



National Obesity Forum
Pharmacotherapy Guidelines
For Obesity Management in Adults

www.nationalobesityforum.org.uk

Choice of anti-obesity agent

There are two agents currently available for pharmacotherapy as part of a weight management programme for obese and overweight patients; Orlistat and Sibutramine. There is no evidence that bulking agents such as Methylcellulose or Ispaghula husk have any role to play in long term weight management. Metformin can be an effective drug for weight management in diabetic patients, and its effect on insulin resistance has been utilised in obese non-diabetic subjects to aid weight loss, but it should not be prescribed for this purpose in primary care. Unlicensed drugs including Phentermine and Diethylpropion have no place in pharmacotherapy of obesity and have profound safety implications. However they are still prescribed by some sources, and may be encountered in Primary Care.

Orlistat & Sibutramine exhibit different pharmacological profiles, contra-indications & side-effects. NICE Guidance and the SPC Product Licenses for both products have differences with regard to eligibility of drug treatment, requirements prior to starting therapy and continuation of therapy. They cannot be used together.

Comparison of Orlistat & Sibutramine eligibility (SPC & NICE)

| Eligibility for Treatment Initiation | Orlistat (Xenical) | Sibutramine (Reductil) |
|--------------------------------------|--------------------|------------------------|
| BMI over 30 | ✓ | ✓ |
| BMI over 27 + co-morbidity | - | ✓ |
| BMI over 28 + co-morbidity | ✓ | ✓ |

Co-morbidities include diabetes, hyperlipidaemia & hypertension

CHD and stroke may also be included under the heading of 'co-morbidity' for Orlistat

Sibutramine is contra-indicated if blood pressure is not controlled at $\leq 145/90$

Pre-Therapy Requirements prior to receiving 1st Prescription

Orlistat (Xenical): patient is required to display weight loss of at least 2.5kg through lifestyle.

Sibutramine (Reductil): patient has been unable to display weight loss of at least 5% through lifestyle change within the last 3 months.

| Continuation of therapy | Orlistat (Xenical) | Sibutramine (Reductil) |
|-------------------------|--------------------|------------------------|
| 2 week criteria | | BP check fortnightly |
| 1 month criteria | | 2kg weight loss |
| 3 month criteria | 5% weight loss | 5% weight loss |
| 6 month criteria | 10% weight loss | 10% weight loss |

Evidence shows that maintaining 5% weight loss is clinically beneficial.

| | | |
|--|--|---|
| Current Cost (1 year treatment) | £ 537 (1 capsule 3 times daily) | £ 456 - £ 510 (10-15mg once daily) |
|--|--|---|

Drugs for Obesity Management

Populations where drugs are contra-indicated

| | |
|---|------------------------|
| Pre-conception, pregnancy or breast-feeding | children (under 18 yr) |
| Elderly (over 65 yr) | BMI <27 |
| Significant drug interactions | |

Drugs that may cause Weight Gain

- * antipsychotics esp: olanzepine (Zyprexa)
- * antidepressants : tricyclics, SSRIs, MAOIs & mirtazepine (Zispin) and Lithium
- * corticosteroids : all corticosteroids may promote weight gain by 2 mechanisms : fat redistribution causing truncal obesity, buffalo hump & moon face, and fluid retention via mineralocorticoid effects.
- * OCP : progestogenic compounds
- * β-blockers : not only do these agents cause weight gain, they may restrict physical activity due to fatigue.
- * oral hypoglycaemics : Numerous agents shown to increase weight. Most sulphonylureas (except glimepiride) Glitazones.
- * insulin
- * anticonvulsants : weight gain has been documented with some agents (phenytoin, sodium valproate). Topiramate (topamax) is weight neutral or may cause weight loss.
- * antihistamines : many antihistamines may cause weight gain though these effects are more pronounced with older agents.

Orlistat promotes weight loss by reducing the absorption of energy dense fat. It is a potent inhibitor of pancreatic & gastric lipases, which are enzymes responsible for breaking down fat, allowing approximately 30% of dietary fat to pass through the GI tract unabsorbed.

