Abstract
The prevalence of diabetes continues to rise, following the rising rates of obesity. Obesity is not only associated with an increased risk for developing type 2 diabetes but also an elevated probability of developing long-term complications associated with the disease. Weight gain is also an important concern as a potential side effect of therapies that improve glycemic control in diabetes, including insulin therapy. As a result, patients with type 2 diabetes are at risk for a vicious circle of increasing weight and increasing insulin resistance, thus requiring further intensification of glycemic treatment. It is therefore important to address the problem of obesity in patients with type 2 diabetes. In 2012, the US Food and Drug Administration (FDA) approved two new anti-obesity medications: lorcaserin and phentermine/topiramate extended-release. Both agents have demonstrated clinically meaningful weight reduction as well as significant improvements in glycemic control in obese patients with diabetes. Liraglutide has also shown weight loss and improvements in glycemic control in patients with diabetes. Anti-obesity drugs, in conjunction with lifestyle changes, may play a valuable role in the management of diabetes.

Keywords
Diabetes, liraglutide, lorcaserin, obesity, phentermine/topiramate extended-release

The prevalence of overweight and obesity among patients with type 2 diabetes is extremely high. Data from two national surveys indicate that 28% of individuals with diabetes were overweight and 59% were obese.1 Furthermore, a rise in body mass index (BMI) is directly correlated to an increased risk for diabetes.2–4 The prevalence of type 2 diabetes is three to seven times higher in obese adults than in those of normal weight, and adults with a BMI >35 kg/m² are 20 times more likely to develop diabetes than those with a BMI between 18.5 and 24.9 kg/m².5–9 Prediabetes and the metabolic syndrome are also associated with obesity.5 Obesity is not only associated with an increased risk for developing type 2 diabetes but also an elevated probability of developing microvascular,6 neuropathic,5,7 and cardiovascular8–11 complications associated with the disease.

The incidence of type 2 diabetes has risen in parallel with the global increase in obesity, which can be illustrated by examining US data (see Figure 1). The prevalence of obesity is leveling out in the US population, but the prevalence of diabetes is rising. The presence of diabetes parallels the prevalence of obesity, but follows obesity by about 10 years.12 This has important health and economic implications. The total number of people with diabetes worldwide is projected to rise from 366 million in 2012 to 552 million in 2030.13 Projections also suggest that there will be 65 million more obese adults in the US by 2030, resulting in an additional 6–8.5 million cases of diabetes.14 Obesity is also associated with elevated risk for long-term complications, such as cardiovascular disease (CVD), in people with type 2 diabetes.15 Strategies to combat the increasing incidence of diabetes should therefore also focus on the obesity epidemic.

The transition from obesity to type 2 diabetes is characterized by a progressive deficiency in insulin secretion accompanied by a rise in insulin resistance.16 Numerous mechanisms underlie these changes, including adipose tissue dysfunction, which results in impaired insulin sensitivity in adipocytes17 and secretion of numerous factors that are involved in the development of insulin resistance, such as non-esterified or free fatty acids (FFAs), glycerol, hormones, and pro-inflammatory cytokines.18 Chronic elevations in FFAs have also been implicated as a causative factor in pancreatic β-cell dysfunction.19 This article aims to consider the role of pharmacologic therapies to control obesity in individuals with type 2 diabetes.

Effect of Type 2 Diabetes Therapy on Bodyweight
The current treatment goal in type 2 diabetes is to achieve the best possible glycemic control, since intensive glycemic control has been associated with a substantially decreased risk for microvascular complications.20 Clinical evidence has also suggested a beneficial role for glycemic control on CVD, depending on patient characteristics, including age, diabetes duration, previous glucose control, and risk for hypoglycemia.21 CVD is the major cause of death in patients with type 2 diabetes; more than 60% of patients die of myocardial infarction (MI) or stroke.22
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Table 1: Effect of Anti-diabetic Medications on Weight

