

PHARMACY COVERAGE GUIDELINE

WEGOVY® (semaglutide) injection for Non-Weight Loss Indications Generic Equivalent (if available)

This Pharmacy Coverage Guideline (PCG):

- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope

- This PCG applies to Commercial and Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of outof-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance

- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "<u>Definition</u>" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.
- Information about medications that require prior authorization is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to pharmacyprecert@azblue.com.

<u>Purpose</u>: This coverage guideline is used to review Wegovy use <u>for non-weight loss indications, including</u> <u>established cardiovascular disease and noncirrhotic metabolic dysfunction-associated steatohepatitis (MASH)</u>. For use in weight loss, please refer to the member's benefit plan book.

Criteria:

<u>Section A</u>. Established Cardiovascular Disease: WEGOVY (semaglutide)

- <u>Criteria for initial therapy</u>: Wegovy (sematlutide) and/or generic equivalent (if available) are considered medically necessary and will be approved when ALL the following criteria are met:
 - 1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with a Cardiologist

ORIGINAL EFFECTIVE DATE: 05/16/2024 LARCHIVE DATE: LLAST REVIEW DATE: 05/15/2025 LLAST CRITERIA REVISION DATE: 11/20/2025



PHARMACY COVERAGE GUIDELINE

WEGOVY® (semaglutide) injection for Non-Weight Loss Indications Generic Equivalent (if available)

- 2. Individual is 45 years of age or older
- 3. Individual has a confirmed diagnosis of **established cardiovascular disease** defined as **ONE** of the following:
 - a. Prior myocardial infarction (MI)
 - b. Prior ischemic or hemorrhagic stroke
 - c. Symptomatic peripheral arterial disease (PAD) demonstrated by **any** of the following:
 - i. Intermittent claudication with ankle-brachial index (ABI) < 0.85 (at rest)
 - ii. Peripheral arterial revascularization procedure
 - iii. Amputation due to atherosclerotic disease
- 4. Requested medication use is to reduce the risk for cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke in an adult individual with established cardiovascular disease with a-body mass index (BMI) of at least 27 kg/m²
- 5. Individual is on guideline directed standard of care for their established cardiovascular condition which can include <u>any</u> of the following as clinically appropriate:
 - a. Lipid-lowering therapy
 - b. Platelet aggregation inhibitors
 - c. Angiotensin converting enzyme inhibitors or angiotensin II receptor blockers
 - d. Beta blockers
 - e. Calcium channel blockers
 - f. Angiotensin receptor-neprilysin inhibitor
- 6. Individual is currently **not** taking any of the following medications:
 - a. Glucagon-like Peptide 1 Receptor Agonists (GLP-1) (e.g., Ozempic, Rybelsus, Trulicity, etc)
 - b. Glucose-Dependent Insulinotropic Polypeptide (GIP)/Glucagon-Like Peptide (GLP-1) Receptor Agonist GIP-GLP-1 agonists (e.g., tirzepatide)
- 7. Requested medication will be used as an adjunct to diet and increased physical activity in combination with a program supporting a reduced calorie diet of at least 500 kcal/day and activity for at least 150 minutes per week
- 8. <u>If available</u>: Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see <u>Definitions section</u>)
- 9. There are **NO** FDA-label contraindications such as:
 - Personal or family history of medullary thyroid carcinoma (MTC) or Multiple Endocrine Neoplasia syndrome type 2 (MEN 2)
 - b. A prior serious hypersensitivity reaction to semaglutide (e.g., anaphylaxis, angioedema)
- 10. Individual does not have a history of suicidal attempt or active suicidal ideation
- 11. Individual does not have a history or presence of chronic pancreatitis or recent (within the prior 180 days) acute pancreatitis

ORIGINAL EFFECTIVE DATE: 05/16/2024 | ARCHIVE DATE:

| LAST REVIEW DATE: 05/15/2025 | LAST CRITERIA REVISION DATE: 11/20/2025



PHARMACY COVERAGE GUIDELINE

WEGOVY® (semaglutide) injection for Non-Weight Loss Indications Generic Equivalent (if available)

- 12. Individual does not have severe gastroparesis
- 13. Individual does not have New York Heart Association (NYHA) Class IV heart failure
- 14. Individual has a HbA1c less than 6.5% in the past 12 months
- 15. Individual does not have a diagnosis of diabetes mellitus type 1 or type 2 (excludes gestational diabetes)

