NHS Tayside

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REVISED GUIDELINES FOR USE OF ANTI-OBESITY AGENTS: ORLISTAT (XENICAL®) and SIBUTRAMINE (REDUCTIL®)

Produced by Tayside Medicines Information Centre

*Orlistat (Xenical®) and sibutramine (Reductil®) are agents used for the management of obesity. Orlistat acts locally by blocking fat absorption from the gastro-intestinal tract. Sibutramine enhances satiety through its action on central neurotransmitters. Individually, these drugs may be tried in the management of obesity (combination therapy **not** recommended) but their use should be governed by strict criteria. The following guidelines are provided, and are based on the Tayside Drug & Therapeutics Committee recommendations for each drug.*

WHICH PATIENTS?

Anti-obesity drugs MAY be considered for the following patients…

Obese patients with a BMI ≥ 30, or BMI ≥ 27/28 (sibutramine/orlistat respectively) with one or more weight-associated risk factors.

Such risk factors include:

- Cardiovascular disease ie angina, heart failure **(NOT sibutramine)**
- Uncontrolled hypertension (**NOT sibutramine**)
- Diabetes mellitus
- Pituitary problems
- Sleep apnoea
- Hyperlipidaemia despite lipid-lowering therapy
- Severe respiratory problems including COPD or asthma
- Surgery: when weight loss is necessary in order for surgery to proceed. For example:
  - Hip replacement and other joint/orthopaedic operations
  - Coronary artery bypass operations
  - Aneurysm repair - abdominal and peripheral
  - Significant abdominal herniation

… but ONLY after diet and lifestyle change has failed …

Anti-obesity drugs are **only** indicated for patients who cannot achieve or maintain an appropriate weight loss (suggested target 5-10% or more of body weight) over a course of dietetic surveillance (they should otherwise continue to receive diet and lifestyle advice and support). Drugs should **never** be used as the sole element of treatment. Thus patients should first be entered into a minimum 3 month structured weight management programme on the advice of a health care professional (may include a hospital or community dietician or practice nurse) trained in obesity management including the provision of diet and lifestyle advice and support. If some weight loss occurs but the target is not achieved, the opportunity should be given for a further 3 months attempt with diet alone. Orlistat's license no longer requires a 2.5kg weight loss prior to prescription but adherence to a reduced fat diet before starting orlistat may assist in the reduction of unwanted GI side-effects.

WHO SHOULD NOT BE TREATED?

- Orlistat (Xenical®) is **contraindicated** in breast-feeding, cholestasis and chronic malabsorption and is not recommended in pregnancy. There is **no data** to support its use in the elderly and it is **not intended** to be used in children. NICE guidance states that it should be used in those aged 18-75 only.

- Sibutramine (Reductil®) is **contraindicated** in those with psychiatric illness, major eating disorder, history of drug or alcohol abuse, or on current antidepressant or neuroleptic drug therapy. Avoid also in uncontrolled hypertension (>145/90 mm Hg), hyperthyroidism, severe hepatic or renal impairment, symptomatic BPH, phaeochromocytoma, narrow angle glaucoma, or if a history of coronary artery disease, congestive heart failure, arrhythmia, tachycardia, peripheral arterial occlusive disease or TIA or stroke. It is also **contraindicated** in pregnancy and breast-feeding and is **unlicensed** for those aged < 18 years or > 65 years. Women of childbearing potential should use an adequate method of contraception while taking sibutramine.

WHICH DRUG?

Each agent is unique in its site of action, either local in the GI tract (orlistat) or systemic in the CNS (sibutramine). Site of action may therefore have a bearing on the choice of drug since it influences their side effect profiles, potential interactions and precautions and contraindications. In any event, these agents should only be used within the terms of their individual product licenses. Combination therapy is **not recommended.**

DISCONTINUING TREATMENT

- Sibutramine is only licensed for continuous use up to 1 year. NICE recommends that orlistat treatment should not usually continue beyond 12 months, and never beyond 24 months. Evidence of efficacy and safety is limited beyond these periods.

- Treatment **must be discontinued** after 3 months in patients who have failed to lose 5% of their starting body weight. They are otherwise at risk of drug side effects in the absence of any therapeutic benefit.

- The value of continuing therapy is also in doubt if there is significant weight regain (eg 3-5 kg) on treatment after an initial weight loss.

ADVERSE EFFECTS and MONITORING

Orlistat (Xenical®)

Common side effects (ie occurring in 10-25%) are limited by dietary compliance (ie decreased fat intake) and it is therefore essential that these are discussed with the patient beforehand. They include flatus, oily discharge, faecal urgency and incontinence, oily stools and increased defecation.

