



Off-label drug use

The off-label use of pharmaceutical products is widely practised by medical practitioners. The term 'off-label' means that the medicine is used in another way or for an indication other than those specified in the conditions of registration of the medicine and as reflected on its labelling. Two papers^{1,2} and an accompanying editorial³ in this journal address clinical, legal and ethical implications arising from the use of such products.

In one example dinoprostone is registered for use in South Africa for the induction of labour, yet is commonly used in South Africa for the emergency maintenance of ductal patency in newborn babies.¹ The temporary lack of dinoprostone due to logistical problems at the pharmaceutical company led to difficulties in managing a small infant with pulmonary atresia. The authors plead for information to be provided concerning the shortage of any drug, including those for off-label use, in order to plan effectively.

The other paper² considers the implications of the intra-ocular (off-label) use of bevacizumab (Avastin), which is registered for treating metastatic colorectal and breast cancer. Avastin blocks vascular endothelial growth factor (VEGF), thus preventing further growth of blood vessels. It is effective in the treatment of age-related 'wet' macular degeneration. Its off-label use has been controversial mainly because two other anti-VEGF drugs are on the market, but at very much higher prices that would put them out of reach of poorer patients. The South African Vitreoretinal Society has developed protocols endorsed by the Ophthalmological Society for administering Avastin and other intra-ocular medication intravitreally.

In the guidelines on thromboembolism published in this journal⁴ it is noted that there are no drugs registered for prophylaxis in pregnancy and that their recommendations are also off-label.

The off-label use of any medication carries a higher risk for the patient and the medical practitioner than its registered use. From a legal/ethical point of view the off-label use of medication represents a delicate balance between the statutory regulation of medication to safeguard patients against unsafe and ineffective medications, and the prerogative of a physician to prescribe medication that, in his or her opinion, will benefit the patient.

Venous thromboembolism: Prophylactic and therapeutic guideline

In the absence of anticoagulation, the risk of deep-vein thrombosis (DVT) in medically ill patients is comparable to that observed in moderate-risk surgical patients: 10 - 20%. Pulmonary embolism is the most common preventable cause of death in hospital patients, accounting for 10% of all hospital deaths. Pharmacological prophylactic anticoagulation in many

countries, including South Africa, is under-prescribed resulting in unacceptable morbidity and mortality in substantial numbers of patients. A concise, practical guideline for thromboprophylaxis and treatment in medical and surgical patients, endorsed by several major specialist societies, has therefore been produced for South African conditions.⁴

Prophylaxis is not required for patients who are mobile. In patients at high risk of bleeding, the use of mechanical prophylaxis such as graduated compression stockings or intermittent pneumatic compression devices should be considered as an alternative if the thrombosis risk is high.

In surgical patients both patient-related and procedure-related factors should be considered when assessing an individual's risk of developing venous thromboembolism. Details for anticoagulation therapy are provided including the use of low-molecular-weight heparin and warfarin as well as the management of patients with bleeding.

Predicting fetal weight in labour at term

Clinicians frequently estimate fetal weight when examining women in labour at term. This may help in predicting cephalopelvic disproportion when labour progress is poor or give early warning of possible shoulder dystocia. Eckart Buchmann and Karabo Tlale report on their derivation and validation of a simple formula for birth weight based on symphysis-fundal height (SFH) measurement during labour and determining a useful SFH cut-off value for prediction of birth weight.⁵ They conclude that this formula may be useful for intrapartum use in term pregnancies.

Aminoglycoside-induced hearing loss

South Africa's TB epidemic and the threat to TB control posed by the emergence of multidrug-resistant and extensively drug-resistant TB strains put patients at risk of hearing loss because of the necessity of prolonged chemotherapy. Drug-related adverse effects of aminoglycosides include ototoxicity that is permanent. In their editorial on the topic,⁶ Bardien, De Jong and colleagues explore ways of dealing with this potential problem, including the proposal to introduce genetic testing for patients at risk of aminoglycoside-induced hearing loss.

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4. Jacobson BE, Louw S, Mer M, et al. Venous thromboembolism – prophylactic and therapeutic practice guideline. *S Afr Med J* 2009; 99: 467-473.
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6. Bardien S, de Jong G, Schaaf HS, Harris T, Fagan J, Petersen L. Aminoglycoside-induced hearing loss: South Africans at risk. *S Afr Med J* 2009; 99: 440-441.