Initial approval duration: 6 months

- <u>Criteria for continuation of coverage (renewal request)</u>: Wegovy (sematlutide) and/or generic equivalent (if available) are considered *medically necessary* and will be approved when ALL the following criteria are met (samples are not considered for continuation of therapy):
 - 1. Individual continues to be seen by a physician specializing in the individual's diagnosis or is in consultation with a Cardiologist
 - Individual has a confirmed diagnosis of established cardiovascular disease defined as ONE of the following:
 - a. Prior myocardial infarction (MI)
 - b. Prior ischemic or hemorrhagic stroke
 - c. Symptomatic peripheral arterial disease (PAD) demonstrated by **any** of the following:
 - i. Intermittent claudication with ankle-brachial index (ABI) < 0.85 (at rest)
 - ii. Peripheral arterial revascularization procedure
 - iii. Amputation due to atherosclerotic disease
 - 3. Individual is currently **not** taking any of the following medications:
 - a. Glucagon-like Peptide 1 Receptor Agonists (GLP-1) (e.g., Ozempic, Rybelsus, Trulicity, etc)
 - b. Glucose-Dependent Insulinotropic Polypeptide (GIP)/Glucagon-Like Peptide (GLP-1) Receptor Agonist GIP-GLP-1 agonists (e.g., tirzepatide)
 - 4. Requested medication will be used as an adjunct to diet and increased physical activity in combination with a program supporting a reduced calorie diet of at least 500 kcal/day and activity for at least 150 minutes per week
 - 5. Individual continues to be adherent with the medication including guideline directed standard of care for their established cardiovascular condition
 - 6. Individual has documentation of positive clinical response to therapy defined as achieving and maintaining **ONE** of the following:
 - a. Reduction of 5% or more in body weight from baseline
 - b. Reduction of 3% body weight from baseline with **ONE** or more of the following:
 - i. Decrease in low density lipoprotein (LDL) or triglycerides
 - ii. Decrease in waist circumference
 - iii. Decrease in blood pressure
 - 7. Requested dose is at least 1.7 mg weekly

ORIGINAL EFFECTIVE DATE: 05/16/2024 | ARCHIVE DATE: | LAST REVIEW DATE:

| LAST REVIEW DATE: 05/15/2025 | LAST CRITERIA REVISION DATE: 11/20/2025

BLUE CROSS®, BLUE SHIELD® and the Cross and Shield Symbols are registered service marks of the Blue Cross and Blue Shield Association, an association of independent Blue Cross and Blue Shield Plans. All other trademarks and service marks contained in this guideline are the property of their respective owners, which are not affiliated with BCBSAZ.

P324.2 Page 3 of 12



PHARMACY COVERAGE GUIDELINE

WEGOVY® (semaglutide) injection for Non-Weight Loss Indications Generic Equivalent (if available)

- 8. <u>If available</u>: Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see <u>Definitions section</u>)
- 9. Individual has not developed any contraindications or other significant adverse drug effects that may exclude continued use such as:
 - a. Acute pancreatitis
 - b. Suicidal behavior or ideation
 - c. Sustained increase in resting heart rate
 - d. Individual of childbearing potential is pregnant
- 10. Individual does not have a history of suicidal attempt or active suicidal ideation
- 11. Individual does not have a history or presence of chronic pancreatitis or recent (within the prior 180 days) acute pancreatitis
- 12. Individual does not have severe gastroparesis
- 13. Individual does not have New York Heart Association (NYHA) Class IV heart failure
- 14. Individual has a HbA1c less than 6.5% in the past 12 months
- 15. Individual does not have a diagnosis of diabetes mellitus type 1 or type 2 (excludes gestational diabetes)

Renewal duration: 12 months

- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:
 - 1. Off-Label Use of Non-Cancer Medications
 - 2. Off-Label Use of Cancer Medications

<u>Section B</u>. Noncirrhotic Metabolic Dysfunction-Associated Steatohepatitis (MASH): WEGOVY (semaglutide)

- <u>Criteria for initial therapy</u>: Wegovy (sematlutide) and/or generic equivalent (if available) are considered medically necessary and will be approved when ALL the following criteria are met:
 - Prescriber is a physician specializing in the patient's diagnosis or is in consultation with a Gastroenterologist or Hepatologist
 - 2. Individual is 18 years of age or older

