13. Roberts GW, Druskeit T, Jorgenson LE, Wing LM, Gallus AS, Miller C, et al. Comparison of an age adjusted warfarin loading protocol with empirical dosing and Fennerty's protocol. Aust N Z J Med 1999;29:731-6.
14. Oates A, Jackson PR, Austin CA, Channer KS. A new regimen for starting warfarin therapy in out-patients. Br J Clin Pharmacol 1998;46:157-61.
15. The International Warfarin Pharmacogenetics Consortium. Estimation of the warfarin dose with clinical and pharmacogenetic data. N Engl J Med 2009;360:753-64.
16. Garber AM, Phelps CE. Economic foundations of cost-effectiveness analysis. J Health Econ 1997;16:1-31.

Conflict of interest: none declared

Self-test questions

The following statements are either true or false (answers on page 87)

7. Increased dietary intake of vitamin K reduces a patient's warfarin requirements.
8. Most of the inter-individual variation in warfarin requirements can be explained by genetic variation in cytochrome P450 2C9.

Dental notes

*Prepared by **Michael McCullough**, Chair, Therapeutics Committee, Australian Dental Association*

Pharmacogenetics of warfarin

The international normalised ratio (INR) is a simple test commonly used by dentists to gauge the likelihood that a patient taking warfarin will have excessive haemorrhage following tooth extraction. There is a clearly defined range of INR values within which simple local post-extraction measures, such as suturing, pressure and tranexamic acid mouth rinses, are adequate to control bleeding. Patients within this range can continue warfarin.[1]

The large variation in INR values, related to genetic and dietary factors, particularly the intake of vitamin K, reinforces the need to have this test undertaken shortly before the dental procedure.

The metabolism of warfarin can be reduced by azole antifungals such as miconazole. Topical oral miconazole can profoundly increase the INR and thus the risk of bleeding due to over-anticoagulation.[2,3] Similarly metronidazole, which is commonly used in the management of oral infections, can greatly increase the INR. Dentists therefore need to review patients' current medication before prescribing any drugs, even those topically applied, for possible interactions with warfarin.

References

1. Therapeutic Guidelines: Oral and Dental. Version 1. Melbourne: Therapeutic Guidelines Limited; 2007.
2. Pemberton MN, Oliver RJ, Theaker ED. Miconazole oral gel and drug interactions. Br Dent J 2004;196:529-31.
3. Morgan L. Topical drug with systemic risk. Aust Prescr 2003;26:35.

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 January 2007 and January 2009. The Editorial Executive Committee of *Australian Prescriber* is pleased to report that there has been an improvement since the previous reports were published.[1,2] 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.

References

1. Two-way transparency. Aust Prescr 2005;28:103. www.australianprescriber.com/magazine/28/4/artid/704/ [cited 2009 May 5]
2. New drugs: transparency. Aust Prescr 2007;30:26-7. www.australianprescriber.com/magazine/30/1/26/7/ [cited 2009 May 5]

Table 1

Pharmaceutical company responses to requests for clinical evaluation data 2007–2009

Company	Drug
T T T manufacturer provided clinical evaluation	
Amgen	romiplostim
Baxter Healthcare	factor VIII inhibitor bypassing fraction
Bristol-Myers Squibb	abatacept, dasatinib, perflutren
Ferring	carbetocin
Genzyme	anti-thymocyte globulin
Hospira	ibandronic acid
Pfizer	maraviroc, varenicline, ziprasidone
Wyeth	temsirolimus
T T manufacturer provided additional useful information	
Boehringer Ingelheim	pramipexole
Janssen-Cilag	paliperidone
Merck Sharp & Dohme	fosaprepitant
Servier	ivabradine
T manufacturer provided only the product information	
Abbott	paricalcitol
Amgen	panitumumab
Baxter Healthcare	human protein C
Biogen Idec	natalizumab
Boehringer Ingelheim	tipranavir
Cedarglen Investments	galsulfase
CSL	sitaxentan
Delpharm	nitric oxide
Eli Lilly	duloxetine
Genzyme	idursulfase, laronidase
GlaxoSmithKline	human papillomavirus vaccine, lapatinib
Merck Sharp & Dohme	zoster virus vaccine
Novartis	nilotinib, ranibizumab, telbivudine
Pharmatel Fresenius Kabi	pentastarch
Sanofi-Aventis	insulin glulisine
Schering-Plough	olmesartan
UCB Pharma	rotigotine
T manufacturer declined to supply data	
AstraZeneca	fulvestrant
Celgene	lenalidomide
Eli Lilly	exenatide
Janssen-Cilag	darunavir
X manufacturer did not respond to request for data	
Genzyme	alglucosidase
Merck Sharp & Dohme	raltegravir, sitagliptin