Recommendation No. 121/2021 of 18 October 2021 of the President of the Agency for Health Technology Assessment and Tariff System on the assessment of Rybelsus (semaglutide) in the following indication:

type 2 diabetes, in patients taking at least two oral hypoglycaemic agents or basal insulin in combination with at least two oral hypoglycaemic agents or basal insulin in combination with at least one oral hypoglycaemic agent, with HbA1c ≥ 8%, with obesity defined as BMI ≥ 30 kg/m^2 and very high cardiovascular risk defined as: confirmed cardiovascular disease or damage to other organs manifested by: proteinuria or left ventricular hypertrophy, or retinopathy, or the presence of 2 or more major risk factors from among the following: age ≥ 55 of age for men, ≥ 60 of age for women, dyslipidaemia, hypertension, smoking

The President of the Agency recommends the reimbursement of Rybelsus (semaglutide) in the following indication: type 2 diabetes, for patients taking at least two oral hypoglycaemic agents or basal insulin in combination with at least one oral hypoglycaemic agent, with HbA1c ≥ 8%, with obesity defined as BMI ≥ 30 kg/m2 and with very high cardiovascular risk defined as: confirmed cardiovascular disease or damage to other organs manifested by: proteinuria or left ventricular hypertrophy, or retinopathy, or the presence of ^{2} or more major risk factors from among the following: age ≥ 55 for men, ≥ 60 for women, dyslipidaemia, hypertension, smoking, **only provided that [information protected as a trade secret]**

Grounds for the recommendation

Semaglutide (Ozempic, solution for injection) is included in the reimbursement scheme and is reimbursed in the following indication (narrower than the one covered in this recommendation): type 2 diabetes before insulin initiation, treated with at least two oral hypoglycaemic agents for at least 6 months, with HbA1c ≥ 8%, with obesity defined as BMI ≥35 kg/m^2 and very high cardiovascular risk. In addition, on 12 February 2021, Ozempic (semaglutide) was granted a conditional positive reimbursement recommendation (Recommendation No. 14/2021) in a population identical to that assessed in this recommendation for Rybelsus (semaglutide in the form of tablets).

The results of clinical analysis, which indicate that the use of semaglutide in patients with type 2 diabetes significantly reduces HbA1c level compared to both the placebo used together with insulin and metformin, and to SGLT-2 inhibitors, were taken into consideration. However, it should be emphasised that a statistically significant superiority in results over SGLT-2 inhibitors was not achieved for all endpoints, including those relating to achieving HbA1c<7% or weight reduction.
Undoubtedly, a limitation of the clinical analysis is the lack of conclusions based on study results for the specific subpopulation of patients with type 2 diabetes covered in the reimbursement

application. This limitation is the primary reason why it is justified to seek to equate the cost of Rybelsus therapy to the cost of therapy with the cheapest of the SGLT -2 inhibitors.

An account has also been taken of the estimates in the economic analysis indicating that [information protected as a trade secret] In turn, the results of the analysis of the impact on the budget of the applicant show [information protected as a trade secret]

However, it should be noted that the drug consumption estimated based on the indications and data about the population that can use the drug is many times higher than the applicant's estimates (approx. 60,000 patients may become eligible for the reimbursement of the drug based on the indications adopted and the above result is shown for the population [information protected as a trade secret] in the first and second year of reimbursement, respectively).

In view of the expected budget impact analysis, which is many times higher than predicted in the applicant's analyses, it is justified to introduce a risk-sharing scheme that will secure the total impact on the payer's budget due to reimbursement of the above-mentioned technology.

The opinion also notes that most of the clinical indications recommend the use of GLP-1 receptor agonists in obese patients and in the presence or risk of cardiovascular co-morbidities. In the indications found, GLP-1 receptor agonists can also be used in further stages of treatment: in two-drug therapy, three-drug therapy, as well as in a simple and combined insulin therapy.

