Active Ingredient Summary Table
Weight Loss

Active Pharmaceutical Ingredient	Mechanism of Action (MoA) for Weight Loss	FDA Approved Products (FDA approval not specifically for weight loss)	Studied Routes of Administration (not limited to routes studies specifically for weight loss)	Dosing Studied for Weight Loss	Chemical and Physical Stability Information
Acarbose[1]	Acarbose is a complex oligosaccharide, it delays ingested carbohydrates resulting in decreased blood glucose elevation following meals Very little acarbose is absorbed as active drug	Tablet (25, 50, 100mg)	Oral	Given 25mg to 50mg three times daily, the maximum allowed dosage is 100mg three times daily	Information not available
Bupropion HCl[2-4]	Bupropion stimulates pro-opiomelanocortin cells (POMC) to produce an anorexic effect, when paired with naltrexone HCl, a negative feedback loop that may reduce efficacy of bupropion is inhibited	IR and ER tablets Tablet combo with Naltrexone (Contrave) (8mg naltrexone/90mg bupropion)	Oral	Studied dosing typically follows an escalation pattern starting at 90mg twice daily and escalating to 180mg twice daily in combination with naltrexone HCl Bupropion HCl has also been studied as a solo agent for weight loss at 300 to 400mg total per day	One study found minimal bupropion HCl degradation in solution at pH ≤5 at up to 90hr at 60˚C Some studies suggest better aqueous stability in acidic solutions below pH 5
Canagliflozin[69,70]	Sodium-glucose co-transporter 2 (SGLT2) inhibitor – prevents reabsorption of glucose in the kidneys leading to increased glucose secretion into the urine	IR or XR alone or in combination with metformin	Oral	Studied at 300mg in combination with phentermine 15mg for weight loss	Limited information available, one HPLC degradation study found degradation with long term (48hr) exposure to 70C

Active Ingredient Summary Table
Weight Loss

Empagliflozin[68,71]	Sodium-glucose co-transporter 2 (SGLT2) inhibitor – prevents reabsorption of glucose in the kidneys leading to increased glucose secretion into the urine	IR or XR tablets alone or in combination with metformin or linagliptin at doses of 5-25mg	Oral	Studied at 10mg once daily in combination with topiramate 25mg twice daily for weight loss	Poor thermal stability, prolonged exposure to 40C can result in significant degradation.
Liraglutide[5-9]	GLP-1 receptor agonist Liraglutide causes delayed gastric emptying and decreases appetite, increasing satiety	Injectable Solution 6mg/ml	Subcutaneous Injection Limited studies via other routes in animal studies found 0.03% nasal bioavailability and 0.006% oral bioavailability Planned studies for sublingual use at 3,12, and 30mg, but no information yet	Dose is typically titrated up from 0.6mg to 3mg SC daily	Stored refrigerated long term, but stable for 30 days at controlled room temperature and up to 30˚C per the package insert Degradation studies have noted limited thermal stability of liraglutide at up to 60˚C pH stability at 7-9 (commercially available injectable pH ~8.15)
Lisdexamfetamine[10-12]	Lisdexamfetamine (LDX) is a prodrug of dextroamphetamine. It is currently approved for binge eating disorder but not for weight loss, despite this, LDX facilitates NE neurotransmission, which may contribute to weight loss	Capsule (10-70mg) Chewable tab (10-60mg)	Oral	Mainly studied at 20-70mg per day for binge eating disorder	Some degradation studies suggest good stability at slightly acidic pH ~4
Metformin[13-22]	MoA may be related to modulation of hypothalamic appetite-regulatory centers as	Tablet (ER and IR) 500mg, 850mg, 1000mg	Oral Transdermal Buccal	Studied at 500mg twice daily usually as an adjunct to other therapies	Studies on various oral liquid formulations found minimal degradation with long term exposure to 40C, another suggested thermal stability

Active Ingredient Summary Table
Weight Loss

	well as alteration of gut microbiome	Oral Solution Various combination products, mainly with other APIs for type 2 diabetes			above 40C, but noted the influence of excipients such as mannitol or lactose may decrease temperature stability Stable from slightly acidic (above pH 4) to neutral pH
Methionine/Inositol/ Choline[72,73]	These "lipotropic" injectable products are intended to facilitate increased fat burning and decreased lipid synthesis	No commercially available products	Used most commonly via the IM route, though some use orally as well	Extremely limited information available on the safety and efficacy of these lipotropic products. Anecdotally, methionine is often used at 12.5-25mg/mL and inositol and choline are used at 25-50mg/mL Injections are typically given once or twice weekly	Limited data available suggests aqueous stability at slightly acidic pH around 5-6 Data on temperatures consistent with autoclave sterilization is not available
Naltrexone HCl[23-33]	MoA may be related to its opioid blockade and its effect on endorphins potentially decreasing the feeling of "reward" associated with food In combo with bupropion it prevents a negative feedback loop that would normally reduce the effectiveness of bupropion alone for weight loss, results in anorexic effect	Tablet (50mg) IM Injection Tablet combo with Bupropion (Contrave) (8mg naltrexone/90mg bupropion)	Oral Injection Some literature on ophthalmic use Some literature on nasal use Some literature on buccal use	Studied dosing typically follows an escalation pattern starting at 8mg twice daily and escalating to 16mg twice daily in combination with bupropion HCl	Evidence suggests good thermal stability for naltrexone HCl, with one study noting stability of the aqueous solution to autoclave sterilization Information on extemporaneous oral suspensions suggests good stability at slightly acidic pH in the range of 4-5