<table>
<thead>
<tr>
<th>Medication Class</th>
<th>Examples</th>
<th>Effect on Weight</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insulin</td>
<td>Insulin glargine, detemir</td>
<td>Most associated with weight gain, insulin detemir less so</td>
<td>20, 31</td>
</tr>
<tr>
<td>Thiazolidinediones</td>
<td>Pioglitazone</td>
<td>Weight gain often occurs but is not inevitable. Favorable shift in fat distribution from visceral to subcutaneous adipose depots</td>
<td>25</td>
</tr>
<tr>
<td>Sulfonylureas</td>
<td>Glyburide, glipizide, gimepiride</td>
<td>Mixed data though some studies have made associations with weight gain</td>
<td>28</td>
</tr>
<tr>
<td>Meglitinides</td>
<td>Repaglinide, nateglinide, mitiglinide</td>
<td>Weight gain of up to 3 kg in 3 months reported</td>
<td>29</td>
</tr>
<tr>
<td>Alpha-glucosidase inhibitors</td>
<td>Acarbose, miglitol, voglibose</td>
<td>No clinically relevant effect on bodyweight</td>
<td>32</td>
</tr>
<tr>
<td>Bile acid sequestrants</td>
<td>Colesevelam</td>
<td>No effect on bodyweight</td>
<td>34</td>
</tr>
<tr>
<td>Biguanides</td>
<td>Metformin</td>
<td>Some beneficial effects on weight/weight neutral</td>
<td>35–37</td>
</tr>
<tr>
<td>GLP-1 agonists</td>
<td>Exenatide, liraglutide, lisenatide</td>
<td>Associated with modest weight loss</td>
<td>38</td>
</tr>
<tr>
<td>DPP-IV inhibitors</td>
<td>Sitagliptin, vildagliptin, saxagliptin, linagliptin</td>
<td>Neutral effects on bodyweight</td>
<td>33</td>
</tr>
<tr>
<td>SGLT-2 inhibitors</td>
<td>Dapaglirozin, canaglirozin</td>
<td>Associated with reduction in bodyweight</td>
<td>42</td>
</tr>
</tbody>
</table>

**Table 2: US Food and Drug Administration-approved Anti-obesity Medication—Clinical Data in Patients with Type 2 Diabetes and Obesity**

<table>
<thead>
<tr>
<th>Agent</th>
<th>Impact on Weight</th>
<th>Adverse Events</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Orlistat</td>
<td>In a 1-year, multicenter RCT, patients with type 2 diabetes on metformin were given orlistat or metformin</td>
<td>Intestinal cramps, flatus, fecal incontinence, oily spotting, and flatus with discharge in up to a third of patients</td>
<td>68</td>
</tr>
<tr>
<td>PHEN/TPM ER</td>
<td>Sustained 2-year weight reduction of 6.8 % (7.5/46 mg) to 8.8 % (15/92 mg) was reported in the diabetic population versus 1.9 % in the placebo group</td>
<td>Paresthesia (14–21 %), constipation (15–17 %), dizziness (7–10 %), dygeusia, depression-related and anxiety-related symptoms in 5–10 %</td>
<td>76</td>
</tr>
<tr>
<td>Lorcaserin</td>
<td>Results at 1 year showed that more patients lost ≥ 5 % bodyweight with lorcaserin BID (37.5 %; p&lt;0.001) or lorcaserin QD (44.7 %; p&lt;0.001) versus placebo (16.1 %). Mean (± SEM) weight reduction was 4.5 ± 0.35 % with lorcaserin BID and 5.0 ± 0.5 % with lorcaserin QD versus 1.5 ± 0.36 % with placebo (p&lt;0.001 for each)</td>
<td>Headache (14.5–16.8 %), back pain (8.4–11.7 %), nasopharyngitis (11.3–23.2 %), and nausea, urinary tract infection, cough, fatigue, gastroenteritis, and dizziness in 5–10 %</td>
<td>74</td>
</tr>
</tbody>
</table>

**BID = twice a day; PHEN/TPM ER = phentermine/topiramate extended-release; QD = daily; RCT = randomized controlled trial; SEM = standard error of the mean.**

The American Diabetes Association (ADA) guidelines currently recommend a glycemic goal of glycated hemoglobin (HbA1c) <7.0 %. However, they recommend that glucose goals should be individualized for patient depending on various risk factors. Glycemic goals present a challenge to the obese patient with diabetes, as improvement in glycemic control necessitates the administration of higher dosages of insulin, or the addition of insulin to pharmacologic regimes that promote weight gain. A vicious circle may ensue. Strategies to overcome insulin-associated weight gain include increasing insulin sensitivity through diet and exercise, enabling dose reductions, or by the use of co-medications, such as pramlintide or metformin. Newer, long-lasting basal insulin analogs, such as insulin detemir, are associated with lower levels of weight gain compared with shorter-acting insulin formulations.