ORIGINAL EFFECTIVE DATE: 05/16/2024 | ARCHIVE DATE:

| LAST REVIEW DATE: 05/15/2025 | LAST CRITERIA REVISION DATE: 11/20/2025



PHARMACY COVERAGE GUIDELINE

WEGOVY® (semaglutide) injection for Non-Weight Loss Indications Generic Equivalent (if available)

- 3. Individual has a confirmed diagnosis of **noncirrhotic metabolic dysfunction-associated steatohepatitis (MASH)** with moderate to advanced liver fibrosis (consistent with stages F2 to F3 fibrosis) [**Note**: MASH is formally known as NASH (see Definitions section)]
- 4. Requested medication will be used as an adjunct to diet and increased physical activity in combination with a program supporting a reduced calorie diet of at least 500 kcal/day and activity for at least 150 minutes per week aiming for a weight loss goal of at least 7-10%
- 5. Individual has at least **THREE** of the following five metabolic risk factors:
 - a. Large waist circumference defined as: men greater than 94 cm (37 inches), women greater than 80 cm (32 inches) **OR** has a body mass index equal to or greater than 30 kg/m²
 - b. Triglyceride level: equal to or greater than 150 mg/dL (1.7 mmol/L) **OR** on specific treatment
 - c. HDL-cholesterol: less than 40 mg/dL (1.03 mmol/L) in males and less than 50 mg/dL (1.29 mmol/L) in females **OR** on specific treatment
 - d. Systolic blood pressure equal to or greater than 140 or diastolic blood pressure equal to or greater than 90 mmHg on two occasions **OR** on specific treatment for hypertension
 - e. Has a diagnosis of type 2 diabetes
- 6. **ONE** of the following criteria that is consistent with NASH (or MASH) liver fibrosis:
 - a. Historical liver biopsy obtained <2 years prior showing Stage 2 or 3 fibrosis with NASH based on existing pathology, in an individual with no significant change in body weight of >5% or use of a medication that might affect NAS or fibrosis stage
 - b. FibroScan with transient elastography (within the prior 3 months) of greater than or equal to 8.5 kPa and controlled attenuation parameter greater than or equal to 280 dB/m
 - c. Historical biochemical test for fibrosis: such as a biomarker that detects the formation of type III collagen (PRO-C3 >14 ng/mL) or enhance liver fibrosis score (ELF ≥9)
 - d. Combination of noninvasive imaging such as vibration-controlled transient elastography (VCTE) or Enhanced Liver Fibrosis (ELF) test <u>plus</u> FIB-4 index or other combination of imaging and serologic tests (<u>see Definitions section</u>)
- 7. **ALL** of the following:
 - a. There is evidence of liver steatosis (>5% by imaging or histology) and <u>one</u> risk factor for cardiometabolic dysfunction (e.g., dyslipidemia, obesity, pre- or established type 2 diabetes mellitus, hypertension)
 - b. There is evidence of liver inflammation and hepatocellular injury such as lobar inflammation and ballooning injury to hepatocytes
 - c. Individual does not have other causes of steatotic liver disease
 - d. Individual drinks either no alcohol or there is minimal alcohol consumption (i.e., <20 g daily for females and <30 g daily for males) (see Definitions section)
- 8. Individual does not have Stage 4 fibrosis
- 9. Individual is currently **not** taking any of the following medications:
 - a. Glucagon-like Peptide 1 Receptor Agonists (GLP-1) (e.g., Ozempic, Rybelsus, Trulicity, etc.)
 - b. Glucose-Dependent Insulinotropic Polypeptide (GIP)/Glucagon-Like Peptide (GLP-1) Receptor Agonist (e.g., tirzepatide)

ORIGINAL EFFECTIVE DATE: 05/16/2024 | ARCHIVE DATE:

| LAST REVIEW DATE: 05/15/2025 | LAST CRITERIA REVISION DATE: 11/20/2025



PHARMACY COVERAGE GUIDELINE

WEGOVY® (semaglutide) injection for Non-Weight Loss Indications Generic Equivalent (if available)

- 10. <u>If available</u>: Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)
- 11. There are **NO** FDA-label contraindications such as:
 - a. Personal or family history of medullary thyroid carcinoma (MTC) or Multiple Endocrine Neoplasia syndrome type 2 (MEN 2)
 - b. A prior serious hypersensitivity reaction to semaglutide (e.g., anaphylaxis, angioedema)
- 12. Individual does not have a history of suicidal attempt or active suicidal ideation
- 13. Individual does not have a history or presence of chronic pancreatitis or recent (within the prior 180 days) acute pancreatitis
- 14. Individual does not have severe gastroparesis

