

Our 2026 update to the EASO pharmacological management framework for obesity management reflects the rapidly evolving evidence base for obesity management medications, particularly incretin-based therapies. The framework remains a practical, evidence-informed algorithm to support clinical decision-making, not a rigid treatment sequence.

The updated framework is based on 62 randomised controlled trials, incorporating evidence published up to 21 November 2025. It refines the 2025 EASO algorithm by strengthening the evidence around total body weight loss, clarifying the comparative position of available medications, and expanding the liver disease domain to include MASH resolution and, newly for 2026, liver fibrosis improvement.

## KEY UPDATES IN THE FRAMEWORK

### 1. A LIVING FRAMEWORK, NOT A ONE-OFF ALGORITHM



The 2026 update confirms EASO's

intention to maintain the pharmacological framework as a living evidence map, updated as new trials, outcomes, medications and formulations emerge.

### 2. CLEARER EVIDENCE FOR BODY WEIGHT MANAGEMENT



For total body weight loss, all medications

assessed showed clinically meaningful benefit versus placebo. The strongest weight-loss effects were seen with tirzepatide and semaglutide, with tirzepatide maintained above semaglutide in the body weight management domain.

### 3. STRONGER FOCUS ON OBESITY-RELATED COMPLICATIONS



The framework distinguishes between:

- Body weight management in obesity, where no complications are present and the aim is to prevent dysfunction in non-adipose organs.
- Complications management in obesity, where complications are already present and the aim is to reverse or improve dysfunction in non-adipose organs.

### 4. NEW LIVER DISEASE EMPHASIS



The most substantive 2026 update is in the liver domain. The framework now includes:

- MASH resolution, where current evidence supports benefit for both semaglutide and tirzepatide.
- Liver fibrosis improvement, newly added in 2026, where current evidence is strongest for semaglutide, while evidence for tirzepatide remains less mature.

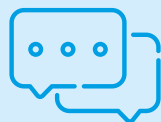
### 5. MECHANISM-INFORMED CARE



The framework supports a more precise understanding of obesity through two concepts:

- Metabolic adiposity: linked to deranged endocrine and immune responses, contributing to complications such as prediabetes, type 2 diabetes, cardiovascular disease, heart failure and MASLD/MASH.
- Mechanical adiposity: linked to altered physical forces, contributing to complications such as obstructive sleep apnoea and knee osteoarthritis.