Taking into account the above arguments, but also the proposed price of the proposed technology, it seems reasonable to reimburse Rybelsus (semaglutide) **only provided that [information protected as a trade secret]**

[information protected as a trade secret]

Subject of the application

The order of the Minister of Health concerns the assessment of the appropriateness of public reimbursement of the following medicinal product:

- Rybelsus (semaglutide), tablets, 3 mg, 30, tablets, GTIN code: 05712249113537; net sales price: [information protected as a trade secret]

- Rybelsus (semaglutide), tablets, 7 mg, 30, tablets, GTIN code:05712249113544; net sales price: [information protected as a trade secret]

- Rybelsus (semaglutide), tablets, 14 mg, 30, tablets, GTIN code:05712249113551; net sales price: [information protected as a trade secret]

Proposed payment and dispensing category: [information protected as a trade secret], the drug available in the pharmacy on prescription for an indication of a given clinical condition, in the existing limit group: "252.0, Antidiabetic agents – GLP-1 agonists". [information protected as a trade secret]

Health problem

Diabetes is a group of metabolic diseases characterised by hyperglycaemia resulting from a defect in insulin secretion and/or activity. Chronic hyperglycaemia is associated with damage, dysfunction and failure of various organs, especially the eyes, kidneys, nerves, heart and blood vessels.

Type 2 diabetes is classified as E11 in the ICD 10 classification (Noninsulin-dependent diabetes), which includes the following disease entities:

- Diabetes (without obesity) (with obesity): adult-onset; young adult-onset (MODY); without ketosis; stable; type 2.
- noninsulin-dependent growth-onset diabetes.

The prevalence of type 2 diabetes in Poland is approx. 9% in the population aged between 20 and 79. The annual incidence in Poland is estimated at approx. 200/100,000 people. Age of onset is generally > 30. The incidence increases with age until 70, and it decreases above this age. The mortality rate in Poland is approx. 15/100,000 people, while in the population aged > 75 years of age it rises up to 120/100,000 people. As many as 70% of deaths are due to cardiovascular complications.

Alternative health technology

Taking into account clinical guidelines and currently publicly-funded technologies, the following comparators have been identified for the proposed technology:

in patients ineffectively treated with ≥ 2 oral antidiabetic agents (OAD) without insulin:

- SGLT-2 inhibitors *(*sodium-glucose co-transporter-2),
- GLP-1 receptor agonists (glucagon-like peptide 1).

in patients ineffectively treated with ≥1 OAD and insulin:

- intensification of insulin treatment.

It should be noted that the selected comparators partly reflect current clinical practice. The Agency also recommends the use of an alpha-glucosidase inhibitor - acarbose among the comparators, in addition to SGLT-2 inhibitor agents and insulin therapy.

Description of the proposed intervention

Rybelsus contains semaglutide, which acts as a GLP-1 receptor agonist; it selectively binds to the GLP-1 receptor by activating it, which is similar to native GLP-1. GLP-1 is a physiological hormone that demonstrates a considerable number of effects in terms of the regulation of appetite and blood sugar levels, as well as effects on cardiovascular function. Its effects on blood sugar levels and appetite are related to GLP-1 receptors in the pancreas and brain.

According to the Summary of Product Characteristics (SmPC), Rybelsus is indicated for the treatment of adults with insufficiently controlled type 2 diabetes to improve glycaemic control as an adjunct to diet and exercise:

- as monotherapy when metformin is considered inappropriate due to intolerance or contraindications;
- in combination with other medicinal products for the treatment of diabetes.

The indication specified in the application is included in the registration indication.

Efficacy, effectiveness and safety assessment

This assessment involves collecting data on the health consequences (efficacy and safety) of the new therapy for the health problem in question and of other therapies that are currently reimbursed from public funds and represent alternative therapies available for the health problem. Furthermore, this assessment requires determination of the reliability of data collected and a comparison of the efficacy and safety results of the new therapy against the therapies already available to treat the health problem in question.