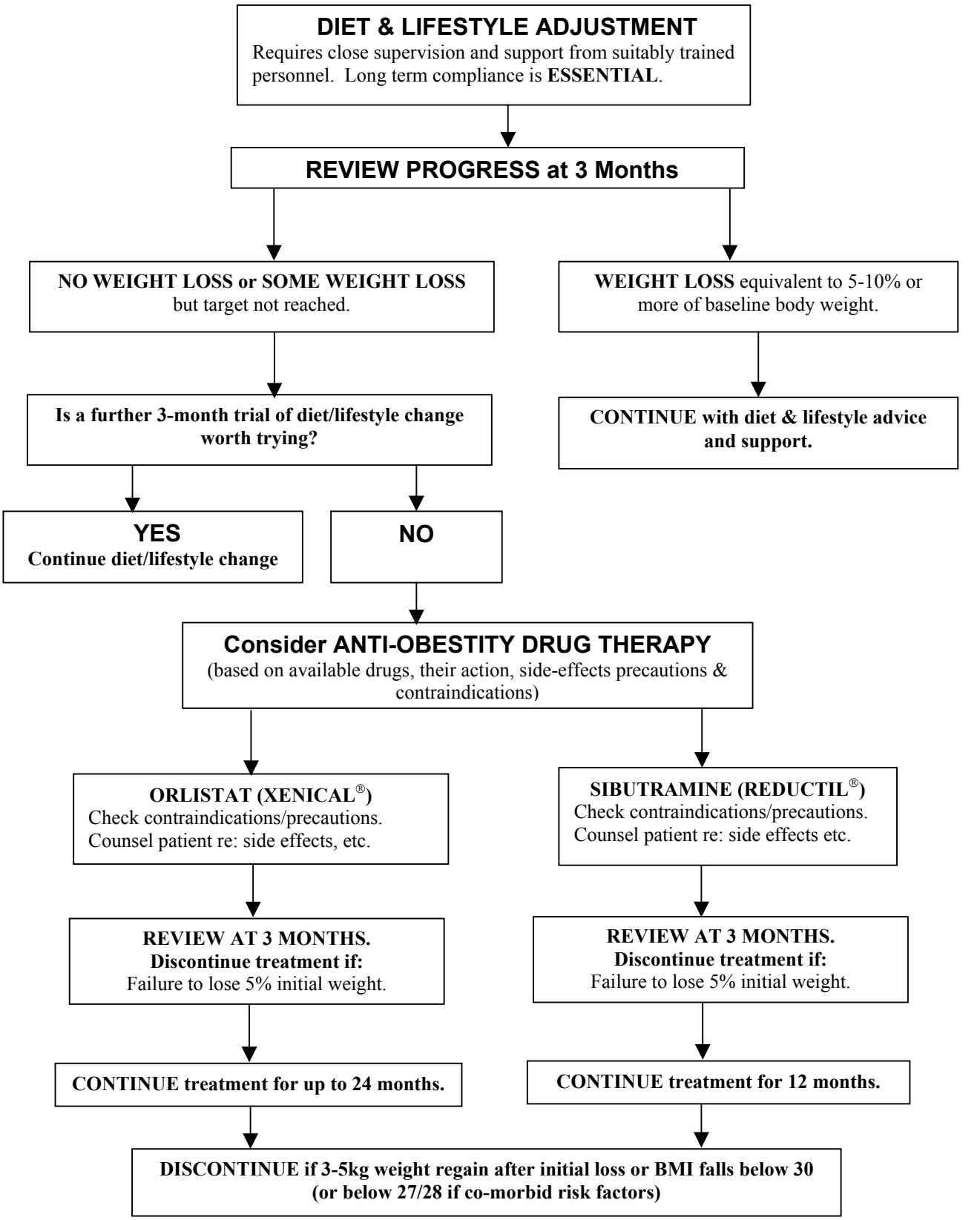
Sibutramine (Reductil®)

These are relatively common and similar to the side-effects seen on SSRI antidepressant therapy They include anxiety, light-headedness, paraesthesia, sleep disturbance, increased sweating, dry mouth, anorexia, altered taste, nausea, constipation (aggravated haemorrhoids), tachycardia, palpitations, generalised vasodilatation/flushing, and raised BP. Monitor blood pressure and pulse rate every two weeks for the first three months, then monthly for the next three months, then at least every 3 months thereafter. Discontinue treatment in patients who have an increase, at 2 consecutive visits, in resting heart rate of ≥10bpm or systolic/diastolic BP of ≥10mmHg. In previously well-controlled hypertensive patients, if blood pressure exceeds 145/90 mmHg at two consecutive readings, treatment should be discontinued

DRUG INTERACTIONS

Drug	Interacts with:	Comments
orlistat	fat soluble vitamins	↓absorption. Advise vitamin A, D & E rich diet or give supplements
	acarbose	Not established but avoid. Close monitoring of oral antidiabetic therapy advised
	warfarin	Monitor INR (Long term use is associated with the possibility of ↓vitamin K absorption.)
	ciclosporin	Possible ↓absorption of ciclosporin
sibutramine	ketoconazole, itraconazole, erythromycin, clarithromycin, ciclosporin	↓sibutramine clearance, possible ↑toxicity (palpitations, etc)
	SSRI antidepressants, MAOIs, sumatriptan & related antimigraine drugs, dihydroergotamine, pethidine, pentazocine, fentanyl	Serotonin syndrome possible (diarrhoea, abdominal pain, ↑BP, tremors, hyper-reflexia, convulsions, etc) and/or increased risk of CNS toxicity
	Antipsychotics	increased risk of CNS toxicity
	Sympathomimetics (eg pseudoephedrine, some cough/cold remedies)	Possible ↑BP. Avoid

GUIDELINES FOR THE USE OF SIBUTRAMINE AND ORLISTAT IN TAYSIDE
Summary and Recommendations



GOOD PRACTICE POINTS

Patients require monitoring and encouragement, consider prescribing no more than one month's treatment.

Sibutramine; blood pressure and pulse rate MUST be monitored every two weeks for first three months, then monthly for three months, then at least every 3 months thereafter.