Initial approval duration: 6 months

- <u>Criteria for continuation of coverage (renewal request)</u>: Wegovy (sematlutide) and/or generic equivalent (if available) are considered *medically necessary* and will be approved when ALL the following criteria are met (samples are not considered for continuation of therapy):
 - 1. Individual continues to be seen by a physician specializing in the individual's diagnosis or is in consultation with a Gastroenterologist or Hepatologist
 - 2. Individual has a confirmed diagnosis of **noncirrhotic metabolic dysfunction-associated steatohepatitis (MASH)**
 - 3. Individual has documentation of positive clinical response to therapy defined as achieving and maintaining **ONE** of the following:
 - a. Resolution of nonalcoholic steatohepatitis with an at least 2-point reduction in nonalcoholic fatty liver (NAFLD) activity score (i.e., NAS) and without worsening of fibrosis as seen by **BOTH** of the following:
 - i. Absence of ballooning (score = 0) and absence or mild lobal inflammation (score = 0 to 1)
 - ii. No worsening of fibrosis as seen by any progression greater than or equal to 1 stage
 - b. Fibrosis response seen by at least a one stage improvement in fibrosis without worsening of NAS
 - c. Blood tests such as aminotransferase levels and non-invasive assessments of liver fibrosis that demonstrate stabilization of fibrosis
 - 4. Individual is currently **not** taking any of the following medications:
 - a. Glucagon-like Peptide 1 Receptor Agonists (GLP-1) (e.g., Ozempic, Rybelsus, Trulicity, etc)
 - b. Glucose-Dependent Insulinotropic Polypeptide (GIP)/Glucagon-Like Peptide (GLP-1) Receptor Agonist GIP-GLP-1 agonists (e.g., tirzepatide)
 - 5. Individual has been adherent with the medication in combination with diet and exercise aiming for a weight loss goal of at least 7-10%

ORIGINAL EFFECTIVE DATE: 05/16/2024 LARCHIVE DATE: LLAST REVIEW DATE: 05/15/2025 LLAST CRITERIA REVISION DATE: 11/20/2025



PHARMACY COVERAGE GUIDELINE

WEGOVY® (semaglutide) injection for Non-Weight Loss Indications Generic Equivalent (if available)

- 6. <u>If available</u>: Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see <u>Definitions section</u>)
- 7. Individual has not developed any contraindications or other significant adverse drug effects that may exclude continued use such as:
 - a. Acute pancreatitis
 - b. Suicidal behavior or ideation
 - c. Sustained increase in resting heart rate
 - d. Individual of childbearing potential is pregnant
- 8. Individual does not have a history of suicidal attempt or active suicidal ideation
- 9. Individual does not have a history or presence of chronic pancreatitis or recent (within the prior 180 days) acute pancreatitis
- 10. Individual does not have severe gastroparesis

Renewal duration: 12 months

- > Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:
 - 1. Off-Label Use of Non-Cancer Medications
 - 2. Off-Label Use of Cancer Medications

Description:

Wegovy (semaglutide) is a glucagon-like peptide-1 (GLP-1) receptor agonist indicated in combination with a reduced calorie diet and increased physical activity to reduce the risk of major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke) in adults with established cardiovascular disease and is either overweight or obese. The exact mechanism of cardiovascular risk reduction has not been established. Coadministration with other semaglutide-containing products or with any other GLP-1 receptor agonist is not recommended.

Wegovy(semaglutide) is indicated in combination with a reduced calorie diet and increased physical activity for the treatment of noncirrhotic metabolic dysfunction-associated steatohepatitis (MASH), formerly known as nonalcoholic steatohepatitis (NASH), with moderate to advanced liver fibrosis (consistent with stages F2 to F3 fibrosis) in adults. The indication for MASH is approved under accelerated approval based on improvement of MASH and fibrosis. Continued approval for this indication may be contingent upon the verification and description of clinical benefit in a confirmatory trial.

