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

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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.[1] 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.[1] 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.[2] It is difficult to obtain reliable data about the frequency of cephalosporin anaphylaxis, but published figures are 0.0001–0.1%.[1]

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.[2] 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.[1,3] 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

cephalosporins it is prudent to take a careful history as to the nature of the penicillin allergy and the specific drug involved. It would be sensible to avoid prescribing drugs with the same or similar side chains, especially if an alternative non-beta-lactam antibiotic is available. If a cephalosporin is prescribed, the first dose should be taken in a monitored setting.

References

1. Kelkar PS, Li JT. Cephalosporin allergy. N Engl J Med 2001;345:804-9.
2. Lin RY. A perspective on penicillin allergy. Arch Intern Med 1992;152:930-7.
3. Baumgart KW, Baldo BA. Cephalosporin allergy [letter]. N Engl J Med 2002;346:380-1.

New drugs: transparency

Access to information about drugs is essential for the quality use of medicines. Since 2003 *Australian Prescriber* has therefore recorded details about the willingness of pharmaceutical companies to disclose the information that supported the Australian approval of their new products.[1] These details are published as the T(ransparency)-score at the end of each new drug comment in *Australian Prescriber*.

Table 1 shows the responses to requests for evaluation data between August 2005 and December 2006. The Editorial Executive Committee of *Australian Prescriber* is pleased to report that there has been an improvement since the previous report was published.[1] Most manufacturers now provide some information to assist in the preparation of the new drug comments. The Editorial Executive Committee hopes this trend to increased transparency continues.

Reference

1. Two-way transparency. Aust Prescr 2005;28:103.

Table1

Pharmaceutical company responses to requests for clinical evaluation data

Company	Drug
Manufacturer provided all requested information	
AstraZeneca	rosuvastatin
Ferring	quinagolide
Pfizer	eplerenone
Pfizer	sunitinib malate
Roche	bevacizumab
Roche	erlotinib
Roche	epoetin beta
Wyeth	tigecycline
Manufacturer provided some data	
Alcon	anecortave acetate
Arrow Pharmaceuticals	butoconazole nitrate
Arrow Pharmaceuticals	solifenacin succinate
Bayer	sorafenib tosylate
Bristol-Myers Squibb	entecavir
CSL	rabies vaccine
EpiPharm	tazarotene
Epitan	eflornithine hydrochloride
GlaxoSmithKline	rotavirus vaccine
Merck Sharp & Dohme	rotavirus vaccine
Merck Sharp & Dohme	human papillomavirus vaccine
Novartis	deferasirox
Orphan	lanthanum carbonate hydrate
Schering-Plough	posaconazole
Servier	strontium ranelate
Manufacturer had no objection to providing data but did not actually provide it	
Novartis	lumiracoxib
Manufacturer declined to supply data	
Amgen	palifermin
Genzyme	sevelamer hydrochloride
Novo Nordisk	insulin detemir
Schering	disodium gadoxetate
Manufacturer did not respond to request	
Alphapharm	cetuximab
Altana Pharma	ciclesonide
Janssen-Cilag	bortezomib
Novartis	darifenacin hydrobromide
Schering	alemtuzumab
Solvay	moxonidine