## KEY MESSAGE

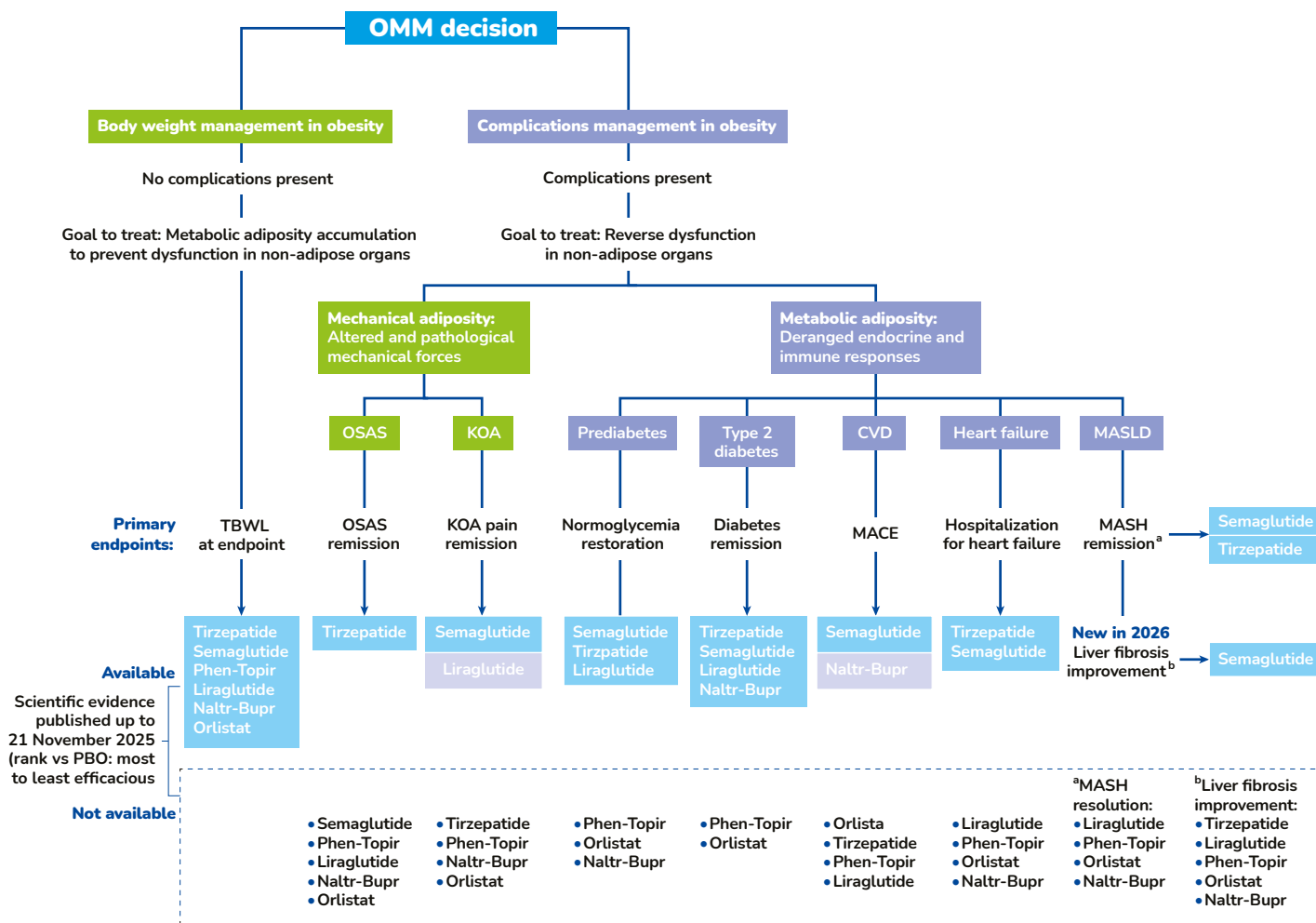


Pharmacological obesity management should be personalised. Treatment decisions should consider not only body weight outcomes, but also the presence and severity of obesity-related complications, including type 2 diabetes, cardiovascular disease, heart failure, obstructive sleep apnoea, knee osteoarthritis and MASLD/MASH.

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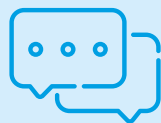


## TREATMENT ALGORITHM FOR INDIVIDUALS WITH OBESITY



This algorithm is based on the presence or absence of obesity related complications and RCT evidence available up to 21 November 2025. Medications are listed in order of efficacy for each endpoint indicated. Within each domain, medications are positioned to reflect comparative efficacy for the stated endpoint(s) based on trial evidence available up to the cut-off; this is not a prescribing sequence and should not be interpreted as a universal ranking across domains. Medications shown at the same level have comparable effects for that domain and/or endpoint. Where comparative evidence is indirect or limited, apparent differences should be interpreted alongside uncertainty and evidence maturity. Blue shading indicates statistically significant effects versus control; grey shading indicates no statistically significant effect or no available evidence for that domain. Algorithm entries reflect doses licensed for chronic weight management in adults in the European Union at the evidence cut-off; higher-dose regimens (for example, semaglutide at 7.2 mg) are acknowledged but are not included as separate nodes. Medications and doses: liraglutide, 3.0 mg; naltrexone-bupropion (Naltr-Bupr), 32 or 360 mg; orlistat, 360 mg; phentermine-topiramate (Phen-Topir), 15 or 92 mg; semaglutide, 2.4 mg; and tirzepatide, 10–15 mg. <sup>a</sup>Limited trial numbers and/or substantial between-study heterogeneity may reduce reliability for selected estimate(s), and clinical judgement is recommended. CVD, cardiovascular disease; HF, heart failure (with preserved ejection fraction); KOA, knee osteoarthritis; MACE, major adverse cardiovascular event; MASLD, metabolic dysfunction-associated steatotic liver disease; OSAS, obstructive sleep apnea; PBO, placebo.

### KEY MESSAGE



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