Most oral anti-diabetic agents have been associated either with weight gain (thiazolidinediones, sulfonylureas, meglitunides) or are weight-neutral (alpha-glucosidase inhibitors; dipetidyl peptidase-IV inhibitors, bile acid sequestrants). Metformin has been associated with beneficial effects on weight in type 2 diabetes, although a Cochrane review concluded that it is weight-neutral. Moderate weight loss has consistently been observed in clinical studies of glucagon-like peptide 1 (GLP-1) agonists in type 2 diabetes. The addition of GLP-1 agonists to insulin therapy in obese patients with diabetes improves both glycemic control and weight. The beneficial effect on weight is thought to be mediated by central regulation of feeding and delayed gastric emptying, promoting early satiety. Sodium-glucose co-transporter 2 (SGLT2) inhibitors, the newest class of diabetic medications, have also been associated with favorable effects on bodyweight, resulting from an initial osmotic diuresis, and in the long term from increased urinary excretion of glucose.

**Impact of Treating Obesity in Diabetes**

Numerous studies have demonstrated that weight loss in patients with diabetes results in improvement in glycemic control. Moderate weight loss (5 % of bodyweight) can improve insulin action, decrease fasting blood glucose concentrations, and reduce the need for diabetes medications, as well as preventing or delaying the development of type 2 diabetes in those with risk factors for the disease, such as impaired glucose tolerance. In a 4-year, double-blind, prospective study, 3,305 patients were randomized to lifestyle changes plus either an anti-obesity drug (orlistat 120 mg) or placebo. Compared with lifestyle changes alone, orlistat plus lifestyle changes resulted in a greater reduction in the incidence of type 2 diabetes over 4 years and produced greater weight loss.
loss in a clinically representative obese population. There is therefore a strong rationale for the use of anti-obesity drugs in overweight and obese patients with type 2 diabetes.

**Anti-obesity Treatment Options in Diabetes**

Lifestyle interventions should be undertaken before initiating drug therapy in obese patients with diabetes. These should include reductions in caloric intake of 500–1,000 calories per day, increases in physical activity, and changes in health behavior. Lifestyle interventions have proved successful in the prevention of diabetes, as well as in achieving weight loss in patients with type 2 diabetes. The Look AHEAD trial randomly assigned 5,145 overweight or obese patients with type 2 diabetes to participate in an intensive lifestyle intervention or to receive diabetes support and education. After a median follow-up of 9.6 years, weight loss was greater in the intervention group than in the control group throughout the study (8.6 % versus 0.7 % at 1 year; 6.0 % versus 3.5 % at study end). The intensive lifestyle intervention also produced greater reductions in HbA1c. However, the trial was stopped early for futility after failing to meet its primary endpoint of reduction in the rate of cardiovascular events.

Although many lifestyle interventions may result in short-term weight loss, most are associated with poor long-term compliance and weight regain. In daily life settings, the implementation of lifestyle interventions is more difficult than in clinical studies. Long-term success with lifestyle modification for weight loss in diabetes is often poor: a systematic review of dietary interventions in obesity between 1931 and 1999 found a median change in body weight of only 2 kg after 1 year.8 In daily life settings, the implementation of lifestyle interventions is more difficult than in clinical studies. Long-term success with lifestyle modification for weight loss in diabetes is often poor: a systematic review of dietary interventions in obesity between 1931 and 1999 found a median change in body weight of only 2 kg after 1 year.

Bariatric surgery is an effective treatment for obesity in the prevention and management of diabetes, and has resulted in rapid improvements in glycemic parameters but is associated with a risk for postoperative complications, including death, as well as being expensive and requiring specialist facilities. It is therefore unlikely to become a first-line treatment strategy for the majority of patients with diabetes and obesity. The ADA and International Diabetes Federation recommend that bariatric surgery should be considered in patients with type 2 diabetes with a BMI ≥35 kg/m². Recent recommendations from the American Society of Bariatric Physicians also suggest that it may be considered for patients with BMI ≥30 kg/m² with one or more adverse health consequences due to excessive body fat.

Both the American College of Physicians and the American Society of Bariatric Physicians recommend that drug therapy is part of an overall strategy for managing overweight and obesity, which should include appropriate recommendations for diet, physical activity, and behavior therapy. Anti-obesity medications have been successfully employed in the management of obese patients with diabetes. However, obesity is a complex disorder, and there is broad variability in the weight-loss response to all therapies for obesity including surgery, lifestyle interventions, and pharmacotherapy. Genome-wide association studies have identified numerous associated genes, suggesting that multiple mechanisms are involved in obesity. Furthermore, inflammation plays a major role in obesity. Studies have identified an imbalance between the levels of proinflammatory cytokines, such as interleukins and tumor necrosis factors, and the levels of anti-inflammatory cytokines. It is therefore unlikely that a single drug will be effective in all cases and there is a need for a range of anti-obesity therapies with differing mechanisms of action.
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**Figure 3: Effect of Phentermine/Topiramate Extended-release on Bodyweight in the CONQUER Trial**