ORIGINAL EFFECTIVE DATE: 05/16/2024 | ARCHIVE DATE:

| LAST REVIEW DATE: 05/15/2025 | LAST CRITERIA REVISION DATE: 11/20/2025

PHARMACY COVERAGE GUIDELINE

WEGOVY® (semaglutide) injection for Non-Weight Loss Indications Generic Equivalent (if available)

Definitions:

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting MedWatch Forms for FDA Safety Reporting I FDA

Established cardiovascular disease:

- Prior myocardial infarction (MI)
- Prior ischemic or hemorrhagic stroke
- Symptomatic peripheral arterial disease (PAD) defined as intermittent claudication with ankle-brachial index (ABI) <0.85 (at rest) OR peripheral arterial revascularization procedure OR amputation due to atherosclerotic disease

Some causes of Steatotic Liver Disease (SLD): steatosis of any etiology

- Drug induced liver disease
- Monogenic liver disease
- Alcohol induced liver disease (ALD)
- Cryptogenic liver disease
- Metabolic dysfunction-associated liver disease (MASLD)

Steatotic (fatty) liver disease (SLD):

- A comprehensive term defined as hepatic steatosis of any etiology identified on radiologic imaging or by liver biopsy.
- Steatotic liver disease (SLD) is further classified as:
 - Metabolic dysfunction-associated steatotic liver disease (MASLD) Individuals with MASLD have fatty liver (>5% hepatic steatosis) with at least one risk factor for cardiometabolic dysfunction (such as dyslipidemia or obesity), no other causes of SLD, and minimal or no alcohol consumption (i.e., <20 g daily for females and <30 g daily for males). This category was previously known as nonalcoholic fatty liver disease (NAFLD).</p>
 - MASLD with metabolic dysfunction-associated steatohepatitis (MASH) Individuals with MASH have <u>histologic evidence of inflammation and hepatocellular injury</u>, such as ballooning of hepatocytes, <u>with or without fibrosis</u>. This category was previously known as nonalcoholic steatohepatitis (NASH).
 - MASH cirrhosis Individuals with MASH cirrhosis have cirrhosis with current or previous histologic evidence of MASH or history of MASLD.
 - Metabolic dysfunction- and alcohol-associated liver disease (MetALD) Individuals with liver steatosis, have at least one metabolic risk factor, and a history of moderate (but not heavy) alcohol use. This category recognizes that SLD can involve a combination of metabolic dysfunction and alcohol.

Cirrhosis:

- A late stage of liver fibrosis that in advanced stages is considered to be irreversible
- Cirrhosis often has multiple signs and symptoms including fatigue, loss of appetite, jaundice, abdominal distension, bleeding and bruising, and many others

ORIGINAL EFFECTIVE DATE: 05/16/2024 | ARCHIVE DATE: | LAST REVIEW DATE: 05/15/2025 | LAST CRITERIA REVISION DATE: 11/20/2025

PHARMACY COVERAGE GUIDELINE

WEGOVY® (semaglutide) injection for Non-Weight Loss Indications Generic Equivalent (if available)

Compensated Cirrhosis:

- Cirrhosis without evidence of decompensation
- Some individuals with compensated cirrhosis may be asymptomatic

Decompensated Cirrhosis:

 Cirrhosis with signs and symptoms such as confusion (hepatic encephalopathy), fluid in the abdomen (ascites), yellowing of the skin and mucous membranes (jaundice), or kidney failure

Examples of some Noninvasive Imaging:

- Vibration-controlled Transient elastography (VCTE)
- Magnetic resonance elastography (MRE)
- Acoustic radiation force impulse (ARFI)
- Two-dimensional shear wave elastography (2D-SWE)

Examples of some Fibrosis Assessment by Serologic Testing:

- Aspartate aminotransferase to platelet ratio (APRI)
- Enhanced Liver Fibrosis (ELF) score (3 elements involved in matrix turnover: hyaluronic acid, tissue inhibitor of metalloproteinase-1, and N-terminal procollagen III peptide)
- FIB-4 index (platelet count, ALT, AST, age)
- FibroScan
- FibroSpect
- FibroTest/FibroSure
- Hepascore

FIB-4 calculator:

https://www.mdcalc.com/calc/2200/fibrosis-4-fib-4-index-liver-fibrosis#why-use **OR** FIB-4 = age (years) X AST Level (U/L) / platelet count (109/L) X square root of ALT (U/L)

