LifeWise
Health Plan of Washington

PHARMACY POLICY – 5.01.621

Drugs for Weight Management

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Introduction

Excess weight is associated with many health risks such as diabetes, high blood pressure, high cholesterol, and heart disease along with an increased risk of death. Many individuals are able to lose weight by changing their diet and increasing their exercise. The challenge for most people is keeping off the weight they have lost. Initiation of drug therapy in overweight individuals should be made after consideration of the benefits and risks. There are a number of medications approved by the US Food and Drug Administration (FDA), when used in combination with diet and exercise, for the treatment of weight management. This policy describes when drugs for chronic weight management may be considered medically necessary.

Note: The Introduction section is for your general knowledge and is not to be taken as policy coverage criteria. The rest of the policy uses specific words and concepts familiar to medical professionals. It is intended for providers. A provider can be a person, such as a doctor, nurse, psychologist, or dentist. A provider also can be a place where medical care is given, like a hospital, clinic, or lab. This policy informs them about when a service may be covered.

Policy Coverage Criteria

Drug	Medical Necessity
Contrave (naltrexone/bupropion) • **Chronic weight management (adults)**	**Contrave (naltrexone/bupropion) may be considered medically necessary for chronic weight management when all the following criteria are met:** • The individual is aged 18 years or older **AND** • Has engaged in a trial of behavioral modification and dietary restriction for at least 3 months **AND** • Has a body mass index (BMI) of greater than or equal to 30 kg/m^2 **OR** • Has a BMI of greater than or equal to 27 kg/m^2 and one or more of the following weight-related comorbid conditions: ○ Asthma ○ Cardiovascular disease ○ Chronic obstructive pulmonary disease (COPD) ○ Coronary artery disease ○ Dyslipidemia ○ Hypertension ○ Knee osteoarthritis ○ Metabolic-dysfunction associated steatotic liver disease/non-alcoholic fatty liver disease ○ Obstructive sleep apnea ○ Polyendocrine metabolic ovarian syndrome (PMOS) ○ Type 2 diabetes mellitus **AND** • Medication is being used as an adjunct to a reduced-calorie diet and increased physical activity **AND** • Dose is limited to four Contrave 8 mg/90 mg tablets per day (taken as two tablets in the morning and two tablets in the evening) **AND** • Medication is not being used concurrently with other medications intended for weight loss (e.g., Alli, benzphetamine, diethylpropion, Foundayo, liraglutide 18 mg/3 mL pen, phendimetrazine, phentermine, phentermine and topiramate

Drug	Medical Necessity
	extended-release, Qsymia, Saxenda, Wegovy, Xenical, and Zepbound) **Note:** Drugs for weight management are excluded under many benefit plans. Therefore, the use of Contrave (naltrexone/bupropion) for weight management may not be covered. Please refer to the applicable benefit plan document to determine benefit availability (see **Benefit Application** for further information).
Foundayo (orforglipron) • **Chronic weight management (adults)**	**Foundayo (orforglipron) may be considered medically necessary for chronic weight management when all the following criteria are met:** • The individual is aged 18 years or older **AND** • Has engaged in a trial of behavioral modification and dietary restriction for at least 3 months **AND** • Has a body mass index (BMI) of greater than or equal to 30 kg/m^2 **OR** • Has a BMI of greater than or equal to 27 kg/m^2 and one or more of the following weight-related comorbid conditions: ○ Asthma ○ Cardiovascular disease ○ Chronic obstructive pulmonary disease (COPD) ○ Coronary artery disease ○ Dyslipidemia ○ Hypertension ○ Knee osteoarthritis ○ Metabolic-dysfunction associated steatotic liver disease/non-alcoholic fatty liver disease ○ Obstructive sleep apnea ○ Polyendocrine metabolic ovarian syndrome (PMOS) ○ Type 2 diabetes mellitus **AND** • Does not have severe hepatic impairment (Child-Pugh Class C) **AND**

Drug	Medical Necessity
	• Medication is being used as an adjunct to a reduced-calorie diet and increased physical activity **AND** • Medication is not being used concurrently with other medications intended for weight loss (e.g., Alli, benzphetamine, Contrave, diethylpropion, liraglutide 18 mg/3 mL pen, phendimetrazine, phentermine, phentermine and topiramate extended-release, Qsymia, Saxenda, Wegovy, Xenical, and Zepbound) **AND** • Dose is limited to 17.2 mg daily **AND** • The quantity is limited to 30 tablets per 30 days **Note:** Drugs for weight management are excluded under many benefit plans. Therefore, the use of Foundayo (orforglipron) for weight management may not be covered. Please refer to the applicable benefit plan document to determine benefit availability (see **Benefit Application** for further information).

Generic liraglutide 18 mg/3 mL pen
• **Chronic weight management (adults)**
• **Chronic weight management (pediatrics)**
	Generic liraglutide 18 mg/3 mL pen may be considered medically necessary for chronic weight management in adult individuals when all the following criteria are met:
	• The individual is aged 18 years or older
	AND
	• Has engaged in a trial of behavioral modification and dietary restriction for at least 3 months
	AND
	• Has a body mass index (BMI) of greater than or equal to 30 kg/m^2
	OR
	• Has a BMI of greater than or equal to 27 kg/m^2 and one or more of the following weight-related comorbid conditions:
	  ○ Asthma
	  ○ Cardiovascular disease
	  ○ Chronic obstructive pulmonary disease (COPD)
	  ○ Coronary artery disease

Drug	Medical Necessity
	○ Dyslipidemia ○ Hypertension ○ Knee osteoarthritis ○ Metabolic-dysfunction associated steatotic liver disease/non-alcoholic fatty liver disease ○ Obstructive sleep apnea ○ Polyendocrine metabolic ovarian syndrome (PMOS) ○ Type 2 diabetes mellitus **AND** • Medication is being used as an adjunct to a reduced-calorie diet and increased physical activity **AND** • Dose is limited to 3 mg per day **AND** • Quantity is limited to 5 pens per 30 days **AND** • Medication is not being used concurrently with other medications intended for weight loss (e.g., Alli, benzphetamine, Contrave, diethylpropion, Foundayo, phendimetrazine, phentermine, phentermine and topiramate extended-release, Qsymia, Saxenda, Wegovy, Xenical, and Zepbound) **Generic liraglutide 18 mg/3 mL pen may be considered medically necessary for chronic weight management in pediatric individuals when all the following criteria are met:** • The individual is aged between 12 and 17 years **AND** • Has engaged in a trial of behavioral modification and dietary restriction for at least 3 months **AND** • Currently has a BMI greater than or equal to 95th percentile for age and sex (see **Appendix**) **AND** • Medication is being used as an adjunct to a reduced-calorie diet and increased physical activity **AND** • Dose is limited to 3 mg per day

Drug	Medical Necessity
	AND • Quantity is limited to 5 pens per 30 days **AND** • Medication is not being used concurrently with other medications intended for weight loss (e.g., Alli, benzphetamine, Contrave, diethylpropion, Foundayo, phendimetrazine, phentermine, phentermine and topiramate extended-release, Qsymia, Saxenda, Wegovy, Xenical, and Zepbound) **Note:** Drugs for weight management are excluded under many benefit plans. Therefore, the use of generic liraglutide 18 mg/3 mL pen for weight management may not be covered. Please refer to the applicable benefit plan document to determine benefit availability (see **Benefit Application** for further information).
Generic phentermine and topiramate extended-release • **Chronic weight management (adults)** • **Chronic weight management (pediatrics)**	**Generic phentermine and topiramate extended-release may be considered medically necessary for chronic weight management when all the following criteria are met:** • The individual is aged 18 years or older **AND** • Has engaged in a trial of behavioral modification and dietary restriction for at least 3 months **AND** • Has a body mass index (BMI) of greater than or equal to 30 kg/m^2 **OR** • Has a BMI of greater than or equal to 27 kg/m^2 and one or more of the following weight-related comorbid conditions: ○ Asthma ○ Cardiovascular disease ○ Chronic obstructive pulmonary disease (COPD) ○ Coronary artery disease ○ Dyslipidemia ○ Hypertension ○ Knee osteoarthritis ○ Metabolic-dysfunction associated steatotic liver disease/non-alcoholic fatty liver disease

Drug	Medical Necessity
	○ Obstructive sleep apnea ○ Polyendocrine metabolic ovarian syndrome (PMOS) ○ Type 2 diabetes mellitus **AND** • Medication is being used as an adjunct to a reduced-calorie diet and increased physical activity **AND** • Dose is limited to 15 mg/92 mg daily (1 capsule daily) **AND** • Medication is not being used concurrently with other medications intended for weight loss (e.g., Alli, benzphetamine, Contrave, diethylpropion, Foundayo, liraglutide 18 mg/3 mL pen, phendimetrazine, phentermine, Saxenda, Wegovy, Xenical, and Zepbound) **Generic phentermine and topiramate extended-release may be considered medically necessary for chronic weight management in pediatric individuals when all the following criteria are met:** • The individual is aged between 12 and 17 years **AND** • Has engaged in a trial of behavioral modification and dietary restriction for at least 3 months **AND** • Currently has a BMI greater than or equal to 95th percentile for age and sex (see **Appendix**) **AND** • Medication is being used as an adjunct to a reduced-calorie diet and increased physical activity **AND** • Dose is limited to 15 mg/92 mg capsule daily (1 capsule daily) **AND** • Medication is not being used concurrently with other medications intended for weight loss (e.g., Alli, benzphetamine, Contrave, diethylpropion, Foundayo, liraglutide 18 mg/3 mL pen, phendimetrazine, phentermine, Saxenda, Wegovy, Xenical, and Zepbound)

Drug	Medical Necessity
	Note: Drugs for weight management are excluded under many benefit plans. Therefore, the use of generic phentermine and topiramate extended-release for weight management may not be covered. Please refer to the applicable benefit plan document to determine benefit availability (see **Benefit Application** for further information).
Qsymia (phentermine and topiramate extended-release) • **Chronic weight management (adults)** • **Chronic weight management (pediatrics)**	**Qsymia (phentermine and topiramate extended-release) may be considered medically necessary for chronic weight management when all the following criteria are met:** • The individual is aged 18 years or older **AND** • Has engaged in a trial of behavioral modification and dietary restriction for at least 3 months **AND** • Has a body mass index (BMI) of greater than or equal to 30 kg/m^2 **OR** • Has a BMI of greater than or equal to 27 kg/m^2 and one or more of the following weight-related comorbid conditions: ○ Asthma ○ Cardiovascular disease ○ Chronic obstructive pulmonary disease (COPD) ○ Coronary artery disease ○ Dyslipidemia ○ Hypertension ○ Knee osteoarthritis ○ Metabolic-dysfunction associated steatotic liver disease/non-alcoholic fatty liver disease ○ Obstructive sleep apnea ○ Polyendocrine metabolic ovarian syndrome (PMOS) ○ Type 2 diabetes mellitus **AND** • Medication is being used as an adjunct to a reduced-calorie diet and increased physical activity **AND**

Drug	Medical Necessity
	• Has tried and had an inadequate response or intolerance to generic phentermine and topiramate extended-release **AND** • Dose is limited to 15 mg/92 mg daily (1 capsule daily) **AND** • Medication is not being used concurrently with other medications intended for weight loss (e.g., Alli, benzphetamine, Contrave, diethylpropion, Foundayo, liraglutide 18 mg/3 mL pen, phendimetrazine, phentermine, Saxenda, Wegovy, Xenical, and Zepbound) **Qsymia (phentermine and topiramate extended-release) may be considered medically necessary for chronic weight management in pediatric individuals when all the following criteria are met:** • The individual is aged between 12 and 17 years **AND** • Has engaged in a trial of behavioral modification and dietary restriction for at least 3 months **AND** • Currently has a BMI greater than or equal to 95th percentile for age and sex (see **Appendix**) **AND** • Medication is being used as an adjunct to a reduced-calorie diet and increased physical activity **AND** • Has tried and had an inadequate response or intolerance to generic phentermine and topiramate extended-release **AND** • Dose is limited to 15 mg/92 mg daily (1 capsule daily) **AND** • Medication is not being used concurrently with other medications intended for weight loss (e.g., Alli, benzphetamine, Contrave, diethylpropion, Foundayo, liraglutide 18 mg/3 mL pen, phendimetrazine, phentermine, Saxenda, Wegovy, Xenical, and Zepbound)