Throughout the past decade, many medications have been introduced and approved by the US Food and Drug Administration (FDA) for the treatment of obesity. However, most of them have subsequently been withdrawn following the postmarketing discovery of serious adverse events (AEs). The anti-obesity drug rimonabant showed clinically meaningful reductions in HbA1c in obese patients with type 2 diabetes as an adjunct to oral anti-diabetic therapy, as monotherapy, and in insulin-treated individuals. However, its use was suspended because of an associated risk for psychiatric problems. Silibutramine was withdrawn in 2010 due to cardiovascular risks, phenylpropanolamine was withdrawn in 2000 due to risk for hemorrhagic stroke and fenfluramine and dexfenfluramine were withdrawn after reports of valvular heart disease and primary pulmonary hypertension in 1997.

Prior to 2012, orlistat, (Xenical® , Roche) an inhibitor of pancreatic lipase, was the only weight-loss drug approved by the FDA for long-term use. Orlistat is associated with moderate weight loss and confers additional HbA1c reductions of 0.3–0.5 % at 1 year when given in combination with oral anti-diabetic drugs or insulin, but is associated with gastrointestinal side effects in up to a third of patients including intestinal cramps, flatus, fecal incontinence, oily spotting, and flatus with discharge. More recently, rare cases of serious liver injury have been reported. Celitistat, a highly lipophilic benzoazoxamine that inhibits lipases with a similar action to orlistat, is in clinical development in Japan. In a phase II study, it demonstrated significantly reduced bodyweight and improved glycemic control relative to placebo in obese patients with diabetes, with fewer discontinuations compared with orlistat. Phase III studies have recently completed.

In 2012, the FDA approved two new drugs for chronic weight management in obese or overweight adults with one or more weight-related comorbidities, to be used in conjunction with a reduced-calorie diet and increased physical activity. Lorcaserin (Belviq® , Arena Pharmaceuticals) is a selective agonist of the serotonin (5-hydroxytryptamine) 2C (5-HT2c) receptor that is associated with the regulation of food intake, and therefore suppresses appetite. Phentermine/topiramate extended-release (PHEN/TPM ER, Qsymia® , Vivus) is a fixed-dose combination of phentermine (an anorectic agent), and the anti-epileptic drug topiramate.

Clinical trial data demonstrating the efficacy and safety of the FDA-approved anti-obesity medications in patients with type 2 diabetes is summarized in Table 2. Lorcaserin produces clinically meaningful weight reductions in obese individuals as well as improvements of glycemic control. The Behavioral modification and Lorcaserin for Overweight and Obesity Management (BLOOM) phase III clinical trial (n=3,182) showed significant weight reduction as well as nonsignificant reduction of HbA1c. In the Behavioral modification and Lorcaserin Second Study for Obesity Management (BLOSSOM) phase III study (n=4,008), significant weight reduction and statistically insignificant reductions in HbA1c were noted. The BLOOM-DM (Behavioral Modification and Lorcaserin for Obesity and Overweight Management in Diabetes Mellitus) clinical trial enrolled 604 patients with a BMI of 27–45 kg/m², a diagnosis of type 2 diabetes, and a HbA1c of 7–10 %. Results at 1 year showed that more patients lost >5 % bodyweight with lorcaserin twice daily (BID) (37.5 %; p<0.001) or lorcaserin once daily (QD) (44.7 %; p<0.001) compared with placebo (16.1 %). The mean weight reduction was 4.5 % with lorcaserin BID and 5.0 % with lorcaserin QD versus 1.5 % with placebo (p<0.001 for each). (see Figure 2). There was a reduction in HbA1c, of 0.9 with lorcaserin BID, 1.0 with lorcaserin QD, and 0.4 with placebo (p<0.001 for each); fasting glucose decreased by 27.4 mg/dl, 28.4 mg/dl, and 11.9 mg/dl, respectively (p<0.001 for each).

