



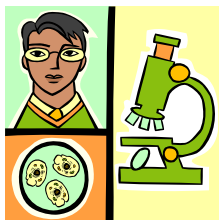
# Therapeutics Today

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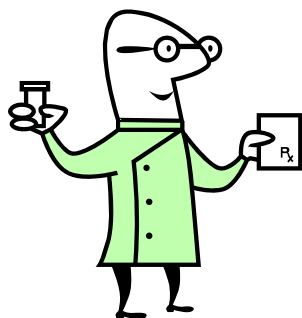
**Withdrawal of Reductil® from the market.** The Committee for Human Medicinal Products (CHMP) of the European Medicines Agency has recommended the suspension of the marketing authorisation (MA) of the anti-obesity agent sibutramine (Reductil®) due to safety concerns. The IMB has confirmed that, in line with the CHMP's recommendation, all stocks of sibutramine are being removed from the marketplace in Ireland with immediate effect. As noted in our January newsletter, the Agency had undertaken a review of the results of the **Sibutramine Cardiovascular Outcome Trial (SCOUT)** which showed an increased risk of serious, non-fatal cardiovascular (CV) events, such as stroke or heart attack, with sibutramine compared with placebo. While this study had been undertaken in patients with existing CV disease, the CHMP concluded that these risks are also considered to be applicable to patients without a diagnosis of CV disease since obesity is a risk factor for CV disease. Moreover, a review of all clinical study data has shown that weight loss achieved with sibutramine is modest in comparison with that obtained with placebo. The CHMP has concluded that the risks of sibutramine use are greater than the benefits and has recommended the suspension of the MA for these medicines across the EU. Further background information on the withdrawal, including a useful Q & A document, is available at [www.ema.europa.eu](http://www.ema.europa.eu); [www.imb.ie](http://www.imb.ie))



**FIT for life!** Colorectal cancer is the second most commonly diagnosed cancer among men and women in Ireland. About 2,200 new cases are diagnosed every year and approximately 1,000 people die from it. The Minister for Health recently announced the introduction of colorectal cancer (CRC) screening in Ireland in early 2012, as part of the government's cancer control programme. The Irish CRC screening programme will involve the use of an immunochemical faecal occult blood test (FIT) with follow-up colonoscopy for all those who test positive with FIT. A recently published study compared participation and detection rates per screened individual for FIT with the well-known guaiac based faecal occult blood test (gFOBT) and flexible sigmoidoscopy (FS) for CRC screening in a region of the Netherlands (n= 5,000/arm) (*GUT 2010; 59: 62-8*). The gFOBT group had to collect a sample from 3 consecutive bowel movements, while the FIT group collected a single faecal sample. The FS group were assigned an appointment for the procedure and provided with the preparatory enema. Results showed highest participation rates for FIT (61.5%) compared with 49.5% for gFOBT and 32% for FS. Detection rates were higher with FS: a diagnostic yield of advanced neoplasia of 2.4/100 invitees compared with 1.5/100 for FIT and 0.6/100 for gFOBT. The authors conclude that FIT screening has demonstrated superior participation and detection rates compared with gFOBT screening. While FS screening demonstrated a higher detection rate, the level of participation was significantly less than with either of the two faecal sampling tests. [Editor's comment: This study confirms the value of FIT as a primary screening tool in CRC screening. Read the full evaluation report on CRC screening in Ireland at: [www.higa.ie](http://www.higa.ie)]



**What's in a name?** The NMIC frequently gets asked by healthcare professionals to identify foreign medications for visitors or people intending to live in Ireland. When dealing with such enquiries it is important to consider several factors, especially the country in which the medication was prescribed. The US Food and Drug Administration (FDA) has highlighted the potential for medication error (<http://www.fda.gov/Drugs/DrugSafety/PublicHealthAdvisories/ucm173134.htm>) as **foreign drugs may use identical or potentially confusing brand names for products with different active ingredients**. For example Acepril® contains lisinopril in Denmark, enalapril in Switzerland and captopril in the UK. Foreign brand names that look or sound alike can also cause difficulties e.g. Inderal® contains propranolol in Ireland but Indiaral® contains loperamide in France. The NMIC is happy to deal with such enquiries from healthcare professionals - in order to ensure that the correct information is provided, it is helpful for us to know the country of origin of the medicine to be identified, and the indication (if known by the patient).