On the basis of the above, the efficacy and safety assessment allows answering the question of the scale of the health outcome (both in terms of efficacy and safety) to be expected from the new therapy compared with other therapeutic options under consideration.

The target population in the analyses are patients with type 2 diabetes treated with at least metformin±sulfonylurea derivative or basal insulin±metformin, with baseline HbA1c ≥8%, BMI ≥ 30 kg/m^2 and patients at very high cardiovascular risk. One primary study

was included in the clinical analysis:

- PIONEER 8 – a randomised controlled trial conducted among 731 ineffectively treated

patients with type 2 diabetes. The study directly compared semaglutide (SEM) administered orally with placebo (PLC) as an add-on therapy to insulin (INS) in monotherapy or an add-on therapy to metformin (INS + MET): SEM + INS ± MET vs PLA + INS ± MET.

In addition, a randomised clinical trial comparing the use of semaglutide with placebo in a population of adult patients with type 2 diabetes with high cardiovascular risk (PIONEER 6) was included.

No studies could be found that would directly compare the use of orally administered semaglutide at the analysed doses with the use of SGLT-2 inhibitors and GLP-1 receptor agonists (at doses reimbursed in Poland) after ineffective therapy with metformin-sulfonylurea derivative.

A comparison of semaglutide with SGLT-2 inhibitors and GLP-1 receptor agonists is provided on the basis of secondary studies:

[information protected as a trade secret]

- Nuhoho 2019 – a systematic review with network meta-analysis to evaluate the efficacy and safety of orally administered semaglutide 14 mg compared with subcutaneously administered GLP-1 receptor agonists in patients with type 2 diabetes who were previously treated with 1-2 oral antidiabetic agents.

Moreover, two additional secondary studies were included in the analysis (Li 2021, Avgerinos

2020). The following primary endpoints were assessed in the primary studies:

- HbA1c change (PIONEER 8);
- time from randomisation to major adverse cardiovascular event (MACE): death from cardiovascular causes, non-fatal myocardial infarction or non-fatal stroke (PIONEER 6).

PIONEER 8 assessed the quality of life using the questionnaires: SF-36v2 *(Short Form Health Survey; Acute Version*), DTSQ (Diabetes Treatment Satisfaction Questionnaire), IWQOL – Lite CT *(Impact of Weight on Quality of Life-Lite Clinical Trial Version*).

Reliability assessment of PIONEER 8 was performed using the Cochrane Collaboration's risk of bias assessment tool based on the Jadad scale criteria (5-point). The study scored 5 on the Jadad scale and the Cochrane analysis of the study showed a low or unknown (in the domains of concealment of randomisation code and blinding of effect assessment) risk of bias. Secondary studies: Nuhoho 2019 and [information protected as a trade secret] were characterised by [information protected as a trade secret] according to the AMSTAR 2 scale.

Efficacy

PIONEER 8, SEM 7 mg and SEM 14 mg vs PLC (results for *trial product estimand*[1] population are shown)

Among the patients with type 2 diabetes, statistically significant (IS) greater reductions in glycated haemoglobin levels were observed in the groups of SEM 7 mg and 14 mg used together with MET and INS after 52 weeks of treatment: HbA1c, fasting plasma glucose levels: FPG, plasma glucose by self-measurement: SMPG, body weight, BMI and waist circumference, and a greater reduction in postprandial glycaemic spikes (only at the 7mg dose, a result at the IS cut-off) compared with the group receiving PLC together with MET and INS:

- SEM 7 mg vs PLC (INS adjustment):
    - HbA1c: MD=-0.9% [95% CI: -1,1; -0.6], p<0.0001;
    - FPG: MD=-1.15 mmol/L [95%CI: -1.72; -0.59], p<0.0001;
    - SMPG: MD=-1.0 mmol/L [95%CI: -1.5; -0.5], p<0.0001;
    - Post-meal glycaemic spikes: MD=-0.6 mmol/L [95%CI: -1.1; -0.2], p=0.0083
    - Body weight: MD=-5.5 kg [95%CI: -4.5; -2.6], p<0.0001;
    - BMI: MD=–1.3 kg/m^2 [95%CI: –1.7; –0.9], p<0,0001;
    - Waist circumference: MD=-2.2 cm [95%CI: -4, 2; -2.1], p<0.0001.