Drug	Medical Necessity
	Note: Drugs for weight management are excluded under many benefit plans. Therefore, the use of Qsymia (phentermine and topiramate extended-release) for weight management may not be covered. Please refer to the applicable benefit plan document to determine benefit availability (see **Benefit Application** for further information).
Saxenda (liraglutide) • **Chronic weight management (adults)** • **Chronic weight management (pediatrics)**	**Saxenda (liraglutide) may be considered medically necessary for chronic weight management in adult individuals when all the following criteria are met:** • The individual is aged 18 years or older **AND** • Has engaged in a trial of behavioral modification and dietary restriction for at least 3 months **AND** • Has a body mass index (BMI) of greater than or equal to 30 kg/m^2 **OR** • Has a BMI of greater than or equal to 27 kg/m^2 and one or more of the following weight-related comorbid conditions: ○ Asthma ○ Cardiovascular disease ○ Chronic obstructive pulmonary disease (COPD) ○ Coronary artery disease ○ Dyslipidemia ○ Hypertension ○ Knee osteoarthritis ○ Metabolic-dysfunction associated steatotic liver disease/non-alcoholic fatty liver disease ○ Obstructive sleep apnea ○ Polyendocrine metabolic ovarian syndrome (PMOS) ○ Type 2 diabetes mellitus **AND** • Medication is being used as an adjunct to a reduced-calorie diet and increased physical activity **AND**

Drug	Medical Necessity
	• Has tried and had an inadequate response or intolerance to generic liraglutide 18 mg/3 mL pen **AND** • Dose is limited to 3 mg per day **AND** • Quantity is limited to 5 pens per 30 days **AND** • Medication is not being used concurrently with other medications intended for weight loss (e.g., Alli, benzphetamine, Contrave, diethylpropion, Foundayo, liraglutide 18 mg/3 mL pen, phendimetrazine, phentermine, phentermine and topiramate extended-release, Qsymia, Wegovy, Xenical, and Zepbound) **Saxenda (liraglutide) may be considered medically necessary for chronic weight management in pediatric individuals when all the following criteria are met:** • The individual is aged between 12 and 17 years **AND** • Has engaged in a trial of behavioral modification and dietary restriction for at least 3 months **AND** • Currently has a BMI greater than or equal to 95th percentile for age and sex (see **Appendix**) **AND** • Medication is being used as an adjunct to a reduced-calorie diet and increased physical activity **AND** • Has tried and had an inadequate response or intolerance to generic liraglutide 18 mg/3 mL pen **AND** • Dose is limited to 3 mg per day **AND** • Quantity is limited to 5 pens per 30 days **AND**

Drug	Medical Necessity
	• Medication is not being used concurrently with other medications intended for weight loss (e.g., Alli, benzphetamine, Contrave, diethylpropion, Foundayo, liraglutide 18 mg/3 mL pen, phendimetrazine, phentermine, phentermine and topiramate extended-release, Qsymia, Wegovy, Xenical, and Zepbound) **Note:** Drugs for weight management are excluded under many benefit plans. Therefore, the use of Saxenda (liraglutide) for weight management may not be covered. Please refer to the applicable benefit plan document to determine benefit availability (see **Benefit Application** for further information).
Wegovy (semaglutide) injection • **Chronic weight management (adults)** • **Chronic weight management (pediatrics)** • **Reduce risk of major adverse cardiovascular events (MACE) with established cardiovascular disease and either obesity or overweight** • **Noncirrhotic metabolic dysfunction-associated steatohepatitis (MASH)** **Wegovy HD (semaglutide) injection** • **Chronic weight management (adults)**	**Wegovy and Wegovy HD (semaglutide) injection may be considered medically necessary for chronic weight management when all the following criteria are met:** • The individual is aged 18 years or older **AND** • Has engaged in a trial of behavioral modification and dietary restriction for at least 3 months **AND** • Has a body mass index (BMI) of greater than or equal to 30 kg/m^2 **OR** • Has a BMI of greater than or equal to 27 kg/m^2 and one or more of the following weight-related comorbid conditions: ○ Asthma ○ Cardiovascular disease ○ Chronic obstructive pulmonary disease (COPD) ○ Coronary artery disease ○ Dyslipidemia ○ Hypertension ○ Knee osteoarthritis ○ Metabolic-dysfunction associated steatotic liver disease/non-alcoholic fatty liver disease ○ Obstructive sleep apnea ○ Polyendocrine metabolic ovarian syndrome (PMOS)

Drug	Medical Necessity
	○ Type 2 diabetes mellitus **AND** • Medication is being used as an adjunct to a reduced-calorie diet and increased physical activity **AND** • Dose is limited to 7.2 mg once weekly **AND** • Quantity is limited to 4 pens per 28 days **AND** • Medication is not being used concurrently with other medications intended for weight loss (e.g., Alli, benzphetamine, Contrave, diethylpropion, Foundayo, liraglutide 18 mg/3 mL pen, phendimetrazine, phentermine, phentermine and topiramate extended-release, Qsymia, Saxenda, Wegovy tablets, Xenical, and Zepbound) **Wegovy (semaglutide) injection may be considered medically necessary for chronic weight management in pediatric individuals when all the following criteria are met:** • The individual is aged between 12 and 17 years **AND** • Has engaged in a trial of behavioral modification and dietary restriction for at least 3 months **AND** • Currently has a BMI greater than or equal to 95th percentile for age and sex (see **Appendix**) **AND** • Medication is being used as an adjunct to a reduced-calorie diet and increased physical activity **AND** • Dose is limited to 2.4 mg once weekly **AND** • Quantity is limited to 4 pens per 28 days **AND** • Medication is not being used concurrently with other medications intended for weight loss (e.g., Alli, benzphetamine,

Drug	Medical Necessity

	Contrave, diethylpropion, Foundayo, liraglutide 18 mg/3 mL pen, phendimetrazine, phentermine, phentermine and topiramate extended-release, Qsymia, Saxenda, Wegovy tablets, Xenical, and Zepbound)
	
	Wegovy (semaglutide) injection may be considered medically necessary to reduce the risk of major adverse cardiovascular events (MACE) in adults with established cardiovascular disease and either obesity or overweight when all the following criteria are met:
	• The individual is aged 18 years or older
	AND
	• Has a body mass index (BMI) of greater than or equal to 27 kg/m^2
	AND
	• Meets 1 of the following:
	  ○ Has experienced a prior heart attack or stroke
	  ○ Has a history of symptomatic peripheral arterial disease as evidenced by one of the following:
	  ▪ Intermittent claudication with ankle-brachial index less than 0.85
	  ▪ Peripheral arterial revascularization procedure
	  ▪ Amputation due to atherosclerotic disease
	AND
	• Medication is used in combination with optimized drug therapy for established cardiovascular disease
	AND
	• Medication is being used as an adjunct to a reduced-calorie diet and increased physical activity
	AND
	• Dose is limited to 2.4 mg once weekly
	AND
	• Quantity is limited to 4 pens per 28 days
	AND
	• Medication is not being used concurrently with other medications intended for weight loss (e.g., Alli, benzphetamine,

Drug	Medical Necessity

	Contrave, diethylpropion, Foundayo, liraglutide 18 mg/3 mL pen, phendimetrazine, phentermine, phentermine and topiramate extended-release, Qsymia, Saxenda, Wegovy tablets, Xenical, and Zepbound)
	
	Wegovy (semaglutide) injection may be considered medically necessary for the treatment of adult individuals with noncirrhotic metabolic dysfunction-associated steatohepatitis (MASH) when all the following criteria are met:
	• The individual is aged 18 years or older
	AND
	• Has evidence of stage F2 or F3 fibrosis confirmed by 1 of the following:
	  ○ Liver biopsy from within 3 years preceding treatment
	  ○ Vibration-controlled transient elastography (VCTE) within 6 months preceding treatment
	  ○ Magnetic resonance elastography (MRE) within 6 months preceding treatment
	  ○ Enhanced Liver Fibrosis (ELF) test within 6 months preceding treatment
	AND
	• Has 1 or more of the following metabolic risk factors that are managed according to standard of care:
	  ○ Elevated fasting plasma glucose indicative of diabetes or pre-diabetes
	  ○ Hypertension
	  ○ Hypertriglyceridemia
	  ○ Obesity
	  ○ Reduced high-density lipoprotein (HDL) cholesterol
	AND
	• Meets 1 of the following:
	  ○ Consumes 15 standard drinks or less per week if male
	  ○ Consumes 10 standard drinks or less per week if female
	AND
	• Does not have cirrhosis (F4)
	AND

Drug	Medical Necessity
	• Medication is being used as an adjunct to a reduced-calorie diet and increased physical activity **AND** • Wegovy (semaglutide) will not be started at the same time as Rezdiffra (resmetirom) for the treatment of MASH **AND** • Medication is not being used concurrently with medications intended for weight loss (e.g., Alli, benzphetamine, Contrave, diethylpropion, Foundayo, liraglutide 18 mg/3 mL pen, phendimetrazine, phentermine, phentermine and topiramate extended-release, Qsymia, Saxenda, Wegovy tablets, Xenical, and Zepbound) **AND** • Medication is prescribed by or in consultation with an endocrinologist, gastroenterologist, or hepatologist **AND** • The dose is limited to 2.4 mg once weekly **AND** • The quantity is limited to 4 pens per 28 days **Note:** Drugs for weight management are excluded under many benefit plans. Therefore, the use of Wegovy (semaglutide) for weight management may not be covered. Please refer to the applicable benefit plan document to determine benefit availability (see **Benefit Application** for further information).
Wegovy (semaglutide) tablets • **Chronic weight management (adults)** • **Reduce risk of major adverse cardiovascular events (MACE) with established cardiovascular disease and either obesity or overweight**	**Wegovy (semaglutide) tablets may be considered medically necessary for chronic weight management when all the following criteria are met:** • The individual is aged 18 years or older **AND** • Has engaged in a trial of behavioral modification and dietary restriction for at least 3 months **AND** • Has a body mass index (BMI) of greater than or equal to 30 kg/m^2 **OR**

Drug	Medical Necessity

	• Has a BMI of greater than or equal to 27 kg/m^2 and one or more of the following weight-related comorbid conditions:
	  ○ Asthma
	  ○ Cardiovascular disease
	  ○ Chronic obstructive pulmonary disease (COPD)
	  ○ Coronary artery disease
	  ○ Dyslipidemia
	  ○ Hypertension
	  ○ Knee osteoarthritis
	  ○ Metabolic-dysfunction associated steatotic liver disease/non-alcoholic fatty liver disease
	  ○ Obstructive sleep apnea
	  ○ Polyendocrine metabolic ovarian syndrome (PMOS)
	  ○ Type 2 diabetes mellitus
	AND
	• Medication is being used as an adjunct to a reduced-calorie diet and increased physical activity
	AND
	• Dose is limited to 25 mg daily
	AND
	• Quantity is limited to 30 tablets per 30 days
	AND
	• Medication is not being used concurrently with other medications intended for weight loss (e.g., Alli, benzphetamine, Contrave, diethylpropion, Foundayo, liraglutide 18 mg/3 mL pen, phendimetrazine, phentermine, phentermine and topiramate extended-release, Qsymia, Saxenda, Wegovy injection, Xenical, and Zepbound)
	
	Wegovy (semaglutide) tablets may be considered medically necessary to reduce the risk of major adverse cardiovascular events (MACE) in adults with established cardiovascular disease and either obesity or overweight when all the following criteria are met:
	• The individual is aged 18 years or older
	AND

Drug	Medical Necessity

	• Has a body mass index (BMI) of greater than or equal to 27 kg/m^2
	AND
	• Meets one of the following:
	  ○ Has experienced a prior heart attack or stroke
	  ○ Has a history of symptomatic peripheral arterial disease as evidenced by one of the following:
	  ▪ Intermittent claudication with ankle-brachial index less than 0.85
	  ▪ Peripheral arterial revascularization procedure
	  ▪ Amputation due to atherosclerotic disease
	AND
	• Medication is used in combination with optimized drug therapy for established cardiovascular disease
	AND
	• Medication is being used as an adjunct to a reduced-calorie diet and increased physical activity
	AND
	• Dose is limited to 25 mg daily
	AND
	• Quantity is limited to 30 tablets per 30 days
	AND
	• Medication is not being used concurrently with other medications intended for weight loss (e.g., Alli, benzphetamine, Contrave, diethylpropion, Foundayo, liraglutide 18 mg/3 mL pen, phendimetrazine, phentermine, phentermine and topiramate extended-release, Qsymia, Saxenda, Wegovy injection, Xenical, and Zepbound)
	
	Note: Drugs for weight management are excluded under many benefit plans. Therefore, the use of Wegovy (semaglutide) for weight management may not be covered. Please refer to the applicable benefit plan document to determine benefit availability (see **Benefit Application** for further information).