The most common AEs associated with lorcaserin are headache, nausea, dizziness, fatigue, dry mouth, and constipation. In the BLOOM-DM study, headache was reported in 14.5 % and 16.8 % of the BID and QD lorcaserin groups, respectively; back pain was reported in 11.7 % and 8.4 % of the BID and QD lorcaserin groups, respectively; however, most were mild and self-limiting. Concerns have been expressed in terms of the risk for valvulopathy associated with activation of the serotonin 2B (5-HT2B) receptors on cardiac interstitial cells; an association with valvulopathy resulted in the withdrawal of fenfluramine and dexfenfluramine from the market. However, data from in vitro assays indicated that lorcaserin at recommended doses is unlikely to activate the 5-HT2B receptor. Furthermore, among 2,472 patients evaluated at 1 year and 1,127 evaluated at 2 years in the BLOOM study, the rate of cardiac valvulopathy was not increased with the use of lorcaserin. In the BLOOM-DM study, higher rates of valvulopathy were seen in lorcaserin-treated patients (2.5 % on lorcaserin BID, 3.9 % on lorcaserin QD) versus placebo (1.9 %) group; however, this was considered to be due to the unusually low rate of valvulopathy in the placebo group. Prescribing information recommends discontinuation if 5 % weight loss is not achieved by week 12, or if signs or symptoms of valvular heart disease develop.

The Effects of low-dose, controlled-release, phentermine plus topiramate combination on weight and associated comorbidities in overweight and obese adults (CONQUER) phase III clinical trial of PHEN/TPM ER (n=2,487) randomized patients to placebo, PHEN 7.5 mg/TPM ER 46 mg (7.5/46a), or PHEN 15 mg/TPM ER 92 mg (15/92). Significant weight loss was demonstrated in all patient groups (see Figure 3). Among the patient population that had type 2 diabetes (16 %), the placebo-subtracted weight loss at 1 year was 4.9 % in the 7.5/46 group and 6.9 % in the 15/92 group.
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In the Longer-Term Safety, Efficacy of Phentermine + Topiramate for Weight Reduction Among Overweight or Obese individuals with Cardio metabolic Disease (SEQUEL) extension study (n=676), a sustained 2-year weight reduction of 9 % was reported in patients with type 2 diabetes compared with 2 % in the placebo group (p=0.0003 for 7.5/46 and p<0.0001 for 15/92). Improvements in glycemic parameters were also noted in the treatment group compared with placebo. In a recently published subanalysis of the SEQUEL study, 475 high-risk overweight or obese patients with prediabetes and/or the metabolic syndrome at baseline were monitored for progression to type 2 diabetes. Patients in the PHEN/TPM 7.5/46 and 15/92 treatment groups experienced reductions of 71 % and 79 % in the annualized incidence rate of type 2 diabetes, respectively, compared with placebo. This was related to degree of weight lost (10.9 % and 12.1 %, respectively versus 2.5 % with placebo; p<0.0001).81

AEs reported in the CONQUER trial included paresthesia (14 % in the 7.5/46 versus 21 % in the 15/92 group), constipation (15 % in the 7.5/46 group versus 27 % in the 15/92 group), and insomnia, dizziness, dysgeusia, depression-related symptoms, and anxiety-related symptoms in 5–10 %.82 Safety concerns about PHEN/TPM ER include teratogenicity and elevation in resting heart rate.82 However, a large population-based cohort study (n=837,795) did not find an increased incidence of birth defects.82 Other concerns include the risk for metabolic acidosis, glaucoma, and psychiatric and cognitive AEs.82

The weight reduction associated with GLP-1 analogs in diabetes has led to studies investigating the efficacy and safety of liraglutide (Victoza®; Novo Nordisk) as an anti-obesity treatment. A 20-week clinical trial (n=564) provided evidence that higher doses of liraglutide than are usually indicated for glycemic control led to significant weight loss and may be used in the treatment of obesity.83,84 As a result, the Satiety and Clinical Adiposity – Liraglutide Evidence in Non-Diabetic and Diabetic Subjects (SCALE) clinical development program was initiated. One of the phase III clinical trials in this program enrolled 846 patients with type 2 diabetes. Weight reductions of 6 % and 5 % have recently been reported in patients treated with liraglutide 3 mg and liraglutide 1.8 mg after 56 weeks were 6 % and 5 %, respectively, compared with a 2 % weight loss for people treated with placebo. The proportion of people achieving a weight loss of at least 5 % or 10 % was 50 % and 22 % for liraglutide 3 mg, 35 % and 13 % for liraglutide 1.8 mg, and 13 % and 4 % for placebo treatment, respectively.85