- SEM 14 mg vs PLC (INS adjustment):
    - HbA1c: MD=-1.2 %[95% CI: -1.5; -1.0], p<0.0001;
    - FPG: MD=-1.53 mmol/L [95%CI: [-2.09; -0.97], p<0.0001;
    - SMPG: MD=-1.4 mmol/L [95%CI: -1.8; -0.9], p<0.0001;
    - Body weight: MD=-4.9 kg [95%CI: -5.9; -3.9], p<0.0001;
    - BMI: MD=-1.8 kg/m^2 [95%CI: -2.2; -1.5], p<0.0001;
    - Waist circumference: MD=-4.7 cm [95%CI: -5.8; -3.6], <0.0001.

Quality of life assessment

After 52 weeks, the SEM 7 mg and SEM 14 mg groups showed statistically significant greater improvement in overall health as measured by the SF36v2 questionnaire and statistically significant greater improvement in overall satisfaction with treatment, recommendation of therapy or continuation of therapy as assessed by the DTSQ specific questionnaire.

In the SEM 7 mg group, no IS differences were observed between the evaluated technology and the intensification of insulin treatment in terms of the effect on the subject weight reduction using the IWQOL-Lite CT questionnaire. In contrast, the SEM 14 mg group showed IS greater improvement in the overall IWQOL-Lite CT questionnaire score and the psychosocial domain score.

PIONEER 6

Statistical significance was not reached between semaglutide treatment and PLC for the risk assessment of the primary composite endpoint of cardiovascular death, non-fatal myocardial infarction or non-fatal stroke (HR=0.79 [95%CI: 0.57; 1.11], p=NS).

[information protected as a trade secret]

[information protected as a trade secret]

Nuhoho 2019, indirect comparison of SEM 14 mg vs GLP-1 agonists

There was no demonstrated advantage of SEM 14 mg over other GLP-1 agonists (administered subcutaneously) in terms of glycaemic control (reduction in HbA1c, percentage of patients achieving HbA1c<7%, HbA1c≤6.5%) and cardiovascular effects (reduction in systolic and diastolic blood pressure).

The use of SEM 14 mg was associated with a statistically significant greater reduction in body weight in diabetic patients
than the use of dulaglutide 1.5 mg.

Avgerinos 2020 Li 2021

The results of the efficacy analysis of the other reviews are consistent with the results of PIONEER 8 and also show the efficacy of semaglutide in reducing HbA1c levels and body weight in patients with type 2 diabetes compared to placebo. It should be noted, however, that they relate, among other things, to the same studies that were included in the clinical analysis.

Safety

PIONEER 8 (SEM 7 mg and SEM 14 mg vs PLC)

The incidences of total adverse events were similar in patients with type 2 diabetes

2 treated with semaglutide 14 mg, 7 mg and those treated with insulin (treatment intensification).

Incidence of total adverse events (AEs) leading to treatment discontinuation was statistically significantly higher in patients treated with SEM 14 mg and 7 mg compared to the comparator.

Nausea, diarrhoea, decreased appetite and vomiting were statistically significantly more frequent in the semaglutide 14 mg and 7 mg groups compared to the intensification of insulin treatment.

Constipation and abdominal discomfort were statistically significantly more frequent in the semaglutide 7 mg group compared to intensified insulin treatment.

Hypertension occurred at a statistically significantly lower frequency in the SEM 14 mg group than in the group treated with insulin.