Drug	Medical Necessity
Xenical (orlistat), brand orlistat • **Chronic weight management (adults)** • **Chronic weight management (pediatrics)**	**Xenical (orlistat) and brand orlistat may be considered medically necessary for chronic weight management in adult individuals when all the following criteria are met:** • The individual is aged 18 years or older **AND** • Has engaged in a trial of behavioral modification and dietary restriction for at least 3 months **AND** • Has a body mass index (BMI) of greater than or equal to 30 kg/m^2 **OR** • Has a BMI of greater than or equal to 27 kg/m^2 and one or more of the following weight-related comorbid conditions: ○ Asthma ○ Cardiovascular disease ○ Chronic obstructive pulmonary disease (COPD) ○ Coronary artery disease ○ Dyslipidemia ○ Hypertension ○ Knee osteoarthritis ○ Metabolic-dysfunction associated steatotic liver disease/non-alcoholic fatty liver disease ○ Obstructive sleep apnea ○ Polyendocrine metabolic ovarian syndrome (PMOS) ○ Type 2 diabetes mellitus **AND** • Medication is being used as an adjunct to a reduced-calorie diet and increased physical activity **AND** • Dose is limited to three 120 mg capsules daily (taken as one capsule three times a day) **AND** • Medication is not being used concurrently with other medications intended for weight loss (e.g., Alli, benzphetamine, Contrave, diethylpropion, Foundayo, liraglutide 18 mg/3 mL pen, phendimetrazine, phentermine, phentermine and

Drug	Medical Necessity
	topiramate extended-release, Qsymia, Saxenda, Wegovy, and Zepbound) **Xenical (orlistat) and brand orlistat may be considered medically necessary for chronic weight management in pediatric individuals when all the following criteria are met:** • The individual is aged between 12 and 17 years **AND** • Has engaged in a trial of behavioral modification and dietary restriction for at least 3 months **AND** • Currently has a BMI greater than or equal to 95th percentile for age and sex (see **Appendix**) **AND** • Medication is being used as an adjunct to a reduced-calorie diet and increased physical activity **AND** • Dose is limited to three 120 mg capsules daily (taken as one capsule three times a day) **AND** • Medication is not being used concurrently with other medications intended for weight loss (e.g., Alli, benzphetamine, Contrave, diethylpropion, Foundayo, liraglutide 18 mg/3 mL pen, phendimetrazine, phentermine, phentermine and topiramate extended-release, Qsymia, Saxenda, Wegovy, and Zepbound) **Note:** Drugs for weight management are excluded under many benefit plans. Therefore, the use of Xenical (orlistat) or brand orlistat for weight management may not be covered. Please refer to the applicable benefit plan document to determine benefit availability (see Benefit Application for further information).
Zepbound (tirzepatide) • **Chronic weight management (adults)** • **Moderate to severe obstructive sleep apnea**	**Zepbound (tirzepatide) may be considered medically necessary for chronic weight management when all the following criteria are met:** • The individual is aged 18 years or older

Drug	Medical Necessity
(OSA) in adults with obesity	**AND** • Has engaged in a trial of behavioral modification and dietary restriction for at least 3 months **AND** • Has a body mass index (BMI) of greater than or equal to 30 kg/m^2 **OR** • Has a BMI of greater than or equal to 27 kg/m^2 and one or more of the following weight-related comorbid conditions: ○ Asthma ○ Cardiovascular disease ○ Chronic obstructive pulmonary disease (COPD) ○ Coronary artery disease ○ Dyslipidemia ○ Hypertension ○ Knee osteoarthritis ○ Metabolic-dysfunction associated steatotic liver disease/non-alcoholic fatty liver disease ○ Obstructive sleep apnea ○ Polyendocrine metabolic ovarian syndrome (PMOS) ○ Type 2 diabetes mellitus **AND** • Medication is being used as an adjunct to a reduced-calorie diet and increased physical activity **AND** • Dose is limited to 15 mg once weekly **AND** • Quantity is limited: ○ 4 prefilled pens or single-dose vials per 28 days ○ 1 Kwikpen or multi-dose vial per 28 days **AND** • Medication is not being used concurrently with other medications intended for weight loss (e.g., Alli, benzphetamine, Contrave, diethylpropion, Foundayo, liraglutide 18 mg/3 mL pen, phendimetrazine, phentermine, phentermine and topiramate extended-release, Qsymia, Saxenda, Xenical, and Wegovy)

Drug	Medical Necessity

	Zepbound (tirzepatide) may be considered medically necessary for the treatment of moderate to severe obstructive sleep apnea (OSA) in adults with obesity when all the following criteria are met:
	• The individual is aged 18 years or older
	AND
	• Has a body mass index (BMI) of greater than or equal to 30 kg/m^2
	AND
	• Has had a sleep study within the past 12 months that shows an apnea-hypopnea index of at least 15 events per hour
	AND
	• Has NOT been diagnosed with any of the following conditions:
	  ○ Central sleep apnea with percent of central apneas/hypopneas at least 50%
	  ○ Cheyne Stokes respiration
	AND
	• Medication is being used as an adjunct to a reduced-calorie diet and increased physical activity
	AND
	• Dose is limited to 15 mg once weekly
	AND
	• Quantity is limited:
	  ○ 4 prefilled pens or single-dose vials per 28 days
	  ○ 1 Kwikpen or multi-dose vial per 28 days
	AND
	• Medication is not being used concurrently with other medications intended for weight loss (e.g., Alli, benzphetamine, Contrave, diethylpropion, Foundayo, liraglutide 18 mg/3 mL pen, phendimetrazine, phentermine, phentermine and topiramate extended-release, Qsymia, Saxenda, Xenical, and Wegovy)
	
	Note: Drugs for weight management are excluded under many benefit plans. Therefore, the use of Zepbound (tirzepatide) for weight management

Drug	Medical Necessity
	may not be covered. Please refer to the applicable benefit plan document to determine benefit availability (see Benefit Application for further information).

Drug	Investigational
As listed	**The medications listed in this policy are subject to the product's US Food and Drug Administration (FDA) dosage and administration prescribing information.** **All other uses of the medications listed in this policy are considered investigational.**

Length of Approval	
Approval	**Criteria**
Initial authorization	**Contrave (naltrexone/bupropion) may be approved for 4 months.** **Foundayo (orforglipron) may be approved for 7 months.** **Generic phentermine and topiramate extended-release and Qsymia (phentermine and topiramate extended-release) may be approved for 6 months.** **Liraglutide 18 mg/3 mL pen and Saxenda (liraglutide) may be approved for 4 months.** **Wegovy (semaglutide) for chronic weight management may be approved for 7 months.** **Wegovy (semaglutide) to reduce the risk of major adverse cardiovascular events (MACE) in adults with established cardiovascular disease and either obesity or overweight, and adult individuals with noncirrhotic metabolic dysfunction-associated steatohepatitis (MASH) may be approved for 12 months.**

Length of Approval	
Approval	**Criteria**
	Xenical (orlistat) and brand orlistat may be approved for 6 months. **Zepbound (tirzepatide) for chronic weight management may be approved for 7 months.** **Zepbound (tirzepatide) for the treatment of moderate to severe obstructive sleep apnea may be approved for 12 months.**
Re-authorization criteria	**All reviews for Contrave (naltrexone/bupropion) may be approved for 1 year when clinical benefit/response at the time of re-authorization show:** • Weight loss of greater than or equal to 5% baseline body weight after 15 weeks of treatment **AND** • The individual continues to adhere to a reduced-calorie diet and increased physical activity **All reviews for Foundayo (orforglipron) may be approved for 1 year when clinical benefit/response at the time of re-authorization show:** • Weight loss of greater than or equal to 5% baseline body weight after 7 months of treatment **AND** • The individual continues to adhere to a reduced-calorie diet and increased physical activity **All reviews for generic phentermine and topiramate extended-release and Qsymia (phentermine and topiramate extended-release) for adults may be approved for 1 year when clinical benefit/response at the time of re-authorization show:** • Weight loss of greater than or equal to 5% baseline body weight after 26 weeks of treatment **AND**

Length of Approval	
Approval	**Criteria**
	• The individual continues to adhere to a reduced-calorie diet and increased physical activity **All reviews for generic phentermine and topiramate extended-release and Qsymia (phentermine and topiramate extended-release) for pediatric individuals at least 12 years of age and less than 18 years of age may be approved for 1 year when clinical benefit/response at the time of re-authorization show:** • Weight loss of greater than or equal to 5% baseline BMI after 26 weeks of treatment **AND** • The individual continues to adhere to a reduced-calorie diet and increased physical activity **All reviews for liraglutide 18 mg/3 mL pen and Saxenda (liraglutide) for adults may be approved for 1 year when clinical benefit/response at the time of re-authorization show:** • Weight loss of greater than or equal to 4% baseline body weight after 16 weeks of treatment **AND** • The individual is able to tolerate the maintenance dose of 3 mg once daily **AND** • Continues to adhere to a reduced-calorie diet and increased physical activity **All reviews for liraglutide 18 mg/3 mL pen and Saxenda (liraglutide) for pediatric individuals at least 12 years of age and less than 18 years of age may be approved for 1 year when clinical benefit/response at the time of re-authorization show:** • Weight loss of greater than or equal to 1% baseline BMI after 16 weeks of treatment **AND**

Length of Approval	
Approval	**Criteria**
	• The individual is able to tolerate the maintenance dose of 2.4 mg once daily or 3 mg once daily **AND** • Continues to adhere to a reduced-calorie diet and increased physical activity **All reviews for Wegovy and Wegovy HD (semaglutide) injection for chronic weight management in adults may be approved for 1 year when clinical benefit/response at the time of re-authorization show:** • Weight loss of greater than or equal to 5% baseline body weight after 7 months of treatment **AND** • Continues to adhere to a reduced-calorie diet and increased physical activity **All reviews for Wegovy (semaglutide) injection for chronic weight management in pediatric individuals at least 12 years of age and less than 18 years of age may be approved for 1 year when clinical benefit/response at the time of re-authorization show:** • Weight loss of greater than or equal to 1% baseline BMI after 7 months of treatment **AND** • The individual is able to tolerate a Wegovy maintenance dose of 1.7 mg once weekly or 2.4 mg once weekly **AND** • Continues to adhere to a reduced-calorie diet and increased physical activity **All reviews for Wegovy (semaglutide) injection to reduce the risk of major adverse cardiovascular events (MACE) in adults with established cardiovascular disease and either obesity or**

Length of Approval	
Approval	**Criteria**

	overweight may be approved for 12 months when clinical benefit/response at the time of re-authorization show:
	• The individual is aged 18 years or older
	AND
	• At baseline prior to treatment with Wegovy (semaglutide), the individual had a body mass index (BMI) of greater than or equal to 27 kg/m^2
	AND
	• Meets one of the following:
	  ○ Has experienced a prior heart attack or stroke
	  ○ Has a history of symptomatic peripheral arterial disease as evidenced by one of the following:
	  ▪ Intermittent claudication with ankle-brachial index less than 0.85
	  ▪ Peripheral arterial revascularization procedure
	  ▪ Amputation due to atherosclerotic disease
	AND
	• Medication is used in combination with optimized drug therapy for established cardiovascular disease
	AND
	• Medication is being used as an adjunct to a reduced-calorie diet and increased physical activity
	AND
	• The dose is limited to 2.4 mg once weekly
	AND
	• Quantity is limited to 4 pens per 28 days
	AND
	• Medication is not being used concurrently with other medications intended for weight loss (e.g., Alli, benzphetamine, Contrave, diethylpropion, Foundayo, liraglutide 18 mg/3 mL pen, phendimetrazine, phentermine, phentermine and topiramate extended-release, Qsymia, Saxenda, Wegovy tablets, Xenical, and Zepbound)
	
	All reviews for Wegovy (semaglutide) injection for the treatment of adult individuals with noncirrhotic metabolic

Length of Approval	
Approval	**Criteria**

	dysfunction-associated steatohepatitis (MASH) may be approved up to 12 months as long as the drug-specific coverage criteria are met, and chart notes demonstrate that the individual continues to show a positive clinical response to therapy as documented by:
	• Has not had worsening of fibrosis or MASH
	AND
	• Metabolic risk factors are managed according to standard of care
	AND
	• Meets 1 of the following:
	  ○ Consumes 15 standard drinks or less per week if male
	  ○ Consumes 10 standard drinks or less per week if female
	AND
	• Medication is being used as an adjunct to a reduced-calorie diet and increased physical activity
	
	All reviews for Wegovy (semaglutide) tablets for chronic weight management in adults may be approved for 1 year when clinical benefit/response at the time of re-authorization show:
	• Weight loss of greater than or equal to 5% baseline body weight after 7 months of treatment
	AND
	• Is able to tolerate a Wegovy maintenance dose of 25 mg daily
	AND
	• Continues to adhere to a reduced-calorie diet and increased physical activity
	
	All reviews for Wegovy (semaglutide) tablets to reduce the risk of major adverse cardiovascular events (MACE) in adults with established cardiovascular disease and either obesity or overweight may be approved for 1 year when clinical benefit/response at the time of re-authorization show:
	• The individual is aged 18 years or older
	AND

