TAYSIDE PRIMARY CARE NHS TRUST

# TAYSIDE PRESCRIBER

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Issue 2

# NEW DRUG SUPPLEMENT. No. 2

**Issue 2** **June 2001**

*Produced by Tayside Medicines Information Service and the Prescribing Team, Tayside PCT*

*This supplement to the Tayside Prescriber is produced in response to demand for early information on new drugs from a neutral source. The following is a summary of the evidence from published sources. It does not comment on the role, if any, that such drugs might have, nor does it endorse their use in practice. A system exists in Tayside whereby advice on new drugs for local prescribers will follow from the Area Drug & Therapeutics Committee after assessment by the Drug Evaluation Panel. Anyone wishing to introduce a new drug in hospital practice must first complete a Submission Form before any such assessment can take place. Copies of the Submission Form are available on request from the Secretary, Area Drug & Therapeutics Committee, Medicines Information Service, Department of Pharmacy, Ninewells Hospital. The situation regarding primary care is currently under consideration.*

## SIBUTRAMINE (Reductil®)

- Sibutramine has recently obtained a licence for obese patients (BMI >30kg/m$^2$) or BMI >27kg/m$^2$ in the presence of other obesity-related risk factors (e.g. type 2 diabetes, dyslipidaemia) in combination with a reduced-calorie diet, exercise and behaviour modification. The licence states that sibutramine should only be used if patients have not responded adequately to a weight-reducing regime alone (i.e. those with difficulty achieving or maintaining >5% weight loss within 3 months). Treatment must be discontinued if weight loss is, or stabilises at <5% of initial body weight, or if >3kg are regained after previously achieved weight loss. Maximum treatment duration is one year.

### Background

- The treatment of obesity with drugs that promote satiety and reduce food intake through an action on central noradrenergic and serotoninergic mechanisms is not new. Hence the past use of amphetamine and its derivatives and the fenfluramines as appetite suppressants. Sibutramine is a new anti-obesity agent, which at first glance seems little different from the antidepressant venlafaxine (Efexor®). Both drugs act by blocking re-uptake of serotonin and noradrenaline in the brain. Hence sibutramine and venlafaxine are selective serotonin-noradrenaline re-uptake inhibitors or SSNRIs. It follows that sibutramine is antidepressant while it is already apparent that the SSRI/SSNRI antidepressants are more likely to cause weight loss than weight gain. This also explains why these drugs share the same side-effect profile and why their use in combination must be avoided. *See Safety issues, below*.

### Evidence from clinical trials

- Most published studies are short-term only. There are no outcome data beyond 18 months.
- Treatment with sibutramine 10-15 mg daily for 6 months resulted in >5% weight loss in 50-90% of obese subjects without co-morbidities and >10% weight loss in 15-50%[1,2,3,4]. Rate of weight loss was generally highest in the first 3 months.
- The effect of sibutramine on weight maintenance following initial weight loss of >5% body weight (achieved by a 6 month course of sibutramine + calorie restriction) has been studied in obese subjects with baseline BMI 30-45kg/m$^2$. Almost half of those who continued to take sibutramine for a further 18 months maintained 80% or more of their original weight loss compared with only 16% who took placebo. However 50% required an increase in

sibutramine dosage from 10mg to 20mg daily in order to achieve this outcome[5]. (*Note: doses greater than 15mg and treatment duration of greater than 1 year are outwith licence*)

- The importance of prescribing anti-obesity drugs only in conjunction with effective dietary and lifestyle modification is highlighted by the results of a trial of sibutramine alone versus sibutramine plus lifestyle advice and calorie restriction. At the end of 1 year the mean weight loss as a percentage of initial body weight was only 4.1% +/- 6.3% for drug alone versus 10.8% +/- 10.3% for drug plus lifestyle modification and 16.5% +/- 8.0% for drug plus controlled dietary and lifestyle intervention[6].
- Treatment with sibutramine + calorie restriction over 3 months in type 2 diabetics resulted in a mean weight loss of 2.4 kg, an associated reduction in fasting blood glucose (mean -0.3 mmol/l) and blood glucose after a test meal (mean -1.1 mmol/l), and a reduction in $HbA_{1c}$ of at least 1% in one-third of patients[7].

## Safety issues

- Safety issues with sibutramine are similar to those with the SSRI and SSNRI antidepressants. Thus common side effects include nausea, headache, dry mouth, insomnia, constipation, sweating and anxiety.
- Sibutramine should not be co-prescribed with MAOIs or antidepressants that block serotonin re-uptake since the risk of developing a serotonin syndrome is increased.
- Other contraindications include a history of coronary artery disease, congestive heart failure, arrhythmia, peripheral artery occlusive disease or cerebrovascular disease, inadequately controlled hypertension, bipolar disorder, hyperthyroidism, severe renal or hepatic impairment, symptomatic BPH, narrow angle glaucoma, phaeochromocytoma and a history of drug or alcohol abuse.
- Sibutramine has been shown to increase blood pressure and heart rate, it is not clear whether this offsets any subsequent benefits. Blood pressure and heart rate must be monitored regularly.
- Sibutramine should be avoided in pregnancy and is not licensed for patients under 18 years of age and the over 65s, owing to insufficient data.

## In summary

*Treatment with sibutramine from 3 months to 1 year as part of a programme that includes dietary and lifestyle modification has been shown to produce short-term reduction in body weight of >5-10%. These results are similar to those obtained with the fat blocker, orlistat (XenicalÒ) which also produces >10% weight loss and blunts weight regain over the same timescale. However the results from long-term outcome studies are awaited with interest, to establish if weight loss with sibutramine translates into a reduction in obesity related morbidity and/or mortality. Sibutramine is similar to the SSRI and related antidepressants, particularly venlafaxine and this has an important bearing on its suitability for some patients. A number of other contraindications to its use exist.*

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| Comparative costs of 28 days' treatment: | Sibutramine | 10-15mg daily | £35-£39 |
| | Orlistat | 240-360mg daily | £27-£41 |

### References


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