Dosage, Side-effects & Contra-Indications :

- * One capsule (120mg) before, during or up to 1 hour after main meal, up to 3 times a day
- * Dose can be missed if meal is missed
- * ADR : oily spotting with flatus, faecal urgency & anal leakage (if inappropriate diet is consumed)
- * Patients on orlistat should adhere to a diet that is nutritionally balanced, mildly hypocaloric & contains less than 30% of calories from fat.

Special Warnings & Contra-Indications :

- * Rarely malabsorption of fat soluble vitamins (A,D,E & K) may occur, although this is not an issue for the majority of patients in primary care
- * Physicians may choose to supplement those who are on therapy for longer than 1 year
- * Orlistat is contra-indicated in patients with cholestasis or malabsorptive syndromes
- * There is no evidence to associate Orlistat with increase in breast cancer

Drug Interactions

- * Treatment with Orlistat may reduce the absorption of ciclosporin – monitor blood levels
- * Treatment with Orlistat may reduce vitamin K absorption – always monitor INR on warfarin patients

Patient Considerations for Discussion :

- * GI side-effects may reduce compliance if patient is not forewarned.
- * Some patients learn which food types give them side-effects and modify their diets to reduce this
- * Some patients may chose to omit doses when dining out or eating fatty food; discuss with patient
- * Patients who supplement multi-vitamins should leave a 2 hour gap either side of Orlistat dosing.

Patients on Orlistat may be encouraged to contact the Medical Action Plan

Helpline supported by Roche : 0800-731-7138.

Reductil (Sibutramine)

Sibutramine is not an appetite suppressant. It inhibits the reuptake of both serotonin & noradrenaline in the brain. Weight loss is mediated via 2 mechanisms. Firstly, Sibutramine's central action on neurotransmitters results in early satiety (feeling of fullness) with reported 20% reduction in food intake. Secondly, sympathetically mediated thermogenesis maintains original Basal Metabolic Rate (BMR) which usually falls as weight is lost. This results in energy expenditure and contributes to further weight loss.

Dosage, Side-effects & Contra-Indications :

- * One 10mg capsule once daily This may be increased to a maximum of 15mg once daily
- * Increase from 10mg to 15mg daily should be considered at 1 month if less than 2kg has been lost
- * ADR : headache, dizziness, sweating, palpitations, constipation & dry mouth

Contra-Indications : Sibutramine should not be used in the following situations * History of CHD, Cardiac Arrhythmias or Uncontrolled Hypertension

- * History of Stroke or Heart Failure
- * History of Eating Disorders or Psychiatric Illness
- * Patients on Antipsychotics or Antidepressants

The European Committee for Proprietary Medicinal Products (CPMP) has investigated Sibutramine and concluded that it exhibits a positive favourable risk profile for the management of obesity (May 2002) *

Sibutramine can be used safely in hypertensives who are well controlled (BP not over 145/90)

* Patients require pulse & BP monitoring (*every 2 weeks for 3m, then every 4 weeks for 3m, then every 3 months thereafter*)

- * STOP THERAPY : If blood pressure rises by 10mmHg, 2 readings
- * STOP THERAPY : If pulse rises by 10 beats per minute
- * INVESTIGATE reports of breathing problems, palpitations or chest pain

Patient Considerations for Discussion : * Sibutramine should only be used in conjunction with appropriate lifestyle changes to diet and physical activity.

- * The satiety effect of this agent should be emphasised– expect to eat less at meals; encourage the use of smaller plates and portion sizes, and reduce snacking.
- * Most patients on Sibutramine actually show reductions in BP. Reassure the patient of this.
- * Non-responders to Sibutramine are more likely to show increases in blood pressure
- * The SPC confirms the incidence of patients experiencing blood pressure increase is less than 10%
- * Patients should be cautioned on use of OTC decongestants (sympathomimetics) as they may increase BP

Patients on Sibutramine may be encouraged to contact the Change for Life programme supported by Abbott: 0800-389-4669.