Length of Approval	
Approval	**Criteria**

	• At baseline prior to treatment with Wegovy (semaglutide), the individual had a body mass index (BMI) of greater than or equal to 27 kg/m^2
	AND
	• Meets one of the following:
	  ○ Has experienced a prior heart attack or stroke
	  ○ Has a history of symptomatic peripheral arterial disease as evidenced by one of the following:
	  ▪ Intermittent claudication with ankle-brachial index less than 0.85
	  ▪ Peripheral arterial revascularization procedure
	  ▪ Amputation due to atherosclerotic disease
	AND
	• Medication is used in combination with optimized drug therapy for established cardiovascular disease
	AND
	• Medication is being used as an adjunct to a reduced-calorie diet and increased physical activity
	AND
	• The dose is limited to 25 mg daily
	AND
	• Quantity is limited to 30 tablets per 30 days
	AND
	• Medication is not being used concurrently with other medications intended for weight loss (e.g., Alli, benzphetamine, Contrave, diethylpropion, Foundayo, liraglutide 18 mg/3 mL pen, phendimetrazine, phentermine, phentermine and topiramate extended-release, Qsymia, Saxenda, Wegovy injection, Xenical, and Zepbound)
	
	All reviews for Xenical (orlistat) and brand orlistat for adults may be approved for 1 year when clinical benefit/response at the time of re-authorization show:
	• Weight loss of greater than or equal to 5% baseline body weight after 6 months of treatment

Length of Approval	
Approval	**Criteria**
	AND • Continues to adhere to a reduced-calorie diet and increased physical activity **All reviews for Xenical (orlistat) and brand orlistat for pediatric individuals at least 12 years of age and less than 18 years of age may be approved for 1 year when clinical benefit/response at the time of re-authorization show:** • Weight loss of greater than or equal to 5% baseline BMI after 6 months of treatment **AND** • Continues to adhere to a reduced-calorie diet and increased physical activity **All reviews for Zepbound (tirzepatide) for chronic weight management in adults may be approved for 1 year when clinical benefit/response at the time of re-authorization show:** • Weight loss of greater than or equal to 5% baseline body weight after 7 months of treatment **AND** • The individual is able to tolerate a Zepbound (tirzepatide) maintenance dose of up to 15 mg once weekly **AND** • Continues to adhere to a reduced-calorie diet and increased physical activity **All reviews for Zepbound (tirzepatide) to treat moderate to severe obstructive sleep apnea may be considered medically necessary for the treatment of moderate to severe obstructive sleep apnea (OSA) in adults with obesity when all the following criteria are met:** • The individual is aged 18 years or older **AND** • At baseline, had a body mass index (BMI) of at least 30 kg/m^2

Length of Approval	
Approval	**Criteria**
	AND • Weight loss of greater than or equal to 10% baseline body weight after 12 months of treatment **AND** • Has stability in OSA signs or symptoms such as snoring, excessive daytime sleepiness, and fatigue **AND** • Medication is being used as an adjunct to a reduced-calorie diet and increased physical activity

Documentation Requirements
The individual's medical records submitted for review for all conditions should document that medical necessity criteria are met. The record should include the following: • Office visit notes that contain the individual's baseline body weight, body mass index (BMI), relevant history including any weight-related comorbidities, dietary plan, physical activity plan, and medication dosage

Coding

N/A

Related Information

Consideration of Age

The ages stated in this policy for which Contrave (naltrexone/bupropion), Foundayo (orforglipron), generic liraglutide 18 mg/3 mL pen, generic phentermine and topiramate extended-release, Qsymia (phentermine/topiramate extended-release), Saxenda (liraglutide), Wegovy (semaglutide), Xenical (orlistat), brand orlistat, and Zepbound (tirzepatide) are considered medically necessary are based on the ages approved in the FDA labeling.

Benefit Application

Some plans provide coverage for certain medications (e.g., GLP-1s) used for weight management only when the member's body mass index (BMI) meets a specified threshold. This threshold may differ from the BMI criteria outlined in this medical policy. Please review the plan terms in your benefit booklet or contact customer service.

Dyslipidemia

Dyslipidemia can be detected by a blood test measuring different lipids levels. The optimal lipid level varies depending on the individual's age, sex, and other risk factors, but generally, the following ranges are recommended:

- LDL cholesterol: less than 100 mg/dL
- HDL cholesterol: greater than 40 mg/dL for individuals assigned male at birth and greater than 50 mg/dL for individuals assigned female at birth
- Triglycerides: less than 150 mg/dL
- Total cholesterol: less than 200 mg/dL

Criteria for Diagnosis of Prediabetes and Diabetes in Nonpregnant Individuals

Test	Prediabetes	Diabetes
A1C	5.7% - 6.4%	6.5% or higher
Fasting Plasma Glucose (FPG)	100 mg/dl to 125 mg/dL	126 mg/dL or higher
Oral Glucose Tolerance Test (OGTT)	140 to 199 mg/dL	200 mg/dL or higher
Random Plasma Glucose Test		In an individual with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose ≥200 mg/dL (≥11.1 mmol/L). Random is any time of the day without regard to time since previous meal.

American Diabetes Association Standards of Care

Lifestyle Behavior Change and Pharmacologic Interventions for Prevention or Delay of Diabetes and Associated Comorbidities Recommendations:

- Refer adults with overweight or obesity at high risk of type 2 diabetes, as seen in the Diabetes Prevention Program (DPP), to an intensive lifestyle behavior change program to achieve and maintain a weight reduction of at least 7% of initial body weight through healthy reduced-calorie diet and ≥150 min/week of moderate-intensity physical activity.
- Prescribe an eating pattern known to be effective in preventing type 2 diabetes to individuals with prediabetes. A variety of eating patterns, such as Mediterranean style, intermittent fasting, and low carbohydrate, have shown benefit.
- Given the cost-effectiveness of lifestyle behavior modification programs for diabetes prevention, such diabetes prevention programs should be offered to adults at high risk of type 2 diabetes.
- Metformin for the prevention of type 2 diabetes should be considered in adults at high risk of type 2 diabetes, as typified by the DPP, especially those aged 25–59 years with BMI ≥35 kg/m^2, higher fasting plasma glucose (e.g., ≥110 mg/dL [≥6 mmol/L]), and higher A1C (e.g., ≥6.0% [≥42 mmol/mol]), and in individuals with prior gestational diabetes mellitus.

Pharmacologic Therapy for Adults with Type 2 Diabetes:

A person-centered shared decision-making approach should guide the choice of glucose-lowering medications for adults with type 2 diabetes. Use medications that provide sufficient effectiveness to achieve and maintain intended treatment goals with consideration of the effects on cardiovascular, kidney, weight, and other relevant comorbidities; hypoglycemia risk; cost and access; risk for adverse reactions and tolerability; and individual preferences. Medications for glucose lowering in type 2 diabetes may include:

- Metformin
- Sodium-Glucose Cotransporter 2 (SGLT2) Inhibitors: bexagliflozin, canagliflozin, dapagliflozin, empagliflozin, ertugliflozin
- Glucagon-Like Peptide-1 Receptor Agonist (GLP-1 RA): dulaglutide, liraglutide, semaglutide

- Dual Glucose-Dependent Insulinotropic Polypeptide (GIP) and Glucagon-Like Peptide-1 Receptor Agonist (GLP-1 RA): tirzepatide
- Dipeptidyl Peptidase 4 (DPP-4) inhibitors: alogliptin, linagliptin, saxagliptin, sitagliptin
- Pioglitazone
- Sulfonylureas (2nd generation): glimepiride, glipizide, glyburide
- Insulin

American College of Cardiology/American Heart Association Hypertension Definitions and Staging System

Definitions	Blood Pressure (mmHg)
Stage 1 Hypertension	Systolic 130 to 139 mmHg or diastolic 80 to 89 mmHg
Stage 2 Hypertension	Systolic ≥140 mmHg or diastolic ≥90 mmHg
Severe Hypertension	Systolic >180 mmHg or diastolic >120 mmHg

American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines

Lifestyle and Psychosocial Approaches

- In adults who have overweight or obesity, weight loss is recommended with a goal of at least 5% of body weight reduction to prevent or treat elevated blood pressure and hypertension
- In adults with or without hypertension, a heart-healthy eating pattern, such as the DASH eating plan, is recommended to prevent or treat elevated blood pressure and hypertension
- In adults with or without hypertension, increasing physical activity, through a structured exercise program that includes aerobic exercise and/or resistance training, is recommended to prevent or treat elevated blood pressure and hypertension

Medical Management of Blood Pressure

The decision to initiate antihypertensive treatment should be based on blood pressure (BP) level and risk for cardiovascular disease (CVD). Based on BP level alone, all adults with hypertension benefit from antihypertensive therapy at a threshold of ≥140/90 mm Hg. Adults with hypertension and clinical CVD (coronary heart disease, stroke, or HF) are at increased risk for CVD events and benefit from antihypertensive therapy at a lower BP threshold of ≥130/80 mm Hg to prevent recurrent events. Among adults without clinical CVD, identification of individuals at increased risk for CVD selects those who derive greatest benefit from antihypertensive therapy at a threshold of ≥130/80 mm Hg. When initiating pharmacological therapy, primary consideration should be given to comorbidities (e.g., coronary artery disease, HF, stroke, diabetes, CKD) for which specific BP-lowering medication classes are indicated. Initial medication management may include the following:

- Angiotensin-Converting Enzyme (ACE) Inhibitor: benazepril, captopril, enalapril, fosinopril, lisinopril, moexipril, perindopril, quinapril, ramipril, trandolapril
- Angiotensin II Receptor Blocker (ARB): azilsartan, candesartan, eprosartan, irbesartan, losartan, olmesartan, telmisartan, valsartan
- Calcium Channel Blocker (CCB)-dihydropyridines: amlodipine, felodipine, isradipine, nicardipine LA and SR, nisoldipine
- CCB-nondihydropyridines: diltiazem ER, verapamil IR/SR/delayed onset ER
- Diuretics
    - Aldosterone antagonist: eplerenone, spironolactone
    - Loop: bumetanide, furosemide, torsemide
    - Potassium sparing: amiloride, triamterene
    - Thiazide-type: chlorthalidone, hydrochlorothiazide, indapamide
- Beta blockers
    - Cardioselective: atenolol, betaxolol, bisoprolol, metoprolol tartrate, metoprolol succinate
    - Cardioselective and vasodilatory: nebivolol
    - Non-cardioselective: nadolol, propranolol IR, propranolol LA
    - Intrinsic sympathomimetic activity: acebutolol, penbutolol, pindolol

- Combined alpha and beta blockers: carvedilol, labetalol
- Direct renin inhibitor: aliskiren
- Alpha-1 blockers: doxazosin, prazosin, terazosin
- Central alpha-2-agonist and other centrally acting drugs: clonidine, methyldopa, guanfacine
- Direct vasodilators: hydralazine, minoxidil
- Dual endothelin receptor antagonist: aprocitentan

CDC Classification of Obesity in Adults

BMI Category	BMI Range (kg/m^2)
Obesity	30 or greater
Class 1 Obesity	30 to less than 35
Class 2 Obesity	35 to less than 40
Class 3 Obesity	40 or greater

American Association for the Study of Liver Diseases (AASLD) Practice Guidance: Liver Protective Healthy Behaviors and Lifestyle Interventions

- Weight loss improves hepatic steatosis, NASH, and hepatic fibrosis in a dose-dependent manner.
- Individuals with NAFLD who are overweight or obese should be prescribed a diet that leads to a caloric deficit. When possible, diets with limited carbohydrates and saturated fat and enriched with high fiber and unsaturated fats (e.g., Mediterranean diet) should be encouraged due to their additional cardiovascular benefits.
- Individuals with NAFLD should be strongly encouraged to increase their activity level to the extent possible. Individualized prescriptive exercise recommendations may increase sustainability and have benefits independent of weight loss.

American Association for the Study of Liver Diseases (AASLD) Guidance Statements Lipid Lowering Medications

- Statins are safe and recommended for cardiovascular disease (CVD) risk reduction in individuals with NAFLD across the disease spectrum, including compensated cirrhosis.
- Limited data exist on the safety and efficacy of statins in individuals with decompensated cirrhosis, although statin use with careful monitoring could be considered in individuals with high CVD risk.
- Hypertriglyceridemia can be managed through lifestyle changes and supplementation with omega-3 fatty acids, icosapent ethyl, or fibrates.

Evidence Review

Summary of Evidence

Contrave (naltrexone/bupropion)

The effects of Contrave on weight loss in conjunction with reduced caloric intake and increased physical activity was studied in double-blind, placebo-controlled trials (BMI range 27 to 45 kg/m^2) with study durations of 16 to 56 weeks randomized to naltrexone and/or bupropion or placebo.

Four 56-week multicenter, double-blind, placebo-controlled obesity trials (Contrave Obesity Research, or COR-I, COR-II, COR-BMOD, and COR-Diabetes) were conducted to evaluate the effect of Contrave in conjunction with lifestyle modification in 4,536 individuals randomized to Contrave or placebo. The COR-I, COR-II, and COR-BMOD trials enrolled individuals with obesity (BMI 30 kg/m^2 or greater) or overweight (BMI 27 kg/m^2 or greater) and at least one comorbidity (hypertension or dyslipidemia). The COR-Diabetes trial enrolled individuals with BMI greater than 27 kg/m^2 with type 2 diabetes with or without hypertension and/or dyslipidemia.