NMA 2019 (SEM 7 mg in SEM 14 mg vs SGLT-2)

The incidence of total adverse events resulting in treatment discontinuation in patients using SEM and SGLT-2 inhibitors was similar except for the comparison of SEM 14 mg versus CANA, where the use of SEM was more often associated with treatment discontinuation due to AEs: SEM versus CANA: OR=2.57 [95%CI: 1.17; 5.67], p<0.05.

Nuhoho 2019 (SEM 14 mg vs GLP-1)

The incidence of total adverse events in patients using semaglutide 14 mg and other GLP-1 agents were similar (no IS difference in results). Avgerinos 2020 Li 2021 (SEM 7 mg and SEM 14 mg vs PLC) The results of the safety analysis of the other reviews are consistent with the above conclusions. Li 2021 indicates no increase in the incidence of total adverse events, hypoglycaemia, myocardial infarction, heart failure or stroke. In contrast, Avgerinos 2020 review highlights an increased incidence of gastrointestinal adverse events during the use of SEM.

Limitations

The main limitation to the reliability of the analysis presented is the fact that the efficacy and safety analyses concern the general population of patients with diabetes. No results were extracted for the population indicated in the reimbursement application, i.e. patients using at least two oral hypoglycaemic agents or basal insulin in combination with at least one oral hypoglycaemic agent, with HbA1c ≥ 8%, with obesity defined as BMI ≥ 30kg/m^2 and with very high cardiovascular risk defined as confirmed cardiovascular disease or damage to other organs manifested by proteinuria or left ventricular hypertrophy, or retinopathy, or the presence of 2 or more major risk factors among the following: age ≥ 55 for men, ≥ 60 for women, dyslipidaemia, hypertension, smoking.

The uncertainty of the presented clinical analysis results also stems from the lack of studies directly comparing the use of semaglutide at the doses analysed with the use of SGLT-2 inhibitors and other GLP-1 agonists following ineffective therapy with metformin ± sulfonylurea derivative.

In addition, no effectiveness study for orally administered semaglutide in the indication analysed was included in the analysis.

Proposed risk-sharing scheme
[information protected as a trade secret]

Economic evaluation, including a cost-effectiveness estimation

Economic evaluation involves estimating and comparing the costs and health outcomes that may be associated with the administration of the new therapy to an individual patient instead of already reimbursed therapies.

The costs of therapy are estimated in Polish currency, and health outcomes are usually expressed in life-years gained (LYG) or quality-adjusted life years (QALY) as a result of the therapy.

Juxtaposing the values concerning the costs and outcomes of a new therapy and comparing them to the costs and outcomes of already reimbursed therapies allows answering the question of whether the health outcome achieved in an individual patient owing to a new therapy is associated with a higher cost in comparison with already reimbursed therapies.

The obtained results of the cost-effectiveness ratio are compared with the so-called cost-effectiveness threshold, i.e. a result that indicates that given the wealth of Poland (expressed in GDP), the maximum cost of the new therapy that is expected to produce a unit of health outcome (1 LYG or 1 QALY) compared to already available therapies should not exceed three times GDP per capita.

Currently, the cost-effectiveness threshold is PLN 155,514.00 (3 x PLN 51,838.00).

The cost-effectiveness ratio does not estimate or determine the value of life, but it only enables its assessment and on that basis, among other things, choosing the therapy related to potentially best outcome.

The cost-effectiveness assessment included a cost-utility analysis (CUA) over a lifetime horizon (50 years), from the perspective of the public payer – the entity required to fund the benefits with public funds, i.e. the National Health Fund (NHF) and from the joint perspective of the payer and the patient.

The following medical costs were included in the analysis:

- semaglutide (SEM);
- comparators, i.e. SGLT-2 inhibitors (canagliflozin, empagliflozin, dapagliflozin) and insulin;
- oral antidiabetic agents, i.e. metformin and sulphonylurea derivative (glimepiride);
- insulin and insulin therapy needles;
- lances and diabetes test strips;
- treatment of diabetic complications;
- other treatments of diabetes (concomitant treatment, diagnosis of other parameters).

