



Te Kaporeihana Āwhina Hunga Whara

# Considered Judgement Form

*This form is a checklist of issues that may be considered by the Purchasing Guidance Advisory Group when making purchasing recommendations.*

*Meeting date: 20 October 2005*

*Topic: Evidence based review of weight loss medicines*

## *Background and Purpose:*

For people recovering from accident or injury, obesity may significantly impede participation in treatment and rehabilitation. The Evidence Based Healthcare (EBH) group has therefore been asked to update ACC's 2001 purchasing guidance on the obesity management drug Orlistat (Xenical®) and expand it to cover other weight loss products. The 2001 guidance was based on an in-house review of the evidence then available carried out by Dr Nick Kendall and colleagues<sup>1</sup>. That review provided "limited support" for purchasing Orlistat for ACC claimants. The 2001 guidance therefore recommends a targeted purchasing strategy in which Orlistat should be considered as suitable for only three types of claimants:

1. Those who **must** lose weight before surgery.
2. Those with significant obesity and/or transportation difficulties that directly prevent their return to independence or work.
3. Serious injury claimants whose specific rehabilitation needs (e.g. attendant care) are compounded by severe obesity.

In order for ACC to fund Orlistat, the 2001 guidance requires these claimants to meet the following criteria:

- Have a body mass index (BMI) greater than 35 kg/m<sup>2</sup> (groups 1, 2 and 3).
- Have specific rehabilitation goals identified that are (i) achievable and measurable, and (ii) initially unattainable due to the claimant's obesity (groups 1, 2 and 3).
- Successfully complete a "motivational test" by losing at least 2.5 kg over a one month period through diet and exercise alone (groups 1 and 2 only).

It was noted that Orlistat should be used as an adjunct to a low calorie diet and that claimants would need to continue the therapy for at least 6 months.

Since 2001, the number of New Zealanders classified as obese or overweight has risen (and continues to rise) and new weight loss drugs have entered the market. In 2004 the EBH group therefore commissioned the New Zealand Health Technology Assessment unit (NZHTA) to produce an updated and expanded evidence based review covering a wider range of weight loss interventions. These interventions include:

- Orlistat (Xenical®) – as noted in the 2001 review, Orlistat is a relatively new obesity management drug used in conjunction with a reduced calorie diet. It is a lipase inhibitor that works by blocking the absorption of fat. Recommended dose = one 120mg capsule three times per day.
- Sibutramine (Reductil®) - another relatively new drug, Sibutramine is a centrally acting monoamine reuptake inhibitor that works by promoting a feeling of fullness after eating and stimulating energy expenditure. Recommended dose = one 10mg capsule per day (may be increased to 15mg if weight loss after 4 weeks < 2kg).
- Phentermine (Duromine™, Umine) - an appetite suppressant chemically related to amphetamine that has been used for weight management since the 1960s. Recommended dose = one 15 or 30mg Duromine™ capsule OR one 30mg Umine sustained release capsule per day. Phentermine is recommended for short term use only (i.e. up to 3 months).
- Diethylpropion (Tenuate Dospan) - a sympathomimetic amine that works by suppressing the appetite and stimulating the central nervous system (CNS). Recommended dose = one 75mg tablet daily.
- Meal replacement plans - interventions in which one or more regular meals are replaced by vitamin-fortified products such as drinks or snack bars, often as an adjunct to a reduced calorie diet.

The following revised and updated purchasing guidance is based on NZHTA's evidence based review. The review was carried out in 2004 and NZHTA's literature search was repeated in August 2005 to ensure that no relevant studies had been missed while the draft report underwent internal and external peer review.

## 1. Effectiveness, Volume of Evidence, Applicability /Generalisability and Consistency

Comment here on the extent to which the service/product/ procedure achieves the desired outcomes. Specific reference needs to be made to safety. Report number needed to treat and harm where possible, any issues concerning the quantity of evidence and its methodological quality and the extent to which the evidence is directly applicable or generalisable to the New Zealand Population, and the degree of consistency demonstrated by the available evidence. Where there are conflicting results, indicate how the group formed a judgement as to the overall direction of the evidence

The evidence indicates that Orlistat, Sibutramine, Phentermine, Diethylpropion and meal replacement plans are all effective at achieving moderate weight loss in obese individuals.