Active Ingredient Summary Table
Weight Loss

Orlastat[34-37]	Orlistat is a reversible inhibitor of gastrointestinal lipases, inactivation of these enzymes leads to an inability to absorb dietary fats decreasing caloric intake Very little orlistat is absorbed systemically, primary effect is local lipase inhibition after an oral dose	Capsule (60mg OTC, 120mg Rx)	Oral	Dosed at 120mg three times daily with each main meal (or within 1 hour after the meal) Orlistat has also been studied in combination with phentermine (phentermine at 37.5mg once daily and orlistat with typical TID dosing)	Orlistat has a low melting point (~44˚C) and is prone to thermal degradation especially when exposed to humidity
Oxytocin[38-46]	An endogenous hypothalamic hormone, regulates a range of processes including eating behavior and metabolism Oxytocin may reduce food intake and lead to increasing energy expenditure and lipolysis	Injection 10IU/ml	Intravenous Intramuscular Nasal spray/nebulization (approximate nasal bioavailability estimated to be 35% in one small study) Sublingual bioavailability estimates vary, one study of a lingual spray and nasal spray estimated the lingual bioavailability to be about 41.7% of nasal bioavailability	Studies on weight loss generally evaluate nasal use, one study found clinically significant weight loss with 24IU administered four times daily (once before each of 3 meals and again before bed)	Package insert specifies not to freeze, but one study did find stability of oxytocin solution diluted in saline frozen at -20˚C over 30 days. Information exists to suggest stability at 40C for at least one week, some information suggests short term stability at higher temperatures as well Stability at pH 3-5
Phentermine HCl[47-48]	Sympathomimetic amine, often called an anorexigenic MoA is multifaceted but one main effect is increase in	Tablet 37.5mg phentermine HCl (30mg phentermine base)	Oral (Tablet and ODT)	Phentermine HCl is used alone at 18.75mg to 37.5mg once daily (or divided into two doses)	Information on pH and general aqueous stability is not widely available for this API

Active Ingredient Summary Table
Weight Loss

	norepinephrine resulting in appetite suppression	OTD (15mg, 30mg, 37.5mg phentermine HCl) Tablet in combo with topiramate (phentermine base 3.75, 7.5, 11.25, 15mg)		In combination with topiramate dosing is usually started at 3.75mg phentermine/23mg topiramate and tapered up over a period of weeks up to a maximum of phentermine 15mg, topiramate 92mg	
Semaglutide[49-54]	Long acting GLP-1 recetpro agonist Semaglutide causes delayed gastric emptying and decreases appetite, increasing satiety	Injection 0.68, 1.34, 2.68mg/ml Tablet 3,7, 14mg	Subcutaneous Injection Oral (approximate oral bioavailability is 0.4-1%)	Studied doses vary, but doses consistent with type II diabetes management have been associated with weight loss, typically the dose starts at 0.25mg weekly and increases every 4 weeks up to 2.5mg injected SC every week Studies on oral dosing for weight loss are evaluating doses higher than currently offered by commercially available tablets, up to 50mg with an escalation period.	Stored refrigerated long term, but package insert notes 56 days controlled room temperature storage is acceptable. Package insert specifies not to freeze One study on semaglutide dry powder found minimal degradation after exposure to 105˚C for 15hr Stability at pH 7.4, Semaglutide has pH related solubility, poorly soluble at pH 2-6, soluble above pH 6
Tirzepatide[55,56]	A GIP (glucose-dependent insulinotropic polypeptide) and GLP1 receptor agonist, GIP has been shown to reduce food intake and increase energy expenditure	Injectable solution(2.5-15mg/0.5ml)	Subcutaneous injection	Dose is typically titrated up from 2.5mg by adding 2.5mg every 4 weeks up to 10mg or 15mg	Stored refrigerated for long term use, package insert states room temperature storage up to 30C is appropriate for up to 21 days Good stability at 6.5-7.5

Active Ingredient Summary Table
Weight Loss

Topiramate[57-62]	Exact MoA not known, thought to decrease appetite and enhance satiety, may be induced by augmenting activity of gamma-aminobutyrate	Tablet/Capsule (25-200mg) Oral Solution (25mg/ml)	Oral (tablet/liquid) Some literature on buccal films	Studied dosing varies, but commonly strengths between 96-192mg are used for weight loss In combination with phentermine dosing is usually started at 3.75mg phentermine/23mg topiramate and tapered up over a period of weeks up to a maximum of phentermine 15mg, topiramate 92mg	Evidence suggests that topiramate in both liquid and dry powder form may be prone to degradation at elevated heat (80-90˚C) Information on extemporaneous oral suspensions suggests good pH in slightly acidic pH in the range of 3.9-4.9
Zonisamide[63-67]	MoA for weight loss not fully elucidated, but may be associated with suppression of appetite and stimulation of POMC to produce an anorexic effect Some studies have looked at zonisamide and bupropion combinations for weight loss	Oral Suspension (20mg/ml) and Oral capsule (25, 50, 100mg)	Oral use	Studied alone at 200-400mg for weight loss, the 400mg dose was associated with weight loss, but adverse events occurred Also studied in combination with bupropion (zonisamide scaling from 100-400mg, bupropion from 100 to 200mg) with more weight loss noted than with zonisamide alone	Good aqueous stability at slightly acidic pH (3.9-4.9) Some information suggests thermal stability up to 60˚C

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