Treatment was initiated with a three-week dose-escalation period followed by approximately 1 year of continued therapy. Individuals were instructed to take Contrave with food. COR-I and COR-II included a program consisting of a reduced-calorie diet resulting in an approximate 500 kcal/day decrease in caloric intake, behavioral counseling, and increased physical activity. COR-

BMOD included an intensive behavioral modification program consisting of 28 group counseling sessions over 56 weeks as well as a prescribed diet and exercise regimen. COR-Diabetes evaluated individuals with type 2 diabetes not achieving glycemic goal of a HbA1c less than 7% either with oral antidiabetic agents or with diet and exercise alone. Of the overall population from these four trials, 24% had hypertension, 54% had dyslipidemia at study entry, and 10% had type 2 diabetes.

The co-primary endpoints were percent change from baseline body weight and the proportion of individuals achieving at least a 5% reduction in body weight. In the 56-week COR-I trial, the mean change in body weight was -5.4% among individuals assigned to Contrave 32 mg/360 mg compared with -1.3% among individuals assigned to placebo (Intent-To-Treat [ITT] population). In this trial, the achievement of at least a 5% reduction in body weight from baseline occurred more frequently for individuals treated with Contrave 32 mg/360 mg compared with placebo (42% vs 17%). The percentages of individuals who achieved at least 5% or at least 10% body weight loss from baseline were greater among those assigned to Contrave, compared with placebo, in all four obesity trials

Safety

Contrave has a boxed warning regarding suicidal thoughts and behaviors. Contrave contains the antidepressant bupropion and individuals with major depressive disorder, both adult and pediatric, may experience worsening of their depression and/or the emergence of suicidal ideation and behavior (suicidality) or unusual changes in behavior, whether or not they are taking antidepressant medications, and this risk may persist until significant remission occurs. In placebo-controlled clinical trials with Contrave for the treatment of obesity in adult individuals, no suicides or suicide attempts were reported in studies up to 56 weeks duration with Contrave (equivalent to bupropion doses of 360 mg/day). In these same studies, suicidal ideation was reported by 3 (0.20%) of 1,515 individuals treated with placebo compared with 1 (0.03%) of 3,239 treated with Contrave.

In Contrave clinical trials, 24% of subjects receiving Contrave and 12% of subjects receiving placebo discontinued treatment because of an adverse event. The most frequent adverse reactions leading to discontinuation with Contrave were nausea (6.3%), headache (1.7%) and vomiting (1.1%). The top 5 adverse reactions among individuals' treatment with Contrave and more common than placebo are nausea (32.5% vs. 6.7%), constipation (19.2% vs. 7.2%), headache (17.6% vs. 10.4%), vomiting (10.7% vs. 2.9%), and dizziness (9.9% vs. 3.4%).

Foundayo (orforglipron)

Foundayo (orforglipron) is a once-daily small molecule (non-peptide) oral GLP-1 RA. The effectiveness of Foundayo was established in combination with a reduced-calorie diet and increased physical activity to reduce excess body weight and maintain weight reduction long term in adults with obesity or adults with overweight in the presence of at least one weight-related comorbid condition based on adequate and well-controlled trials of an investigational orforglipron formulation (Trials 1 and 2). Labeling presents efficacy data from administration of the investigational orforglipron formulation shown as equivalent dosages of once daily Foundayo. It was studied in two randomized, double-blind, placebo-controlled trials (Trials 1 and 2) in adults aged 18 years and older. In these trials, all individuals received standard lifestyle intervention which included instruction on reduced-calorie diet and physical activity counseling (recommended minimum of 150 minutes/week) that began with the first dose of trial medication or placebo and continued throughout the trials. The ATTAIN-1 was a multicenter, randomized, double-blind, placebo-controlled, 72-week Phase 3 trial.8 Individuals (N=3,127) were randomized to Foundayo 6, 12, or 36 mg or placebo. Of note, the doses of Foundayo were referred to as 5.5, 9, or 17.2 mg in the PI.1 Doses of Foundayo were titrated in monthly increments with the 36 mg arm reaching the intended dose at 20 weeks. All individuals received lifestyle counseling; however, a hypocaloric diet was not implemented. Included individuals were adults with BMI ≥30 kg/m2 or BMI 27-30 kg/m2 with ≥1 obesity complication (hypertension, dyslipidemia, CVD, obstructive sleep apnea) and history of ≥1 unsuccessful attempt at weight loss. Individuals with T2DM were excluded. At baseline, the mean BMI was 37 kg/m2. The primary endpoint of change in body weight from baseline at 72 weeks was significantly greater with all doses of Foundayo (-7.5% to -11.2%) vs placebo (-2.1%) ($p<0.001$ all comparisons). Weight reduction of ≥10% occurred in 33.3%, 40%, and 54.6% of individuals in the 6, 12, and 36 mg Foundayo arms compared to 12.9% with placebo; weight reduction of ≥20% occurred in 6.4%, 9%, 18.4%, and 2.8% respectively. The secondary endpoints of change in SBP, triglycerides, and non-HDL cholesterol were significantly reduced with pooled Foundayo vs placebo ($p<0.001$ all comparisons). The ATTAIN-2 trial was a similarly designed multicenter, randomized, double-blind, placebo-controlled, 72-week Phase III trial. Individuals (N=1,613) were randomized to Foundayo 6, 12, or 36 mg, or to placebo and given lifestyle counseling without implementing a hypocaloric diet. The trials differed in inclusion criteria. The ATTAIN-2 trial included adults with BMI ≥27 kg/m2 and T2DM with HbA1c 7%-10%, and a history of an unsuccessful attempt at weight loss. The mean baseline BMI was 35.6 kg/m2. The primary endpoint of change in weight from baseline to week 72 was significantly greater with all doses of Foundayo (-5.1% to -9.6%) compared to placebo (-2.5%) ($p<0.0001$ all comparisons). Weight reduction of ≥15% occurred in 6.8%, 14.4%, and 26% of individuals in the 6, 12, and 36 mg Foundayo arms compared to 3% with placebo. The key secondary endpoint of change in HbA1c was significantly greater with

Foundayo (-1.22% to -1.66%) than placebo (0.47%) (p<0.0001 all comparisons). Significant improvements in other secondary endpoints of change in SBP, triglycerides, and non-HDL cholesterol were also significantly greater with Foundayo s placebo (p=0.0002, <0.0001, and 0.0124, respectively).

Safety

Common adverse events (AEs) (≥20%) with Foundayo in the ATTAIN trials include gastrointestinal (GI) AEs, most commonly nausea (33.7%-36.4%), diarrhea (23.1%-27.4%), constipation (22.4%-25.4%), and vomiting (23.1%-24%) with the highest dose of Foundayo (36 mg). With the lowest dose of Foundayo (6 mg), nausea occurred in 20.1%-28.9%, diarrhea in 21%-21.3%, constipation in 17.7%-21.7%, and vomiting in 12.8%-13%. Most GI AEs were mild-moderate. Discontinuations due to AEs occurred in 8% of individuals in the ATTAIN trials with 5% due to GI AEs. Of note, discontinuations due to any cause were high in both trials (12.5%-25%), most commonly in the placebo arm (14%). No hepatic safety signals were reported in the ATTAIN trials. Increased cases of pancreatitis were noted in ATTAIN-1 but not in ATTAIN-2.

Foundayo is contraindicated in individuals with personal or family history of medullary thyroid carcinoma (MTC) or in individuals with Multiple Endocrine Neoplasia syndrome type 2. Foundayo is not recommended for use in individuals with severe hepatic impairment (Child-Pugh Class C). Foundayo may cause fetal harm; discontinue Foundayo when pregnancy is recognized.

Qsymia (phentermine/topiramate extended-release)

The effect of Qsymia on weight loss in conjunction with reduced caloric intake and increased physical activity was studied in 2 randomized, double-blind, placebo-controlled studies in obese individuals (Study 1) and in obese and overweight individuals with two or more significant co-morbidities (Study 2). Both studies had a 4-week titration period, followed by 52 weeks of treatment. There were 2 co-primary efficacy outcomes measured after 1 year of treatment (Week 56): 1) the percent weight loss from baseline; and 2) treatment response defined as achieving at least 5% weight loss from baseline.

In Study 1, obese individuals (BMI greater than or equal to 35 kg/m^2) were randomized to receive 1 year of treatment with placebo (N=514), Qsymia 3.75 mg/23 mg (N=241), or Qsymia 15 mg/92 mg (N=512) in a 2:1:2 ratio. Individuals ranged in age from 18-71 years old (mean age 43) and 83% were female. Approximately 80% were Caucasian, 18% were African American, and

15% were Hispanic/Latino. At the beginning of the study the average weight and BMI of individuals was 116 kg and 42 kg/m^2, respectively. Individuals with type 2 diabetes were excluded from participating in Study 1. During the study, a well-balanced, reduced-calorie diet to result in an approximate 500 kcal/day decrease in caloric intake was recommended to all individuals and individuals were offered nutritional and lifestyle modification counseling.

In Study 2, overweight and obese individuals were randomized to receive 1 year of treatment with placebo (N=994), Qsymia 7.5 mg/46 mg (N=498), or Qsymia 15 mg/92 mg (N=995) in a 2:1:2 ratio. Eligible individuals had to have a BMI greater than or equal to 27 kg/m^2 and less than or equal to 45 kg/m^2 (no lower limit on BMI for individuals with type 2 diabetes) and two or more of the following obesity-related co-morbid conditions:

- Elevated blood pressure (greater than or equal to 140/90 mmHg, or greater than or equal to 130/85 mmHg for diabetics) or requirement for greater than or equal to 2 antihypertensive medications;
- Triglycerides greater than 200-400 mg/dL or were receiving treatment with 2 or more lipid-lowering agents;
- Elevated fasting blood glucose (greater than 100 mg/dL) or diabetes; and/or
- Waist circumference greater than or equal to 102 cm for men or greater than or equal to 88 cm for women.

After 1 year of treatment with Qsymia, all dose levels resulted in statistically significant weight loss compared to placebo. A statistically significant greater proportion of the individuals randomized to Qsymia than placebo achieved 5% and 10% weight loss.

The effect of Qsymia on BMI in conjunction with reduced caloric intake and increased physical activity was evaluated in Study 3 (NCT 03922945), a 56-week, randomized, double-blind, placebo-controlled study in pediatric individuals (12 to 17 years of age) with BMI greater than or equal to 95th percentile standardized by age and sex. Individuals were randomized to receive treatment with placebo (N=56), Qsymia 7.5 mg/46 mg (N=54), or Qsymia 15 mg/92 mg (N=113) in a 1:1:2 ratio. During the study, a well-balanced, reduced-calorie diet to result in an approximate 500 kcal/day decrease in caloric intake was recommended to all individuals and individuals were offered a family-based lifestyle modification program for adolescents.

Individuals' mean age was 14 years old, approximately 55% were female, 67% were Caucasian, 26% were African American, and 33% were Hispanic/Latino. At the beginning of the study, the average weight and BMI of individuals was 106 kg and 38 kg/m^2, respectively, with approximately 81% considered severely obese (120% of the 95th percentile or greater for BMI

standardized by age and sex). Thirty-eight (38%) of randomized individuals withdrew from the study prior to week 56.

The primary efficacy parameter was mean percent change in BMI. After 56 weeks of treatment with Qsymia, all dose levels resulted in statistically significant reduction in BMI compared to placebo. A greater proportion of individuals randomized to Qsymia than placebo achieved 5%, 10%, and 15% BMI reduction.

Safety

Adverse reactions in adults occurring at a rate of greater than or equal to 5% and at a rate at least 1.5 times placebo include paresthesia, dizziness, dysgeusia, insomnia, constipation, and dry mouth. Adverse reactions in pediatric individuals occurring at a rate greater than or equal to 4% and higher than placebo include depression, pyrexia, dizziness, arthralgia, influenza, and ligament sprain.

Qsymia is contraindicated in pregnant individuals. The use of Qsymia can cause fetal harm and weight loss offers no clear clinical benefit to a pregnant individual. Available data from a pregnancy registry and epidemiologic studies indicate an increased risk in oral clefts (cleft lip with or without cleft palate) with first trimester exposure to topiramate, a component of Qsymia. When phentermine and topiramate were co-administered to rats at doses of 3.75 and 25 mg/kg, respectively [approximately 2 times the maximum recommended human dose (MRHD) based on area under the curve (AUC)], or at the same dose to rabbits (approximately 0.1 times and 1 time, respectively, the clinical exposures at the MRHD based on AUC), there were no drug-related malformations. However, structural malformations, including craniofacial defects and reduced fetal weights occurred in offspring of multiple species of pregnant animals administered topiramate at clinically relevant doses.

