



# Therapeutics Today

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**Why do patients discontinue medicines?** The use of pharmacotherapy for the management of chronic diseases is a cornerstone of cost-effective preventive care. However, the medication needs to be taken for as long as the illness is active. A recent study (*Clin Ther* 2009; 31: 2628-52) compared the risk of medication discontinuation during the first 30 days of treatment in patients who had received no treatment for the condition in the preceding 180 days (medication-naïve) with those who were already receiving treatments for the condition (medication-experienced). Data from 2.17 million patients (57% female) who had prescriptions

for specific chronic illnesses dispensed from 3,821 US pharmacies during 2007 were analysed. Medicines reviewed included asthma medicines (inhaler and oral forms), cardiovascular medicines, oral anti-diabetic agents and insulin, osteoporosis medicines, oral breast cancer therapies, glaucoma drops and statins. Patients who switched from their initial medicine to another in the same therapeutic class were deemed to have continued with therapy. Results showed that the **absolute rate of discontinuation after the initial prescription was dispensed ranged from 30-72% in the medication-naïve group compared with rates of 8-29% in the medication-experienced group**. Overall, the rate of discontinuation during the first 30 days of treatment was more than 12 times greater for medication-naïve patients and 3.9 times greater in the medication-experienced group relative to the mean monthly rate of discontinuation in subsequent months. A multivariate analysis showed that medication inexperience and younger age (but not patient gender, income, or degree of copayment) were consistently associated with a greater risk of discontinuation. Of particular interest, non-oral medications (inhalers, insulin, drops) showed much higher rates of discontinuation, thought to be due to difficulties with administration and insufficient training for patients prescribed such medicines. However, even breast cancer medications were discontinued (42% vs. 11% respectively). Limitations to the study include a lack of full patient records, which might have provided an explanation for discontinuation for some medicines and lack of information about other possible sources of prescriptions such as mail-order pharmacy dispensing. However, because of the large numbers involved in the study and the relatively consistent results, the authors feel that the current study findings are valid. They conclude that **the results underscore the need for health care professionals to better engage with, and more closely follow, medication-naïve patients during the first 30 days of therapy, regardless of the therapeutic class prescribed in order to improve adherence to, and optimise the benefits from, such therapies.**



**Safety Update: Sibutramine.** The European Medicines Agency recently issued a press release ([www.ema.europa.eu](http://www.ema.europa.eu)) regarding sibutramine (Reductil®). Sibutramine is licensed for use in obese patients and overweight patients who also have other risk factors such as type-2 diabetes or dyslipidaemia. The Agency is currently reviewing safety data from the

longterm SCOUT (Sibutramine Cardiovascular OUTcomes) trial. This was a multicentre double-blind, placebo-controlled trial, designed to evaluate the potential benefits of weight management on cardiovascular (CV) outcomes in overweight and obese patients (n=10,000) at high risk of CV events during a follow-up of around 6 years. Results have suggested an increased risk of serious CV events such as stroke or heart attack with sibutramine treatment. However, since patients not normally considered suitable for sibutramine were also included in the trial, the Agency is currently assessing the implications of the study findings for use of sibutramine in normal clinical practice. In the meantime, it recommends the following:

- Sibutramine-containing medicines should be used with caution and only in accordance with the Summary of Product Characteristics (SmPC available at: [www.medicines.ie](http://www.medicines.ie); [www.imb.ie](http://www.imb.ie))
- Patients should be regularly monitored for increases in blood pressure and heart rate
- Treatment should be discontinued if patients do not lose at least 5% of their body weight within 3 months and treatment duration should not exceed one year

The NMIC will provide further updates when the review has been completed by the Agency.



***Ginkgo biloba does not prevent cognitive decline.*** The herbal product *Ginkgo biloba* (*G biloba*) is frequently taken with the hope of improving, preventing or delaying cognitive impairment associated with aging and neurodegenerative disorders such as Alzheimer's disease (AD). A recent study evaluated whether *G biloba* slowed the rate of global or domain-specific cognitive decline in older adults (*JAMA 2009; 302:2663-70*). This was part of the GEM (**Ginkgo Evaluation of Memory**) study which had previously reported that *G biloba* 120mg twice daily was not effective in reducing the incidence of AD or dementia overall. This part of the study looked at the effect of *G biloba* on the rate of cognitive decline. Patients (n=3,072) mean age 79 years, 54% male, with normal cognition or mild cognitive impairment (MCI) were randomised to receive either 120mg *G biloba* or placebo twice daily. Cognition decline over time was evaluated using validated scales (Modified Mini-Mental State Examination (3MSE); the cognitive subscale of the AD assessment scale (ADAS-Cog)) and via individual tests in the following neuropsychological domains: memory, attention, visual-spatial construction, language and executive functions. Median follow-up was 6.1 years. Results showed no difference in the rates of decline as assessed by the study tests between *G biloba* and placebo groups. Of interest, there was no significant modification of treatment effect on rate of decline by age, sex, race, education or baseline MCI (although there was an under-representation of divergent ethnic backgrounds and relatively few subjects with lower education levels). **The authors note that these results (similar to findings from smaller studies) suggest that *G biloba* affects neither subtle preclinical cognitive changes associated with prodromal dementia nor cognitive changes associated with normal aging.**



***Do antioxidants prevent cancer?*** A recent paper reviewed the current evidence surrounding the use of diet and dietary supplements to prevent cancer (*Aust Pharm 2009; 28: 686-91*). It has been estimated that the majority of cancers are environmentally induced. Experimental studies indicate that free radicals may have a role in the initiation and promotion of cancer. The body has a complex endogenous antioxidant system to counteract the production of these free radicals but factors such as hypertension, hyperlipidaemia, smoking, excess exposure to alcohol, sun or air pollutants can increase oxidative stress. There are a variety of substances, possessing antioxidant properties, that may reduce oxidation, including: Vitamins C, E, beta-carotene (betaC), elements such as selenium and copper and phytochemicals such as isoflavones and flavanols. High levels of antioxidants in fruit and vegetables are believed to contribute to cancer prevention, via a reduction in oxidative stress. Although found in the normal diet many people take high-dose antioxidants as food supplements, which are estimated to constitute >50% of complementary and alternative medicine spending in some developed countries. Several observational studies have shown significant benefit associated with higher intake of fruit and vegetables, in terms of preventing certain cancers such as lung or gastrointestinal (GI) cancers. However studies evaluating the benefit of antioxidant supplementation, have shown contradictory results. A Cochrane review (*2008; Art. No. : CD004183*) involving 20 randomised controlled trials (RCTs) and >174,000 patients, did not show any overall benefit with antioxidant supplements on the risk of GI cancers or the risk of mortality. Moreover, the combination of betaC with vitamin A / E was found to significantly increase mortality risk. The lack of benefit (and apparent increased mortality risk) with betaC and vitamins A / E has been reported in other studies and high-dose vitamin E (doses >150 IU /day, which are 10-fold higher than the recommended daily allowance) has been associated with increased all-cause mortality. Only selenium has shown potential benefit with respect to GI cancers. The author concludes that while a diet high in fruit and vegetables may be beneficial, the available data do not support the use of high-dose antioxidant supplements to prevent cancer or reduce mortality; in fact these supplements may instead result in harm.