**Rout the Gout!** Gout (caused by deposition of monosodium urate crystals (MSC) in joints), is the commonest inflammatory arthritis in developed countries, affecting up to 2% of adults (*Lancet 2010;375:318-328*). It is more common in men, and is associated with increasing age and high consumption of meat, seafood, fructose, beer and spirits. Genetic and environmental factors are causal factors in primary gout. Secondary gout occurs in conditions including renal failure, use of certain drugs such as diuretics, low-dose aspirin and drugs used in organ transplantation. Gout and hyperuricaemia are associated with conditions including: hypertension, diabetes, metabolic syndrome, renal and cardiovascular disease.

**Gout has 3 stages:** asymptomatic hyperuricaemia, episodes of acute gout with asymptomatic intervals and chronic gouty arthritis. The risk of acute gout increases with urate concentration, however **some people with high serum urate never develop gout**. Acute gout has an abrupt onset: the affected joint (initially occurring in the lower limb - usually the first metatarsophalangeal joint) presents as erythematous, warm, swollen and tender. Second attacks occur in many patients, often within 6 months to 2 years. Untreated acute attacks of gout lead to chronic gout characterised by chronic destructive polyarticular involvement. Tophaceous gout (frequently seen on the helix of the ear) develops within 5 years of gout in 30% of untreated patients.

**Clinical diagnosis** based on presentation is reasonably accurate; however analysis of synovial fluid or tophus aspirate for MSC allows a definitive diagnosis, and is included in European recommendations. **Serum uric acid concentrations do not confirm or exclude gout as many people with hyperuricaemia do not develop gout and up to a third of patients may have normal concentrations during acute attacks.** Gout and septic arthritis can coexist in the same joint and synovial fluid should also be analysed for bacteria.

**Treatment** of acute gout includes rest, ice application, NSAIDs +/- colchicine (not authorised in Ireland). Evidence suggests low-dose colchicine may be as effective as high-dose; toxic effects are increased in the elderly, renal or hepatic failure and with concomitant drugs such as macrolides, ciclosporin, verapamil or lipid lowering drugs. Studies suggest that oral prednisolone is as effective as NSAIDs and intra-articular steroids are also effective in acute attacks. **Urate lowering therapy** is indicated for patients with recurrent attacks, chronic arthropathy, tophi and gout with uric acid stones. It should be started 2 weeks after resolution of an acute attack; prevention of acute flares during the first 3-6 months' therapy (with NSAIDs or low-dose colchicine) is advised. Flares should be treated without interruption of urate-lowering therapy. Therapy should be continued indefinitely as gout usually recurs a few years after treatment stops. Allopurinol lowers uricaemia through inhibition of xanthine oxidase activity and is used as first line therapy. The dose needs to be gradually increased and lower doses are required in renal impairment. Side effects are rare, however, severe cutaneous toxic effects do occur in 2% of patients, which can be life threatening (20% mortality). Patients with a history of severe skin rash induced by allopurinol should never be given the drug again. Febuxostat (Adenuric®) is a novel xanthine oxidase inhibitor authorised in the EU for the management of gout. Side effects include raised liver enzymes and a small increase in serious cardiovascular events; it is not recommended in patients with heart disease. Other uricosuric agents (probenecid, sulfapyrazone and benzbromarone - none of which is authorised in Ireland) have been used as second-line therapy. **Patient education, appropriate lifestyle advice, and treatment of comorbidities are an important part of management of patients with gout.**

*Every effort has been made to ensure that this information is correct and is prepared from the best available resources at our disposal at the time of issue. References are available on request. This newsletter is produced by the National Medicines Information Centre, St. James's Hospital (SJH) Dublin 8 and Dept of Therapeutics Trinity College, Trinity Centre, SJH. Tel: Direct Line (01) 473 0589 or 1850 727 727 Fax: (01) 473 0596 Email: nmic@stjames.ie*