Saxenda (liraglutide)

The safety and efficacy of Saxenda for chronic weight management in conjunction with reduced caloric intake and increased physical activity were studied in three 56-week, randomized, double-blind, placebo-controlled trials. In all studies, Saxenda was titrated to 3 mg daily during a 4-week period. All individuals received instruction for a reduced calorie diet (approximately 500 kcal/day deficit) and exercise counseling (recommended increase in physical activity of minimum 150 mins/week) that began with the first dose of study medication or placebo and continued throughout the trial.

Study 1 enrolled 3731 individuals with obesity (BMI greater than or equal to 30 kg/m^2) or with overweight (BMI 27-29.9 kg/m^2) and at least one weight-related comorbid condition such as treated or untreated dyslipidemia or hypertension; individuals with type 2 diabetes mellitus were excluded. Individuals were randomized in a 2:1 ratio to either Saxenda or placebo. Individuals were stratified based on the presence or absence of abnormal blood glucose measurements at randomization. All individuals were treated for up to 56 weeks. Those individuals with abnormal glucose measurements at randomization (2254 of the 3731 individuals) were treated for a total of 160 weeks. At baseline, mean age was 45 years (range 18-78), 79% were women, 85% were Caucasian, 10% were African American, and 11% were Hispanic/Latino. Mean baseline body weight was 106.3 kg and mean BMI was 38.3 kg/m^2.

Study 2 was a 56-week trial that enrolled 635 individuals with type 2 diabetes and with either overweight or obesity (as defined above). Individuals were to have an HbA of 7-10% and be treated with metformin, a sulfonylurea, or a glitazone as single agent or in any combination, or with diet and exercise alone. Individuals were randomized in a 2:1 ratio to receive either Saxenda or placebo. The mean age was 55 years (range 18-82), 50% were women, 83% were Caucasian, 12% were African American, and 10% were Hispanic/Latino. Mean baseline body weight was 105.9 kg and mean BMI was 37.1 kg/m^2.

Study 3 was a 56-week trial that enrolled 422 individuals with obesity (BMI greater than or equal to 30 kg/m^2) or with overweight (BMI 27-29.9 kg/m^2) and at least one weight-related comorbid condition such as treated or untreated dyslipidemia or hypertension; individuals with type 2 diabetes mellitus were excluded. All individuals were first treated with a diet (total energy intake 1200-1400 kcal/day) in a run-in period lasting up to 12 weeks. Individuals who lost at least 5% of their screening body weight after 4 to 12 weeks during the run-in were then randomized, with equal allocation, to receive either Saxenda or placebo for 56 weeks. The mean age was 46 years (range 18-73), 81% were women, 84% were Caucasian, 13% were African American, and 7% were Hispanic/Latino. Mean baseline body weight was 99.6 kg and mean BMI was 35.6 kg/m^2.

For Study 1 and Study 2, the primary efficacy parameters were mean percent change in body weight and the percentages of individuals achieving greater than or equal to 5% and 10% weight loss from baseline to week 56. For Study 3, the primary efficacy parameters were mean percent change in body weight from randomization to week 56, the percentage of individuals not gaining more than 0.5% body weight from randomization (i.e., after run-in) to week 56, and the percentage of individuals achieving greater than or equal to 5% weight loss from randomization to week 56. Because losing at least 5% of fasting body weight through lifestyle intervention during the 4- to 12-week run-in was a condition for their continued participation in the randomized treatment period, the results may not reflect those expected in the general population.

After 56 weeks, treatment with Saxenda resulted in a statistically significant reduction in weight compared with placebo. Statistically significantly greater proportions of individuals treated with Saxenda achieved 5% and 10% weight loss than those treated with placebo. In Study 3, statistically significantly more individuals randomized to Saxenda than placebo had not gained more than 0.5% of body weight from randomization to week 56.

Safety

Saxenda includes a boxed warning since it causes dose-dependent and treatment-duration-dependent thyroid C-cell tumors (adenomas and/or carcinomas) at clinically relevant exposures in both genders of rats and mice. Malignant thyroid C-cell carcinomas were detected in rats and mice. It is unknown whether Saxenda will cause thyroid C-cell tumors, including medullary thyroid carcinoma (MTC), in humans, as the human relevance of liraglutide-induced rodent thyroid C-cell tumors has not been determined.

Cases of MTC in individuals treated with liraglutide have been reported in the post-marketing period; the data in these reports are insufficient to establish or exclude a causal relationship between MTC and liraglutide use in humans. Saxenda is contraindicated in individuals with a personal or family history of MTC or in individuals with MEN 2.

In clinical trials, 9.8% of individuals treated with Saxenda and 4.3% of individuals treated with placebo prematurely discontinued treatment as a result of adverse reactions. The most common adverse reactions leading to discontinuation were nausea (2.9% versus 0.2% for Saxenda and placebo, respectively), vomiting (1.7% versus less than 0.1%), and diarrhea (1.4% versus 0%). The top 5 adverse reactions among individuals' treatment with Saxenda and more common than placebo is nausea (39.3% vs. 13.8%), diarrhea (20.9% vs. 9.9%), constipation (19.4% vs. 8.5%), vomiting (15.7% vs. 3.9%), and headache (13.6% vs. 12.6%).

Wegovy (semaglutide)

The safety and efficacy of Wegovy for chronic weight management (weight loss and maintenance) in conjunction with a reduced calorie diet and increased physical activity were studied in three 68-week, randomized, double-blind, placebo-controlled trials and one 68-week, randomized, double-blind, placebo withdrawal trial. In Studies 1, 2, and 3, Wegovy or matching placebo was escalated to 2.4 mg subcutaneous weekly during a 16-week period followed by 52 weeks on maintenance dose. In Study 4, Wegovy was escalated during a 20-week run-in period,

and individuals who reached Wegovy 2.4 mg after the run-in period were randomized to either continued treatment with Wegovy or placebo for 48 weeks.

In Studies 1, 2 and 4, all individuals received instruction for a reduced calorie meal diet (approximately 500 kcal/day deficit) and increased physical activity counseling (recommended to a minimum of 150 min/week) that began with the first dose of study medication or placebo and continued throughout the trial. In Study 3, individuals received an initial 8-week low-calorie diet (total energy intake 1000 to 1200 kcal/day) followed by 60 weeks of a reduced calorie diet (1200-1800 kcal/day) and increased physical activity (100 mins/week with gradual increase to 200 mins/week).

Study 1 was a 68-week trial that enrolled 1961 individuals with obesity (BMI greater than or equal to 30 kg/m^2) or with overweight (BMI 27-29.9 kg/m^2) and at least one weight-related comorbid condition, such as treated or untreated dyslipidemia or hypertension; individuals with type 2 diabetes mellitus were excluded. Individuals were randomized in a 2:1 ratio to either Wegovy or placebo. At baseline, mean age was 46 years (range 18-86), 74.1% were women, 75.1% were White, 13.3% were Asian and 5.7% were Black or African American. A total of 12.0% were Hispanic or Latino. Mean baseline body weight was 105.3 kg and mean BMI was 37.9 kg/m^2.

Study 2 was a 68-week trial that enrolled 807 individuals with type 2 diabetes and BMI greater than or equal to 27 kg/m^2. Individuals included in the trial had HbA1c 7-10% and were treated with either: diet and exercise alone or 1 to 3 oral anti-diabetic drugs (metformin, sulfonylurea, glitazone or sodium-glucose co-transporter 2 inhibitor). Individuals were randomized in a 1:1 ratio to receive either Wegovy or placebo. At baseline, the mean age was 55 years (range 19-84), 50.9% were women, 62.1% were White, 26.2% were Asian and 8.3% were Black or African American. A total of 12.8% were Hispanic or Latino. Mean baseline body weight was 99.8 kg and mean BMI was 35.7 kg/m^2.

Study 3 was a 68-week trial that enrolled 611 individuals with obesity (BMI greater than or equal to 30 kg/m^2) or with overweight (BMI 27-29.9 kg/m^2) and at least one weight-related comorbid condition such as treated or untreated dyslipidemia or hypertension; individuals with type 2 diabetes mellitus were excluded. The individuals were randomized in a 2:1 ratio to receive either Wegovy or placebo. At baseline, the mean age was 46 years, 81.0% were women, 76.1% were White, 19.0% were Black or African American and 1.8% were Asian. A total of 19.8% were Hispanic or Latino. Mean baseline body weight was 105.8 kg and mean BMI was 38.0 kg/m^2.

Study 4 was a 68-week trial that enrolled 902 individuals with obesity (BMI greater than or equal to 30 kg/m^2) or with overweight (BMI 27-29.9 kg/m^2) and at least one weight-related comorbid condition such as treated or untreated dyslipidemia or hypertension; individuals with type 2

diabetes mellitus were excluded. Mean body weight at baseline for the 902 individuals was 106.8 kg and mean BMI was 38.3 kg/m^2. All individuals received Wegovy during the run-in period of 20 weeks that included 16 weeks of dose escalation. Trial product was permanently discontinued before randomization in 99 of 902 individuals (11%); the most common reason was adverse reactions (n=48, 5.3%); 803 individuals reached Wegovy 2.4 mg and were then randomized in a 2:1 ratio to either continue on Wegovy or receive placebo. Among the 803 randomized individuals, the mean age was 46 years, 79% were women, 83.7% were White, 13% were Black or African American, and 2.4% Asian. A total of 7.8% were Hispanic or Latino. Mean body weight at randomization (week 20) was 96.1 kg and mean BMI at randomization (week 20) was 34.4 kg/m^2.

The proportions of individuals who discontinued study drug in Studies 1, 2, and 3 was 16.0% for the Wegovy-treated group and 19.1% for the placebo-treated group, and 6.8% of individuals treated with Wegovy and 3.2% of individuals treated with placebo discontinued treatment due to an adverse reaction. In Study 4, the proportions of individuals who discontinued study drug were 5.8% and 11.6% for Wegovy and placebo, respectively.

For Studies 1, 2 and 3, the primary efficacy parameters were mean percent change in body weight and the percentages of individuals achieving greater than or equal to 5% weight loss from baseline to week 68.

After 68 weeks, treatment with Wegovy resulted in a statistically significant reduction in body weight compared with placebo. Greater proportions of individuals treated with Wegovy achieved 5%, 10% and 15% weight loss than those treated with placebo.

For Study 4, the primary efficacy parameter was mean percent change in body weight from randomization (week 20) to week 68. From randomization (week 20) to week 68, treatment with Wegovy resulted in a statistically significant reduction in body weight compared with placebo. Because individuals who discontinued Wegovy during titration and those who did not reach the 2.4 mg weekly dose were not eligible for the randomized treatment period, the results may not reflect the experience of individuals in the general population who are first starting Wegovy.

A reduction in body weight was observed with Wegovy irrespective of age, sex, race, ethnicity, BMI at baseline, body weight (kg) at baseline, and level of renal function impairment.

The safety and efficacy of Wegovy to reduce the risk of a major adverse cardiovascular event (MACE) was studied in one multicenter, double-blind, placebo-controlled trial, named the SELECT trial. In the SELECT trial, 17,604 individuals who were 45 years or older, had an initial BMI greater than 27, and established cardiovascular disease were randomized in a 1:1 ratio to receive once-weekly subcutaneous Wegovy at a dose of 2.4 mg (after a 16-week dose escalation period) or placebo.

At baseline, the mean age was 62 years (range 45-93), 72% were male, 84% were White, 4% were Black or African American, and 8% were Asian, and 10% were Hispanic or Latino. Mean baseline body weight was 97 kg and mean BMI was 33 kg/m^2. At baseline, prior myocardial infarction was reported in 76% of randomized individuals, prior stroke in 23%, and peripheral arterial disease in 9%. Heart failure was reported in 24% of individuals. At baseline, cardiovascular disease and risk factors were managed with lipid-lowering therapy (90%), platelet aggregation inhibitors (86%), angiotensin converting enzyme inhibitors or angiotensin II receptor blockers (74%), and beta blockers (70%). A total of 10% had moderate renal impairment (eGFR 30 to less than 60 mL/min/1.73m^3) and 0.4% had severe renal impairment of eGFR less than 30 mL/min/1.73m^2.

The median follow-up duration was 41.8 months. The primary efficacy endpoint was a composite of cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke. Wegovy statistically significantly reduced the risk of MACEs by 20% compared to placebo when added to standard of care.