The safety profile of liraglutide is acceptable; the most common AEs were related to the gastrointestinal system and diminished over time.86 In 2011, the FDA advisory panel issued a safety warning regarding the risk for thyroid C-cell tumors and pancreatic islet with liraglutide.87 Following the discovery that long-term liraglutide exposure is associated with C-cell carcinoma and thyroid C-cell focal hyperplasia in rodents.88 However, a recent study suggested that GLP1 receptor agonist-induced C-cell responses in rodents may not be relevant to primates.89 Concern has also been raised about the potential for pancreatitis; however, liraglutide did not induce pancreatitis in mice, rats, or monkeys when dosed for up to 2 years and at exposure levels up to 60 times higher than in humans.90 Other impediments to the widespread use of liraglutide include its relatively high cost and the fact that it administered by intramuscular injection, reducing its acceptability to patients.

Naltrexone plus bupropion (Contrave) is a dopamine and noradrenaline reuptake inhibitor that has not yet been approved. The Contrave Obesity Research (COR) trials assessed the efficacy of naltrexone/bupropion in both patients with and without diabetes.91,92 Reductions in weight and HbA1c have been reported. The drug was previously rejected by the FDA who, in February 2011, stated that a large-scale study of CV risk would be needed before they could consider approval. The Cardiovascular Outcomes Study of Naltrexone SR/Bupropion SR in Overweight and Obese Subjects With Cardiovascular Risk Factors (Light) Study is a randomized, double-blind, placebo-controlled cardiovascular outcomes trial evaluating the occurrence of major adverse cardiovascular events in patients participating in the study.93 Other agents in late-stage clinical development include tofensine, an inhibitor of the presynaptic uptake of noradrenaline, dopamine, and serotonin.94 Several additional gut hormone-based treatments for obesity are under clinical investigation, including peptide YY, pancreatic polypeptide, amylin, and oxyntomodulin.95

It is evident that new anti-obesity medications provide clinically meaningful weight reductions in patients with diabetes with acceptable safety profiles. There is a need for long-term safety data on these medications, in order to dispel fears associated with the safety of anti-obesity medications and increase their clinical utility. An analysis of data from the National Health and Nutritional Examination Survey in 2007–8 found that 45.4 % of the sample population were eligible for anti-obesity treatment. However, among these, only 0.6 % were taking anti-obesity drugs.94 Reasons for this low usage may include concerns over the limited effectiveness and safety of previously available drugs.

Summary and Concluding Remarks

The twin epidemics of diabetes and obesity continue to rise and intervention is required to prevent a global public health crisis. A large body of clinical data supports the treatment of obesity as a management strategy in type 2 diabetes (see Figure 1).97-105 Lifestyle modification focused on diet and physical activity should be an essential component of weight-management interventions. Anti-obesity medications also play a role in weight management, providing modest additional fat loss to that achieved by lifestyle modification alone, improving quality of life (QoL) and showing improvements in glycemic parameters in patients with type 2 diabetes. However, obesity is a heterogeneous condition: the genetic and pathophysiologic factors underlying obesity are highly variable between individuals and, therefore, the clinical response to anti-obesity medication may also vary. There is therefore a need for need for a variety of drugs with differing mechanisms in the management of obesity in type 2 diabetes in order to achieve individualized and optimized therapy.

The regulatory approval of the pharmacologic treatment of obesity has been characterized by repeated rejections of new agents and the withdrawal of previously approved agents due to serious AEs. The approval of lorcaserin and PHEN/TPM ER by the FDA reflect their favorable benefit: risk profile and may represent recognition of the enormity of the obesity problem and an increasing acceptance of the growing demand for effective and safe medications for the treatment of obesity. Both agents have demonstrated clinically meaningful weight reduction as well as significant improvements in glycemic control of obese patients with diabetes. The submission of liraglutide for FDA approval will hopefully further expand the treatment armamentarium.
It remains to be seen whether the performance of new anti-obesity medications in daily life matches that of controlled clinical settings. The patient's perception of how a new medication affects their QoL is crucial to compliance and ultimately treatment success. The QoL parameters reported in the BLOSSOM, BLOOM, and CONQUER clinical studies suggest that the effect of lorcaserin and PHEN/TRM ER on weight loss correspond to a meaningful improvement in QoL. However, the relatively high dropout rates observed in these trials suggest that compliance may be a limiting factor in day-to-day use of these therapies. Despite these concerns, evidence to date suggests that new anti-obesity medications have been well accepted by patients and, in conjunction with lifestyle modification, offer an effective alternative to bariatric surgery in patients with type 2 diabetes.
The Role of Anti-obesity Drugs in Patients with Type 2 Diabetes

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