March 2025

DISEASE BURDEN

Both the prevalence and incidence of T2DM and obesity are increasing throughout the world, with the rising prevalence of both conditions being the steepest among LMICs. High fasting plasma glucose and high BMI are part of the top three risk variables for years of life lost in 2040, underscoring the global health challenge posed by these conditions.

CLINICAL RELEVANCE

Subcutaneous semaglutide, a once-weekly peptide-based GLP-1 RA, is highly effective in achieving and maintaining glycaemic targets in people with T2DM. It also promotes weight loss in adults with overweight or obesity and reduces the risk of major adverse cardiovascular events in this population . Additionally, semaglutide has been shown to significantly reduce the risk of kidney disease progression in adults with T2DM and chronic kidney disease. A label extension for risk reduction of chronic kidney disease (CKD) related events has been filed based on these findings, with a regulatory decision expected in the first half of 2025.

INTELLECTUAL PROPERTY LANDSCAPE

Primary patents on semaglutide have been or granted in few LMICs where they are expected to expire between 2024-2026. Secondary patents on semaglutide solid compositions with salcaprozate sodium, an important excipient of the finished product, have been filed in about seventeen LMICs, including major manufacturing countries such as India, South Africa, China and Brazil where they are expected to expire in 2031. Novo Nordisk owns many secondary patents that may extend exclusivity until 2040.

SEMAGLUTIDE
SUB-CUTANEOUS
DIABETES & CARDIOVASCULAR HEALTH
Novo Nordisk

SERVICE DELIVERY ENABLERS

Point of care testing for the detection, diagnosis, and monitoring of blood glucose is available in almost 90% primary healthcare facilities in LMICs and almost 50% of LICs. GLP1-RA are not yet included in national guidelines or clinical protocols in LMICs, hence companion treatments might vary. The availability and affordability of metformin, the widely recognized first line therapy, is generally good in LMICs.

REGULATORY

The product is approved by the USFDA and EMA. As semaglutide is a small peptide, potential licensees can follow the typical ANDA pathway (para III) such as small molecules or the EU-M4all pathway. No clinical trials are required. Pharmacokinetic-based bioequivalence studies can be performed.

MANUFACTURING

The API is produced using recombinant DNA technology in yeast (*Saccharomyces cerevisiae*) and chemical modification. However, it is possible to produce the product chemically, though the process is expected to be complex. All excipients are commonly used in injectable formulation, but the product contains phenol which might require precautions during manufacturing. Manufacturing process is simple. However aseptic processing will be required. Finished product is in a pen injector, which is considered a device. Shelf life is 3 years under refrigeration.

MARKET

Semaglutide injections have been registered in most countries, including numerous LMICs. However, commercialisation is limited to only a select number of LMICs.

ANDA: Abbreviated New Drug Application; **API**: Active Pharmaceutical Ingredient; **BMI**: Body Mass Index; **CKD**: chronic kidney disease; **DNA**: Deoxyribonucleic acid; **EU-M4All**: The European Medicines Agency (**EMA**), in cooperation with the World Health Organization (**WHO**), can provide scientific opinions on high priority human medicines, including vaccines, that are intended for markets outside of the European Union (**EU**). The procedure is called EU-Medicines for all or 'EU-M4all'; **GLP-1 RA**: Glucagon-like peptide-1 receptor agonist; **LMICs**: low-income (**LIC**s), lower middle-income and upper middle-income countries as per World Bank classification; **T2DM**: Type 2 diabetes mellitus.

DISEASE BURDEN

Both the prevalence and incidence of T2DM and obesity are increasing throughout the world, with the rising prevalence of both conditions being the steepest among LMICs. High fasting plasma glucose and high BMI are part of the top three risk variables for years of life lost in 2040, underscoring the global health challenge posed by these conditions.

CLINICAL RELEVANCE

Oral semaglutide, a once daily peptide-based GLP-1 RA, is highly effective in achieving and maintaining glycaemic targets while also promoting weight loss in people with T2DM . Clinical trials have demonstrated additional benefits, including a reduction in major adverse cardiovascular events (MACE) in those with T2DM and either cardiovascular disease or chronic kidney disease. A label extension was submitted to the FDA for the prevention of major adverse cardiovascular events (MACE) in patients with type 2 diabetes (T2D) and established cardiovascular disease (CVD) and/or chronic kidney disease (CKD) at the end of 2024.

INTELLECTUAL PROPERTY LANDSCAPE

Primary patents on semaglutide have been or granted in few LMICs where they are expected to expire between 2024-2026. Secondary patents on semaglutide solid compositions with SNAC, an important excipient of the finished product, have been filed in about seventeen LMICs, including major manufacturing countries such as India, South Africa, China and Brazil where they are expected to expire in 2031. Novo Nordisk owns many secondary patents that may extend exclusivity until 2040.

SEMAGLUTIDE
ORAL
DIABETES & CARDIOVASCULAR HEALTH
Novo Nordisk

SERVICE DELIVERY ENABLERS

Point of care testing for the detection, diagnosis, and monitoring of blood glucose are available in almost 90% primary healthcare facilities in LMICs and almost 50% of LICs. GLP1-RA are not yet included in national guidelines or clinical protocols in LMICs, hence companion treatments might vary. However, the availability and affordability of metformin, the widely recognized first line therapy, is generally good in LMICs. The oral formulation of semaglutide may make it appropriate for use in resource limited settings as it is heat stable.

REGULATORY

Product is approved with USFDA and EMA. Since semaglutide is a small peptide, potential licensees can follow typical ANDA pathway (para III) like small molecule or Swissmedic MAGHP or EU-M4all pathway. No clinical studies will be required, pharmacokinetic based bioequivalence studies will be required, preferably with qualitative and quantitative similarity.

MANUFACTURING

Produced using recombinant DNA technology in yeast (*Saccharomyces cerevisiae*) with subsequent chemical modification, this process involves multiple stages, including fermentation, synthesis of the acylating agent, and various purification steps, such as spray drying. However, this process is simpler than producing recombinant proteins like monoclonal antibodies. All excipients are commonly used in oral formulations–Povidone K90, microcrystalline cellulose, and magnesium stearate–except salcaprozate sodium (SNAC). This excipient, a novel addition at the time of oral semaglutide' registration in 2019, acts as an absorption enhancer. The manufacturing process was specifically adapted for this purpose, and by 2023, six Drug Master Files for SNAC had been filed with the FDA, indicating its broader market availability.

MARKET

Oral semaglutide is available primarily in the private markets of a small number of LMICs. However, it is more expensive than standard of care (SGLT2 inhibitors). Access plans are not known yet .

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