The efficacy of Wegovy injection was evaluated based on an efficacy analysis at Week 72 in Study 11 (NCT#04822181), a 240-week, randomized, double-blind, placebo-controlled trial. Enrolled individuals had a baseline or recent liver biopsy showing clinically significant MASLD (metabolic dysfunction-associated steatotic liver disease), defined as MASH with fibrosis stage 2 or 3 and a non-alcoholic fatty liver disease (NAFLD) Activity Score (NAS) ≥4 with a score of 1 or more in steatosis, lobular inflammation, and hepatocyte ballooning. Efficacy determination was based on the effect of Wegovy injection on resolution of steatohepatitis without worsening of liver fibrosis and on at least one stage improvement in liver fibrosis without worsening of steatohepatitis, on post-baseline liver biopsies collected at 72 weeks. Part 2 of the trial will serve as the confirmatory trial; it is anticipated to be completed in 2029 and will use the composite endpoint of progression to cirrhosis, hepatic decompensation events, liver transplant, and mortality as the confirmatory endpoints to elucidate long-term clinical benefits. The clinical data from ESSENCE showed that at week 72, 36.8% of individuals treated with Wegovy achieved improvement in liver fibrosis with no worsening of steatohepatitis compared to 22.4% treated with placebo. 62.9% of individuals treated with Wegovy achieved resolution of steatohepatitis with no worsening of liver fibrosis compared to 34.3% treated with placebo. Another secondary endpoint was the percent change in body weight from baseline to Week 72. Individuals treated with Wegovy (mean baseline body weight 95.4 kg) achieved an average of 10.5% weight loss from baseline at Week 72, and individuals treated with placebo (mean baseline weight 97.6 kg) achieved an average of 2% weight loss from baseline at Week 72; treatment with Wegovy resulted in an average of 8.5% greater weight loss from baseline compared to placebo (95% CI: 7.4% to 9.5%).

Safety

Wegovy includes a boxed warning since it causes dose-dependent and treatment-duration-dependent thyroid C-cell tumors (adenomas and/or carcinomas) at clinically relevant exposures in both genders of rats and mice. Malignant thyroid C-cell carcinomas were detected in rats and mice. It is unknown whether Wegovy will cause thyroid C-cell tumors, including medullary thyroid carcinoma (MTC), in humans, as the human relevance of liraglutide-induced rodent thyroid C-cell tumors has not been determined.

Cases of MTC in individuals treated with liraglutide, another GLP-1 receptor agonist, have been reported in the post-marketing period; the data in these reports are insufficient to establish or exclude a causal relationship between MTC and GLP-1 receptor agonist use in humans. Wegovy is contraindicated in individuals with a personal or family history of MTC or in individuals with MEN 2.

In clinical trials, 6.8% of individuals treated with Wegovy and 3.2% of individuals treated with placebo permanently discontinued treatment as a result of adverse reactions. The most common adverse reactions leading to discontinuation were nausea (1.8% versus 0.2%), vomiting (1.2% versus 0%), and diarrhea (0.7% versus 0.1%) for Wegovy and placebo, respectively.

The safety profile of Wegovy observed in the SELECT trial was consistent with previously published studies. The most common adverse events (AEs) reported in the Wegovy arm were gastrointestinal in nature, including those that lead to treatment discontinuation. Individuals 75 years of age and older reported more fractures of the hip and pelvis on Wegovy than on placebo and reported more serious adverse reactions overall compared to younger adult individuals.

Xenical (orlistat)

The effects of Xenical on weight loss, weight maintenance, and weight regain and on a number of comorbidities (e.g., type 2 diabetes, lipids, blood pressure) were assessed in the 4-year XENDOS study and in seven long-term (1- to 2-years duration) multicenter, double-blind, placebo-controlled clinical trials. During the first year of therapy, the studies of 2-year duration assessed weight loss and weight maintenance. During the second year of therapy, some studies assessed continued weight loss and weight maintenance, and others assessed the effect of

Xenical on weight regain. These studies included over 2800 individuals treated with Xenical and 1400 individuals treated with placebo (age range 17-78 years, 80.2% women, 91.0% Caucasians, 5.7% Blacks, 2.3% Hispanics, 0.9% Other). The majority of these individuals had obesity-related risk factors and comorbidities. In the XENDOS study, which included 3304 individuals (age range 30-58 years, 55% women, 99% Caucasians, 1% other), the time to onset of type 2 diabetes was assessed in addition to weight management. In all these studies, treatment with Xenical and placebo designates treatment with Xenical plus diet and placebo plus diet, respectively.

During the weight loss and weight maintenance period, a well-balanced, reduced-calorie diet that was intended to result in an approximate 20% decrease in caloric intake and provide 30% of calories from fat was recommended to all individuals. In addition, all individuals were offered nutritional counseling.

Pooled data from five clinical trials indicated that the overall mean weight loss from randomization to the end of 1 year of treatment in the intent-to-treat population was 13.4 lbs in the individuals treated with Xenical and 5.8 lbs in the placebo-treated individuals. After 1 year of treatment, the mean percent weight loss difference between Xenical-treated individuals and placebo-treated individuals was 3%. One thousand seventy-two (69%) individuals treated with Xenical and 701 (63%) individuals treated with placebo completed 1 year of treatment. Of the individuals who completed 1 year of treatment, 57% of the individuals treated with Xenical (120 mg three times a day) and 31% of the placebo-treated individuals lost at least 5% of their baseline body weight.

Three studies were designed to evaluate the effects of Xenical compared to placebo in reducing weight regain after a previous weight loss achieved following either diet alone (one study, 14302) or prior treatment with Xenical (two studies, 14119C and 14185). The diet utilized during the 1-year weight regain portion of the studies was a weight-maintenance diet, rather than a weight-loss diet, and individuals received less nutritional counseling than individuals in weight-loss studies. For studies 14119C and 14185, individuals' previous weight loss was due to 1 year of treatment with Xenical in conjunction with a mildly hypocaloric diet. Study 14302 was conducted to evaluate the effects of 1 year of treatment with Xenical on weight regain in individuals who had lost 8% or more of their body weight in the previous 6 months on diet alone.

In study 14119C, individuals treated with placebo regained 52% of the weight they had previously lost while the individuals treated with Xenical regained 26% of the weight they had previously lost ($p<0.001$). In study 14185, individuals treated with placebo regained 63% of the weight they had previously lost while the individuals treated with Xenical regained 35% of the weight they had lost ($p<0.001$). In study 14302, individuals treated with placebo regained 53% of

the weight they had previously lost while the individuals treated with Xenical regained 32% of the weight that they had lost ($p<0.001$).

In the 4-year double-blind, placebo-controlled XENDOS study, the effects of Xenical in delaying the onset of type 2 diabetes and on body weight were compared to placebo in 3304 obese individuals who had either normal or impaired glucose tolerance at baseline. Thirty-four percent of the 1655 individuals who were randomized to the placebo group and 52% of the 1649 individuals who were randomized to the Xenical group completed the 4-year study.

At the end of the study, the mean percent weight loss in the placebo group was -2.75% compared with - 5.17% in the Xenical group ($p<0.001$). Forty-five percent of the placebo individuals and 73% of the Xenical individuals lost greater than or equal to5% of their baseline body weight, and 21% of the placebo individuals and 41% of the Xenical individuals lost greater than or equal to10% of their baseline body weight following the first year of treatment. Following 4 years of treatment, 28% of the placebo individuals and 45% of the Xenical individuals lost greater than or equal to5% of their baseline body weight and 10% of the placebo individuals and 21% of the Xenical individuals lost greater than or equal to10% of their baseline body weight. After 4 years of treatment, the mean % difference in weight loss between Xenical treated individuals and placebo was 2.5%.

Safety

Gastrointestinal (GI) symptoms were the most commonly observed treatment-emergent adverse events associated with the use of Xenical in the seven double-blind, placebo-controlled clinical trials and are primarily a manifestation of the mechanism of action. (Commonly observed is defined as an incidence of greater than or equal to 5% and an incidence in the Xenical 120 mg group that is at least twice that of placebo.) The top 5 adverse events among individuals' treatment with Xenical during year 1 and more common than placebo are oily spotting (26.6% vs. 1.3%), flatus with discharge (23.9% vs. 1.4%), fecal urgency (22.1% vs. 6.7%), fatty/oily stool (20.0% vs. 2.9%), and oil evacuation (11.9% vs. 0.8%). In general, the first occurrence of these events was within 3 months of starting therapy. Overall, approximately 50% of all episodes of GI adverse events associated with Xenical treatment lasted for less than 1 week, and a majority lasted for no more than 4 weeks. However, GI adverse events may occur in some individuals over a period of 6 months or longer.

Zepbound (tirzepatide)

Zepbound is a dual GLP-1 and GIP receptor agonist approved for chronic weight management. The efficacy of Zepbound for chronic weight management (weight reduction and maintenance) in conjunction with a reduced-calorie diet and increased physical activity was studied in two randomized, double-blind, placebo-controlled trials (Study 1 and Study 2), in which weight reduction was assessed after 72 weeks of treatment (at least 52 weeks at maintenance dose). In Study 1, the dose of Zepbound or matching placebo was escalated to 5 mg, 10 mg, or 15 mg subcutaneously once weekly during a 20-week titration period followed by the maintenance period. In Study 2, the dose of Zepbound or matching placebo was escalated to 10 mg or 15 mg subcutaneously once weekly during a 20-week titration period followed by the maintenance period.

In Study 2, the dose of Zepbound or matching placebo was escalated to 10 mg or 15 mg subcutaneously once weekly during a 20-week titration period followed by the maintenance period. In Studies 1 and 2, all individuals received instruction on a reduced-calorie diet (approximately 500 kcal/day deficit) and increased physical activity counseling (recommended to a minimum of 150 min/week) that began with the first dose of study medication or placebo and continued throughout the trial.

Study 1 (NCT04184622) was a 72-week trial that enrolled 2539 adult individuals with obesity (BMI greater than or equal to 30 kg/m2), or with overweight (BMI 27 to less than 30 kg/m^2) and at least one weight-related comorbid condition, such as dyslipidemia, hypertension, obstructive sleep apnea, or cardiovascular disease; individuals with type 2 diabetes mellitus were excluded. Individuals were randomized in a 1:1:1:1 ratio to Zepbound 5 mg, Zepbound 10 mg, Zepbound 15 mg, or placebo once weekly.

Study 2 (NCT04657003) was a 72-week trial that enrolled 938 adult individuals with BMI greater than or equal to 27 kg/m2 and type 2 diabetes mellitus. Individuals included in the trial had HbA1c 7-10% and were treated with either diet and exercise alone, or any oral anti-hyperglycemic agent except dipeptidyl peptidase-4 (DPP-4) inhibitors or GLP-1 receptor agonists. Individuals who were taking insulin or injectable GLP-1 receptor agonists for type 2 diabetes mellitus were excluded. Individuals were randomized in a 1:1:1 ratio to Zepbound 10 mg, Zepbound 15 mg, or placebo once weekly.

The proportions of individuals who discontinued study drug in Study 1 were 14.3%, 16.4%, and 15.1% for the 5 mg, 10 mg, and 15 mg ZEPBOUND-treated groups, respectively, and 26.4% for the placebo-treated group. The proportions of individuals who discontinued study drug in Study 2 were 9.3% and 13.8% for the 10 mg and 15 mg Zepbound-treated groups, respectively, and 14.9% for the placebo-treated group. For Studies 1 and 2, the primary efficacy parameters were

mean percent change in body weight and the percentage of individuals achieving greater than or equal to 5% weight reduction from baseline to Week 72. After 72 weeks of treatment, Zepbound resulted in a statistically significant reduction in body weight compared with placebo, and greater proportions of individuals treated with Zepbound 5 mg, 10 mg, and 15 mg achieved at least 5% weight reduction compared to placebo. Among individuals treated with Zepbound 10 mg and 15 mg, greater proportions of individuals achieved at least 10%, 15%, and 20% weight reduction compared to placebo. A reduction in body weight was observed with Zepbound irrespective of age, sex, race, ethnicity, baseline BMI, and glycemic status.

Safety

Zepbound was evaluated for safety in 2 randomized, double-blind, placebo-controlled trials that included 2519 adult individuals with overweight or obesity treated with Zepbound for up to 72 weeks and a 4-week off drug follow-up period. The majority of individuals who discontinued Zepbound due to adverse reactions did so during the first few months of treatment due to gastrointestinal adverse reactions. There is a black box warning for the risk of thyroid c-cell tumors. Suicidal behavior and ideation have been reported in clinical trials with other chronic weight management products.

2021 Update

Reviewed prescribing information for all drugs listed in policy and no new evidence was identified that would require changes to the coverage criteria. Added a new FDA-approved drug to policy called Wegovy (semaglutide) for the treatment of chronic weight management.

2022 Update

Reviewed prescribing information for all drugs listed in policy and identified a new pediatric indication for Qsymia (phentermine/topiramate extended-release). Added coverage criteria to Qsymia for chronic weight management in pediatric individuals with a BMI greater than or equal to 95th percentile for age and sex. Added coverage for brand orlistat with the identical coverage criteria as Xenical (orlistat). Added specific re-authorization criteria to Qsymia, Xenical, and brand orlistat for pediatric individuals. Updated the re-authorization criteria for all drugs to specify that for adults the weight loss percent is from baseline body weight and for pediatric individuals the weight loss percent is from baseline BMI.

2023 Update

Reviewed prescribing information for all drugs listed in policy. Minor correction made to the pediatric quantity limit for Wegovy (semaglutide). Added a new FDA-approved drug to the policy called Zepbound (tirzepatide) for the treatment of chronic weight management.