Clinical Research Network	System (CRN) Non-alcoholic Fatty	Liver Disease (NAFLD/MASLD) Activity Score – NAS
Histological feature	Score	Category definition
Steatosis	0	<5%
	1	5–33%
	2	34–66%
	3	>66%
Hepatocyte ballooning	0	None
	1	Few or borderline ballooning
	2	Many or predominant ballooning
Lobular Inflammation	0	None
	1	1–2 foci per ×200 field
	2	2–4 foci per ×200 field
	3	>4 foci per ×200 field
NAS is sum of steatosis and lob	ar inflammation and ballooning: ra	anges 0-8

ORIGINAL EFFECTIVE DATE: 05/16/2024 | ARCHIVE DATE:

| LAST REVIEW DATE: 05/15/2025 | LAST CRITERIA REVISION DATE: 11/20/2025

PHARMACY COVERAGE GUIDELINE

WEGOVY® (semaglutide) injection for Non-Weight Loss Indications Generic Equivalent (if available)

Fibrosis	0	No Fibrosis
	1A	Mild zone 3 perisinusoidal fibrosis
	1B	Moderate zone 3 perisinusoidal fibrosis
	1C	Periportal/portal fibrosis
	2	Perisinusoidal & periportal/portal fibrosis
	3	Bridging fibrosis
	4	Cirrhosis

The regions surrounding the hepatic arteries and portal veins are known as periportal (zone 1), while those adjacent to the central vein are called the pericentral areas of the lobule (zone 3), with the cells in between these regions, referred to as mid-lobular hepatocytes (zone 2).

Metabolic dysfunction-associated steatohepatitis (MASH) grading and staging system			
Grade	Description		
Mild (grade 1)	Steatosis (predominantly macrovesicular) involving up to 66% of biopsy; may see occasional ballooned zone 3 hepatocytes; scattered intra-acinar polymorphonuclear cells, intra-acinar lymphocytes; no or mild portal chronic inflammation		
Moderate (grade 2)	Steatosis of any degree; ballooning of hepatocytes (predominantly zone3) obvious; intra-acinar polymorphonuclear cells noted, may be associated with zone 3 pericellular fibrosis; portal and intra-acinar chronic inflammation noted, mild to moderate		
Severe (grade 3)	Panacinar steatosis; ballooning and disarray obvious, predominantly inzone 3; intra-acinar inflammation noted as scattered polymorphonuclear cells, ballooned hepatocytes, mild chronic inflammation; portal chronic inflammation mild or moderate		
Stage	Description		
Fibrosis stage 0 (F0)	Absence of fibrosis		
Fibrosis stage 1 (F1)	Zone 3 perisinusoidal fibrosis; focally or extensively present		
Fibrosis stage 2 (F2)	Zone 3 perisinusoidal fibrosis with portal fibrosis		
Fibrosis stage 3 (F3)	Zone 3 perisinusoidal fibrosis and portal fibrosis with bridging fibrosis		
Fibrosis stage 4 (F4)	Cirrhosis		

Alcohol consumption:

Significant alcohol consumption is defined as greater than or equal to approximately 2 alcoholic drinks per day for males, and approximately 1.5 alcoholic drinks per day for females. One alcoholic drink is equal to 12 ounces (355 mL) of 5% alcohol by volume (ABV) beer, 5 ounces (148 mL) of 12% ABV wine, or 1.5 ounces (44.4 mL) of 40% ABV distilled spirits.

A standard drink in the United States is any drink that contains 14 grams of pure alcohol (about 0.6 fluid ounces) One standard drink (or one alcoholic drink equivalent) is found in:

12 ounces of regular beer, which is usually about 5% alcohol

ORIGINAL EFFECTIVE DATE: 05/16/2024 | ARCHIVE DATE: | LAST REVIEW DATE: 05/15/2025 | LAST CRITERIA REVISION DATE: 11/20/2025



PHARMACY COVERAGE GUIDELINE

WEGOVY® (semaglutide) injection for Non-Weight Loss Indications Generic Equivalent (if available)

- 8-10 ounces of malt liquor or hard seltzer is about 7% alcohol
- 5 ounces of wine, which is typically about 12% alcohol
- 3-4 ounces of fortified wine (sherry or port) is about 17% alcohol
- 2-3 ounces of cordial, liqueur, or aperitif is about 24% alcohol
- 1.5 ounces of distilled spirits (brandy, cognac, gin, rum, tequila, whisky, vodka, etc.) is about 40% alcohol

Moderate amounts of alcohol are defined as 20 to 50 g daily (140 to 350 g per week) for females and 30 to 60 g daily (210 to 420 g per week) for males. This range of alcohol intake defines a spectrum between MASLD-predominant and alcohol-predominant disease. Patients with steatosis and heavy alcohol use (i.e., >50 g daily for females and >60 g daily for males) have alcohol-associated liver disease.

