2. Lipsky BA, Berendt AR, Deery HG, Embil JM, Joseph WS, Karchmer AW, et al. Diagnosis and treatment of diabetic foot infections. *Clin Infect Dis* 2004;39:885-910.  
<http://www.journals.uchicago.edu/CID/journal/issues/v39n7/34365/34365.html> [cited 2007 Jan 15]
3. Edmonds ME, Foster AV. Diabetic foot ulcers. *BMJ* 2006;332:407-10.

## Further reading

Campbell LV, Graham AR, Kidd RM, Molloy HF, O'Rourke SR, Colagiuri S. The lower limb in people with diabetes. Position statement of the Australian Diabetes Society. *Med J Aust* 2000;173:369-72.

[http://www.mja.com.au/public/issues/173\\_07\\_021000/campbell/campbell.html](http://www.mja.com.au/public/issues/173_07_021000/campbell/campbell.html) [cited 2007 Jan 15]

National Institute for Health and Clinical Excellence. Type 2 diabetes – footcare: Algorithm.

<http://www.nice.org.uk/page.aspx?o=208094> [cited 2007 Jan 15]

<http://www.diabetic-foot.com.au> [cited 2007 Jan 15]

<http://www.woundupdate.com> [cited 2007 Jan 17]

<http://www.emedicine.com/orthoped/topic387.htm> [cited 2007 Jan 15]

*Conflict of interest: none declared*

## Self-test questions

*The following statements are either true or false (answers on page 27)*

5. Infected diabetic ulcers may be painless.
6. Antibiotic treatment of a diabetic ulcer should not be started until the infecting organism is known.

# Your questions to the PBAC

## Taxanes

The listing of trastuzumab on the Pharmaceutical Benefits Scheme (PBS) in October 2006 was heralded with much fanfare. Along with this listing, changes to the prescribing requirements for taxanes also occurred. Both docetaxel and paclitaxel are now available on authority prescription for the treatment of HER2 positive early breast cancer in combination with trastuzumab. However, one group of patients will miss out on subsidised treatment. They are women with HER2 positive metastatic breast cancer who have not previously been treated with chemotherapy.

Patients with HER2 positive metastatic breast cancer can access trastuzumab under the Herceptin Access Program run through Medicare Australia. The prescribing restrictions for this program specify that the trastuzumab is to be used as a single drug or in combination with a taxane. Herein lies the problem. The current listing for taxanes on the PBS is 'advanced breast cancer after failure of prior therapy, which includes an anthracycline'. Patients with HER2 positive metastatic breast cancer who are chemotherapy naive cannot have the optimal therapy of

trastuzumab in combination with a taxane, as the latter is not funded by the PBS.

Why were the taxanes made available for HER2 positive early breast cancer and not simply for all patients with HER2 positive breast cancer?

Jim Siderov  
Senior Pharmacist  
Cancer Services  
Austin Health  
Melbourne

*PBAC response:*

The Pharmaceutical Benefits Advisory Committee (PBAC) made its recommendation to subsidise taxanes for the treatment of HER2 positive early breast cancer in combination with trastuzumab because of evidence that this treatment combination met the requirements for PBS listing. The PBAC also recommended that the taxanes, in combination with an anthracycline and cyclophosphamide, be made available for adjuvant treatment for all patients with node positive breast

cancer. Again this recommendation was made on the basis of evidence which showed that this treatment was of acceptable efficacy, safety and cost-effectiveness.

To date, the PBAC has not been presented with evidence to show that the combination of a taxane and trastuzumab in chemotherapy naive patients with metastatic breast cancer meets the requirements for PBS listing. While it may seem reasonable to extend the listing for the taxanes for HER2

positive early breast cancer to include all HER2 positive breast cancer, the efficacy and cost-effectiveness is not necessarily the same in metastatic breast cancer as when the treatment is used in early breast cancer.

The continuing success of the PBS depends upon a rigorous evidence-based assessment of drugs for subsidy. These requirements apply in all cases and ensure consistency and fairness in the listing process.

## Medicinal mishap

### Cross-reactivity of penicillins and cephalosporins

*Prepared by Winnie WY Tong, Basic Physician Trainee, Elizabeth A Anderson, Principal Drug Information Specialist, Department of Pharmacy, and Constance H Katelaris, Senior Consultant, Department of Clinical Immunology and Allergy, Westmead Hospital, Sydney*

#### Case

A 73-year-old man collapsed at home. Ambulance officers noted impalpable blood pressure, shortness of breath and complaints of right-sided chest and epigastric pains.

The man had seen his family doctor earlier that day complaining of sore throat, cough and haemoptysis. He was prescribed cephalexin and had taken the first dose 10 minutes before collapsing. The man had a documented history of amoxycillin allergy with pruritis.

Oxygen and intravenous fluids were given and in the emergency department his blood pressure was 140/70. On examination he had a generalised erythematous rash that was pruritic. Wheeze and tongue swelling were absent and intra-abdominal pathology was excluded. A diagnosis of anaphylaxis to cephalexin was made. Hydrocortisone and antihistamines were given and he was admitted to hospital.

As he was taking propranolol it was ceased, as beta blockers can potentiate further anaphylactic reactions. He remained stable on oral antihistamines and was discharged after three days.

#### Comment

Penicillins and cephalosporins exhibit partial and incomplete cross-reactivity of up to 7% that may be related to the 'generation' of cephalosporin.<sup>1</sup> In clinical practice it is not uncommon for cephalosporins to be given to penicillin-allergic patients, particularly if the history of penicillin reaction was not life-threatening. However, reports of adverse outcomes, including fatalities, appear to be increasing. Over the last six

months, the authors know of four cases from western Sydney including two deaths.

Reactions to beta-lactam antibiotics can be classified into immediate and non-immediate. Immediate reactions are IgE mediated and classically manifest as anaphylaxis, urticaria, angioedema, bronchospasm and allergic rhinoconjunctivitis. Non-immediate reactions such as maculopapular or morbilliform rashes are probably T-cell mediated. The most common clinical manifestation of both penicillin and cephalosporin allergy is skin reactions, occurring with a frequency of 1–3% of courses given.<sup>1</sup> In addition to anaphylaxis, less common but serious adverse reactions to cephalosporins include serum sickness-like reactions, acute interstitial nephritis and cytopenias.

While penicillin-induced anaphylaxis is rare (0.01–0.05% of courses), it may be fatal in 10% of cases.<sup>2</sup> It is difficult to obtain reliable data about the frequency of cephalosporin anaphylaxis, but published figures are 0.0001–0.1%.<sup>1</sup>

Whether a penicillin-allergic patient can safely take cephalosporins remains a difficult question to answer – many people labelled penicillin-allergic can actually take penicillin. Patients with a history of penicillin allergy are four times more likely to have a reaction to cephalosporins than patients without a penicillin allergy, especially if the patient is penicillin skin prick test positive.<sup>2</sup> It is not known if a history of anaphylaxis predicts a more serious allergic reaction. A history of mild reactions to penicillin, such as rashes, does not imply that a reaction to cephalosporins will not be life-threatening.

Side chain specific antibodies may be responsible for cephalosporin allergies rather than antibodies to the core beta-lactam ring.<sup>1,3</sup> This would explain the cross-reactivity between certain penicillins and cephalosporins which share similar side chains, for example, amoxycillin and cephalexin, aztreonam and ceftazidime, benzylpenicillin and cephalothin.

While the risk of a serious reaction to cephalosporins in patients with known penicillin allergy remains low, serious adverse reactions do occur, including fatalities. Before prescribing