2024 Update

Reviewed prescribing information for all drugs listed in policy. Updated Wegovy (semaglutide) coverage criteria to include use in certain individuals with established cardiovascular disease.

2025 Update

Reviewed prescribing information for all drugs listed in policy. Updated Contrave (naltrexone-bupropion), Qsymia (phentermine-topiramate), Saxenda (liraglutide), Wegovy (semaglutide), Xenical (orlistat), brand orlistat, and Zepbound (tirzepatide) adult weight-related comorbid condition criteria from type 2 diabetes, hypertension, sleep apnea, hyperlipidemia, and cardiovascular disease to the following: Asthma, cardiovascular disease, chronic obstructive pulmonary disease (COPD), coronary artery disease, dyslipidemia, hypertension, knee osteoarthritis, metabolic-dysfunction associated steatotic liver disease/non-alcoholic fatty liver disease, obstructive sleep apnea, polycystic ovarian syndrome, and type 2 diabetes mellitus. Clarified that the medications listed in this policy are subject to the product's FDA dosage and administration prescribing information. Clarified that non-formulary exception review authorizations for all drugs listed in this policy may be approved up to 12 months. Updated Zepbound (tirzepatide) coverage criteria to include use in certain individuals with moderate to severe obstructive sleep apnea. Added generic phentermine and topiramate extended-release coverage criteria for certain individuals with overweight or obesity. Updated Qsymia (phentermine and topiramate extended-release) coverage criteria to require trial with generic phentermine and topiramate extended-release first. Updated Contrave (naltrexone-bupropion), Qsymia (phentermine-topiramate), Saxenda (liraglutide), Wegovy (semaglutide), Xenical (orlistat), brand orlistat, and Zepbound (tirzepatide) coverage criteria to clarify that the medication is not to be used concurrently with generic phentermine and topiramate extended-release. Updated Saxenda (liraglutide) coverage criteria to require trial with generic liraglutide 18 mg/3 mL pen. Added generic liraglutide 18 mg/3 mL pen coverage criteria for certain individuals

with overweight or obesity. Updated Wegovy (semaglutide) coverage criteria to clarify that the quantity is limited to 4 pens per 30 days. Updated generic liraglutide 18 mg/3 mL pen and Saxenda (liraglutide) coverage criteria to clarify that the quantity is limited to 5 pens per 30 days. Updated Zepbound (tirzepatide) coverage criteria to clarify that the quantity is limited to 4 pens or vials per 30 days.

2026 Update

Reviewed prescribing information for all drugs listed in policy. Updated coverage criteria for Zepbound (tirzepatide) from quantity is limited to 4 pens or vials per 30 days to quantity is limited to 4 prefilled pens or single-dose vials per 30 days, or 1 Kwikpen or multi-dose vial per 28 days. Updated criteria for Wegovy (semaglutide) injection clarifying the quantity is limited to 4 pens per 28 days.

Appendix

Table 1: BMI Cut-offs for Obesity by Sex and Age for Pediatric Individuals Aged 12 Years and Older (CDC Criteria).

Age (years)	Body mass index (kg/m2) at 85th Percentile		Body mass index (kg/m2) at 95th Percentile	
	Males	Females	Males	Females
12	21.0	21.7	24.2	25.2
12.5	21.4	22.1	24.7	25.7
13	21.8	22.5	25.1	26.3
13.5	22.2	23.0	25.6	26.8
14	22.6	23.3	26.0	27.2
14.5	23.0	23.7	26.4	27.7
15	23.4	24.0	26.8	28.1

15.5	23.8	24.3	27.2	28.5
16	24.2	24.6	27.5	28.9
16.5	24.5	24.9	27.9	29.3
17	24.9	25.2	28.2	29.6
17.5	25.3	25.4	28.6	30.0

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3. Qsymia (phentermine/topiramate extended-release). Prescribing Information. VIVUS, Inc., Campbell, CA. Revised September 2024.
4. Saxenda (liraglutide). Prescribing Information. Novo Nordisk Inc., Plainsboro, NJ. Revised October 2025.
5. Wegovy (semaglutide). Prescribing Information. Novo Nordisk Inc., Plainsboro, NJ. Revised January 2026.
6. Xenical (orlistat). Prescribing Information. H2-Pharma, LLC, Montgomery, AL. Revised November 2022.
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History

Date	Comments
01/01/21	New policy, approved December 8, 2020, effective for dates of service on or after January 1, 2020. Add to Prescription Drug section. Coverage criteria added for Contrave (naltrexone/bupropion), Qsymia (phentermine/topiramate extended-release), Saxenda (liraglutide), and Xenical (orlistat) for the treatment of chronic weight management.
08/01/21	Annual Review, approved July 22, 2021. Added coverage criteria for Wegovy (semaglutide) for the treatment of chronic weight management.
01/01/22	Interim Review, approved December 14, 2021. Updated the initial authorization criteria for all drugs in policy adding requirement the patient has engaged in a trial of behavioral modification and dietary restriction and changed the weight related comorbid conditions for patients with a BMI greater than or equal to 27 kg/m^2. Added Saxenda (liraglutide) and Xenical (orlistat) specific pediatric coverage criteria for patients greater than or equal to 12 years of age and < 18 years of age. Updated the initial authorization duration for Contrave (naltrexone/bupropion) to 4 months, Saxenda to 4 months, and Wegovy (semaglutide) to 7 months. Updated the re-auth criteria for Contrave to weight loss greater than or equal to 5% after 15 weeks of treatment. Updated the re-auth criteria for Qsymia (phentermine/topiramate extended-release) to weight loss greater than or equal to 5% after 26 weeks of treatment. Updated re-auth criteria for Saxenda to weight loss greater than or equal to 4% after 16 weeks of treatment and patient is able to tolerate the Saxenda maintenance dose. Added re-auth criteria for Saxenda for pediatric patients greater than or equal to 12 years of age and < 18 years of age. Updated re-auth criteria for Wegovy to weight loss greater than or equal to 5% after 7 months of treatment and patient is able to tolerate the Wegovy maintenance dose. Updated re-auth criteria for Xenical to weight loss greater than or equal to 5% after 6 months of treatment.
11/01/22	Annual Review, approved October 11, 2022. Added coverage criteria to Qsymia (phentermine/topiramate extended-release) for chronic weight management in pediatric individuals. Added coverage for brand orlistat with the identical coverage criteria as Xenical (orlistat). Added specific re-authorization criteria to Qsymia, Xenical, and brand orlistat for pediatric individuals. Updated the re-authorization criteria for all drugs to specify that for adults the weight loss percent is from baseline body weight and for pediatric individuals the weight loss percent is from baseline BMI. Changed the wording from "patient" to "individual" throughout the policy for standardization.
03/01/23	Interim Review, approved February 14, 2023. Added coverage criteria to Wegovy (semaglutide) for chronic weight management in pediatric individuals. For pediatric coverage for Qsymia, Saxenda, and Xenical the requirement for a trial of behavioral modification and dietary restriction was shortened from 4 months to 3 months, the requirement regarding current BMI was updated to require the individual has a BMI greater than or equal to 95th percentile for age and sex (obesity), and for re-auth the

Date	Comments
	requirement that the individual currently has BMI > 85th percentile was removed. Updated policy criteria for all drugs restricting concurrent use with other medications intended for weight loss. Added an appendix table for BMI cut-offs for obesity by sex and age for pediatric individuals aged greater than or equal to 12.
06/01/23	Annual Review, approved May 22, 2023. Minor correction made to the pediatric quantity limit for Wegovy (semaglutide).
12/01/23	Interim Review, approved November 14, 2023. Added criteria for Zepbound (tirzepatide) for the treatment of chronic weight management.
12/01/24	Annual Review, approved November 12, 2024. Updated Wegovy (semaglutide) coverage criteria to include use in certain individuals with established cardiovascular disease.
02/01/25	Annual Review, approved January 14, 2025. Updated Contrave (naltrexone-bupropion), Qsymia (phentermine-topiramate), Saxenda (liraglutide), Wegovy (semaglutide), Xenical (orlistat), brand orlistat, and Zepbound (tirzepatide) adult weight-related comorbid condition criteria from type 2 diabetes, hypertension, sleep apnea, hyperlipidemia, and cardiovascular disease to the following: Asthma, cardiovascular disease, chronic obstructive pulmonary disease (COPD), coronary artery disease, dyslipidemia, hypertension, knee osteoarthritis, metabolic-dysfunction associated steatotic liver disease/non-alcoholic fatty liver disease, obstructive sleep apnea, polycystic ovarian syndrome, and type 2 diabetes mellitus. Clarified that the medications listed in this policy are subject to the product's FDA dosage and administration prescribing information. Clarified that non-formulary exception review authorizations for all drugs listed in this policy may be approved up to 12 months.
06/01/25	Interim Review, approved May 13, 2025. Updated Zepbound (tirzepatide) coverage criteria to include use in certain individuals with moderate to severe obstructive sleep apnea.
08/01/25	Interim Review, approved July 8, 2025. Added generic phentermine and topiramate extended-release coverage criteria for certain individuals with overweight or obesity. Updated Qsymia (phentermine and topiramate extended-release) coverage criteria to require trial with generic phentermine and topiramate extended-release first. Updated Contrave (naltrexone-bupropion), Qsymia (phentermine-topiramate), Saxenda (liraglutide), Wegovy (semaglutide), Xenical (orlistat), brand orlistat, and Zepbound (tirzepatide) coverage criteria to clarify that the medication is not to be used concurrently with generic phentermine and topiramate extended-release.
12/01/25	Interim Review, approved November 11, 2025. Updated Saxenda (liraglutide) coverage criteria to require trial with generic liraglutide 18 mg/3 mL pen. Added generic liraglutide 18 mg/3 mL pen coverage criteria for certain individuals with overweight or obesity.
01/01/26	Interim Review, approved December 22, 2025. Updated Wegovy (semaglutide) coverage criteria to clarify that the quantity is limited to 4 pens per 30 days. Updated generic liraglutide 18 mg/3 mL pen and Saxenda (liraglutide) coverage criteria to

Date	Comments
	clarify that the quantity is limited to 5 pens per 30 days. Updated Zepbound (tirzepatide) coverage criteria to clarify that the quantity is limited to 4 pens or vials per 30 days.
02/01/26	Interim Review, approved January 13, 2026. Added coverage criteria for Wegovy (semaglutide) tablets to reduce the risk of major adverse CV events in adults with established CV disease and either obesity or overweight; and to reduce excess body weight and maintain weight reduction long term in adults with obesity, or in adults with overweight in the presence of at least one weight-related comorbid condition. Updated coverage criteria of Wegovy (semaglutide) injection to include Wegovy tablets in list of medications not to be used concurrently with.
04/01/26	Annual Review, approved March 23, 2026. Updated coverage criteria for Zepbound (tirzepatide) from quantity is limited to 4 pens or vials per 30 days to quantity is limited to 4 prefilled pens or single-dose vials per 30 days, or 1 Kwikpen or multi-dose vial per 28 days. Updated criteria for Wegovy (semaglutide) injection clarifying the quantity is limited to 4 pens per 28 days.
07/01/26	Interim Review, approved June 9, 2026. Added Wegovy HD to criteria of Wegovy (semaglutide) for chronic weight management and updated the dose is limited from 2.4 mg to 7.2 mg once weekly. Added coverage criteria for Foundayo (orforglipron) for chronic weight management in adult individuals. Updated criteria for Contrave, generic liraglutide, generic phentermine-topiramate extended release, Qsymia, Saxenda, Wegovy, Xenical, and Zepbound adding Foundayo to list of medications not to be used concurrently with. Removed reference to non-formulary exception reviews.
09/01/26	Interim Review, approved August 11, 2026. Updated Wegovy (semaglutide) injection adding coverage criteria for the treatment of noncirrhotic metabolic dysfunction-associated steatohepatitis (MASH). Updated Foundayo (orforglipron) initial length of approval from 12 months to 7 months. Updated criteria for Contrave, Foundayo, liraglutide, phentermine-topiramate ER, Qsymia, Saxenda, Wegovy, Xenical, brand orlistat, and Zepbound treatment of chronic weight management replacing polycystic ovary syndrome (PCOS) with polyendocrine metabolic ovarian syndrome (PMOS).

Disclaimer: This medical policy is a guide in evaluating the medical necessity of a particular service or treatment. The Company adopts policies after careful review of published peer-reviewed scientific literature, national guidelines and local standards of practice. Since medical technology is constantly changing, the Company reserves the right to review and update policies as appropriate. Member contracts differ in their benefits. Always consult the member benefit booklet or contact a member service representative to determine coverage for a specific medical service or supply. CPT codes, descriptions and materials are copyrighted by the American Medical Association (AMA). ©2026 Premera All Rights Reserved.

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benefit booklet or contact a customer service representative to determine whether there are any benefit limitations applicable to this service or supply. This medical policy does not apply to Medicare Advantage.