Resources:

Wegovy (semaglutide) subcutaneous injection product information, revised by Norvo Nordisk 08-2025. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed October 06, 2025.

Sheth SG, Chopra S. Clinical features and diagnosis of metabolic dysfunction associated steatotic liver disease (nonalcoholic fatty liver disease) in adults. In: UpToDate, Reau N, Meyer C (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through September 2025. Topic last updated September 25, 2025. Accessed October 06, 2025.

Curry MP, Afdhal NH. Noninvasive assessment of hepatic fibrosis: Overview of serologic tests and imaging examinations. In: UpToDate, Jaffe T, Kamath PS, Meyer C (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through September 2025. Topic last updated March 13, 2025. Accessed October 06, 2025.

Chopra S, Lai M. Management of metabolic dysfunction-associated steatotic liver disease (nonalcoholic fatty liver disease) in adults. In: UpToDate, Lindor KD, Meyer C (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through September 2025. Topic last updated September 08, 2025. Accessed October 06, 2025.

ClinicalTrials.gov Bethesda (MD): National Library of Medicine (US). Identifier NCT04822181: The Effect of Semaglutide in Subjects With Non-cirrhotic Non-alcoholic Steatohepatitis. Available from: http://clinicaltrials.gov. Last update posted August 21, 2025. Last verified August 2025. Accessed October 05, 2025.

ClinicalTrials.gov Bethesda (MD): National Library of Medicine (US). Identifier NCT03574597: SELECT - Semaglutide Effects on Cardiovascular Outcomes in People With Overweight or Obesity. Available from: http://clinicaltrials.gov. Last update posted April 02, 2024. Last verified March 2024. Accessed April 08, 2024. Re-evaluated March 18, 2025.

Lincoff AM, Brown-Frandsen K, Colhoun HM, et al.: Semaglutide and Cardiovascular Outcomes in Obesity without Diabetes. NEJM 2023; Nov 11; 389:2221-2232. Accessed April 08, 2024. Re-evaluated March 18, 2025.

Lincoff AM, Brown-Frandsen K, Colhoun HM, et al. Semaglutide and cardiovascular outcomes in obesity without diabetes. NEJM 2023;389:2221-32. DOI: 10.1056/NEJMoa2307563. Protocol. Accessed April 08, 2024. Re-evaluated March 18, 2025.

Lingvay I, Brown-Frandsen K, Colhoun HM, et al.: Semaglutide for cardiovascular event reduction in people with overweight or obesity: SELECT study baseline characteristics. Obesity (Silver Spring). 2023;31:111–122. Accessed April 08, 2024. Re-evaluated March 18, 2025.

Ryan DH, Lingvay I, Colhoun HM, et al.: Semaglutide effects on cardiovascular outcomes in people with overweight or obesity (SELECT) rationale and design. Am Heart J 2020;229:61-9. Accessed April 08, 2024. Re-evaluated March 18, 2025.

Sanyal AJ, Newsome PN, Kliers I, et al.: Phase 3 Trial of Semaglutide in Metabolic Dysfunction—Associated Steatohepatitis. NEJM 2025 June 05;392 (21):2089-2099. DOI: 10.1056/NEJMoa2413258. Accessed August 28, 2025.

Newsome PN, Sanyal AJ, Engebretsen KA, et al.: Semaglutide 2.4 mg in Participants With Metabolic Dysfunction-Associated

ORIGINAL EFFECTIVE DATE: 05/16/2024 | ARCHIVE DATE: | LAST REVIEW DATE: 05/15/2025 | LAST CRITERIA REVISION DATE: 11/20/2025



PHARMACY COVERAGE GUIDELINE

WEGOVY® (semaglutide) injection for Non-Weight Loss Indications Generic Equivalent (if available)

Steatohepatitis: Baseline Characteristics and Design of the Phase 3 ESSENCE Trial. Available from Aliment Pharmacol Therap, 2024; 60:1525–1533 https://doi.org/10.1111/apt.18331. Accessed August 28, 2025.