Comparative studies suggest that the newer products Orlistat and Sibutramine are safer, more effective and more acceptable than the earlier amphetamine-related drugs Phentermine and Diethylpropion (both of which are no longer recommended in the UK). Sibutramine appears slightly more effective in reducing weight than Orlistat.

Sibutramine is associated with adverse effects that contraindicate its use in patients with inadequately controlled hypertension or a history of cardiovascular disease. Orlistat is associated with relatively common gastrointestinal side effects which, although not dangerous, may be unacceptable to some patients.

The US Food and Drug Administration (FDA) has approved the use of Orlistat for adolescents. However, its efficacy and safety in patients under 18 have yet to be clearly established. Use of Sibutramine in this age group is cautioned outside clinical trials.

Individuals with a BMI  $\geq 30$  kg/m<sup>2</sup> are generally considered to be obese<sup>1</sup> and should be considered for weight loss therapy (but see section 4 for alternative obesity thresholds in non-Caucasian populations).

## 2. Cost

Comment on any economic costs associated with this service, product or procedure

Sibutramine is reported to be cost-effective under most scenarios, with a lower estimated cost per QALY<sup>ii</sup> gained in patient groups with significant obesity related co-morbidities (e.g. diabetes). The cost per QALY gained with Orlistat is reported to be high and for healthy obese patients Orlistat may not be cost-effective. However, for patients with obesity related co-morbidities such as hypertension and/or hypercholesterolemia, Orlistat may be considered to be good value for money.

It is not clear if Phentermine, Diethylpropion or meal replacement plans are cost-effective treatments for obesity as no economic analyses of these therapies were identified. However, the direct cost of a course of Phentermine or Diethylpropion is much lower than the cost of Orlistat or Sibutramine.

## 3. Clinical impact

Comment on the clinical impact e.g. size of population, magnitude of effect, relative benefit over other management options, resource implications, balance of risk and benefit.

On average, an additional 4 kg may be lost when weight loss drugs or meal replacement products are used as part of an appropriate weight loss programme. A loss of 5 – 10% of initial body weight within six months is considered to be clinically important. The studies included in the NZHTA review reported that a substantial proportion of subjects achieved this goal with the use of weight loss products.

In placebo-controlled trials, the most common side effects reported with Sibutramine use were dry mouth, constipation and insomnia, which were usually mild and transient. Because of its noradrenergic action, Sibutramine treatment is associated with a dose-related increase in blood pressure and heart rate. A dose of 10 to 15 mg/d causes an average increase in systolic and diastolic blood pressure of 2 to 4 mm Hg and an average increase in heart rate of 4 to 6 beats/minute. Some patients experience much larger increases in

<sup>1</sup> With a potential increased risk of co-morbidities. The risk associated with limited participation in rehabilitation is implied, however the evidence is less clear.

blood pressure or heart rate and require dose reduction or discontinuation of therapy.

#### 4. Equity, Maori Health, Pacific Health, Acceptability

Comment on the extent to which the service, product or procedure reduces disparities in health status (equity of access, resources, health outcome), is consistent with the treaty of Waitangi and encourages Maori/ Pacific participation in providing and using service, product and procedures, and is consistent with values and expectations of New Zealanders.

Consideration should be given to the different obesity thresholds that have been recommended in non-Caucasian populations. The World Health Organisation has defined a lower obesity threshold ( $BMI \geq 25 \text{ kg/m}^2$ ) for use in Asian populations and a higher threshold ( $BMI \geq 32 \text{ kg/m}^2$ ) for Polynesians.

#### 5. Possible Purchasing Options

List the possible purchasing options.

ACC currently has a targeted purchasing strategy for Orlistat (Xenical®) based on the 2001 in-house review. It is suggested that this strategy be adapted to incorporate the findings of the updated review by NZHTA.

#### 6. Evidence Statement

Summarise the advisory group's synthesis of evidence relating to this service, product or procedure, taking the above factors into account, and indicate the evidence level that applies.

Evidence statements:

1. Sibutramine and Orlistat are effective at achieving moderate weight loss.
2. Sibutramine may achieve greater weight loss than Orlistat. However the use of Sibutramine is contraindicated in patients with poorly controlled hypertension, coronary heart disease, congestive heart failure, arrhythmias, stroke, severe renal or liver dysfunction or concomitant monoamine oxidase inhibitor therapy. It is relatively contraindicated in people who are at increased cardiovascular risk (i.e. >10% risk of a CVD event over 5 years).
3. Orlistat and Sibutramine are safer, more effective and more acceptable than the earlier amphetamine-related weight loss drugs Phentermine and Diethylpropion.
4. An appropriate obesity threshold is  $BMI \geq 35 \text{ kg/m}^2$

## 7. Purchasing Recommendations

What recommendation(s) does the advisory group draw from this evidence?

Purchasing recommendations:

Purchase under the following conditions:

1. Sibutramine and Orlistat are suitable adjuncts to an appropriate clinical weight loss programme for obese ACC claimants and should be considered for the three categories of ACC claimants originally specified in the 2001 purchasing guidance (see page 1), so long as the following criteria are met:
  - (i) Have a body mass index (BMI) greater than 35 kg/m<sup>2</sup>
  - (ii) Measurable and achievable obesity-related rehabilitation goals should be set for all claimants for whom weight loss products are funded.
  - (iii) Claimants in groups 1 and 2 must first complete the one month “motivational test” as originally specified in the 2001 guidance.Short-term treatment of up to six months should be considered for maximum weight loss<sup>iii</sup>.
2. Sibutramine should **not** be purchased where there are the following contraindications: poorly controlled hypertension, coronary heart disease, congestive heart failure, arrhythmias, stroke, severe renal or liver dysfunction or concomitant monoamine oxidase inhibitor therapy. It is relatively contraindicated in people who are at increased cardiovascular risk (i.e. >10% risk of a CVD event over 5 years).
3. Do not purchase amphetamine-related weight loss drugs Phentermine and Diethylpropion.
4. It may be appropriate to set client-specific time limits and/or endpoints for funding of weight loss drugs. The NZHTA review suggests discontinuing treatment if “reasonable weight loss” (2.5kg/month) does not occur within 12 weeks of starting treatment (p. 66). Similarly, realistic weight loss goals (e.g. 5% of initial weight) may be set at the outset, with funding stopped once the goal is reached.

### **Good Practice Points:**

- Weight loss products should only be prescribed as part of a medically monitored, comprehensive weight loss reduction regime involving a calorie controlled diet, behaviour modification and, where possible, physical exercise and lifestyle changes.
- Multivitamin supplements may be necessary while patients are taking Orlistat.
- A general medical assessment should be carried out prior to prescription of weight loss medicines; genetic and endocrine disorders (e.g. hypothyroidism) must be ruled out before obesity is diagnosed.
- Waist to hip ratio (WHR) may also be used to identify obesity and may be a better predictor of weight related cardiovascular risk than BMI. In Caucasians, men with a WHR > 1.02 and women with a WHR > 0.88 are defined as obese.

### **PGAG Discussions:**

Appropriate outcomes (in terms of weight reduction or obesity thresholds) for rehabilitation and surgery are currently believed to be unknown.

It is difficult to extrapolate the effects of obesity on risks in rehabilitation. It was felt that a more general review to understand the risk of obesity in rehabilitation may be helpful.

The evidence based review recommended lowering the obesity threshold for funding to a BMI  $\geq 30\text{kg/m}^2$  (and using different thresholds for different ethnic groups); this report however related this obesity threshold to risk of co-morbidity and general public health risk. The PGAG decided to continue to support the across-the-board obesity threshold of BMI  $\geq 35\text{kg/m}^2$  as recommended in the 2001 ACC guidance, as the

effects of obesity and therefore weight loss on the ability to participate in treatment and rehabilitation are less clear.

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<sup>i</sup> Kendall N. et al. *Evidence review September 2001: Orlistat (Xenical®)*. Wellington – ACC.

<sup>ii</sup> Quality adjusted life year.

<sup>iii</sup> Clinical trials show that most weight loss occurs within the first six months of treatment.