The results are presented for two subpopulations:

- patients treated ineffectively with ≥ 2 OADs;
- patients treated ineffectively with basal insulin in combination with ≥ 1 OAD.

Population treated ineffectively ≥2 OADs

[information protected as a trade secret]

[information protected as a trade secret]

Population treated ineffectively with basal insulin combined with ≥1 OAD

[information protected as a trade secret]

Limitations

The applicant uses the IMS CORE online model as the basis for its economic analysis. The central, networked nature of the application does not enable checking the calculations performed so the input data could not be verified.

In the patient population treated with ≥2OADs in terms of comparison with SGLT-2 inhibitors, empagliflozin was used as a comparator in the primary analysis. The other SGLT-2 inhibitors (empagliflozin and dapagliflozin), on the other hand, were included in the sensitivity analysis only.

Moreover, semaglutide 3 mg was excluded from the analysis.

Agency's own calculations

No additional own calculations were performed.

Indication whether the circumstances referred to in Art. 13 sec. 3 of the Act of 12 May 2011 on the reimbursement of drugs, foodstuffs for particular nutritional uses and medical devices (Dz. U. /Journal of Laws/ of 2021, item 523 as amended) do arise;

If the applicant's clinical analysis does not include randomised clinical trials proving the superiority of the drug over health technologies already reimbursed, the official selling price of the drug must be calculated so that the cost of the drug to be reimbursed is not higher than the cost of the health technology with the most favourable cost–effectiveness ratio.

As the superiority of semaglutide therapy over reimbursed alternative therapy in the population covered in the application was not demonstrated, in a randomised clinical trial, the circumstances referred to in Art. 13 sec. 3 of the Reimbursement Act do arise.

[information protected as a trade secret]

Assessment of the impact on the healthcare system, including the budget impact

Healthcare system impact assessment has two major parts.

First, the analysis of the impact on the payer's budget allows estimating the potential expenses associated with public reimbursement of the new therapy.

Estimates of the expenses associated with the new therapy (the "tomorrow" scenario) are compared to how much is currently spent on treating the health problem (the "today" scenario). On this basis, it is possible to assess whether a new therapy will require more resources allocated to the treatment of the given health problem or whether it will result in savings in the payer's budget.

A budget impact assessment determines whether a payer has adequate resources to reimburse particular technology.

Healthcare system impact assessment in the second part answers the question of how the decision on the reimbursement of a new therapy may affect the organisation of the provision of services (particularly in terms of adaptation to the requirements of the implementation of the new therapy) and the availability of other healthcare services.

The results of the applicant's budget impact analysis are presented over a two-year horizon. The analysis was conducted from the perspective of public payer (NHF) and joint perspective.

The analysis included the costs of acquiring the active substances of semaglutide, insulin, metformin, sulphonylurea derivative and SGLT-2 inhibitor agents; insulin administration; and blood glucose monitoring costs.

The applicant has estimated the number of patients at:

[information protected as a trade secret]

The results of the basic analysis indicate that the reimbursement of Rybelsus (semaglutide) in the indication covered in this recommendation will entail [information protected as a trade secret]

[information protected as a trade secret]

Limitations

The main limitations of the analysis arise from the uncertainty of estimating the population in which the proposed agent would be used. The greatest uncertainty is associated with parameters based on forecasts and the applicant's assumptions regarding the percentage of patients willing to co-pay and the share of market for orally administered semaglutide.

Agency's own calculations

No additional own calculations were performed. However, it should be noted that the consumption of the agent estimated based on the indications and data on the population that can use the drug is many times higher than estimated by the applicant. There is also uncertainty in the forecasting of the time horizon over which population saturation will occur.

In view of the expected impact on the payer's budget, which is many times higher than predicted in the applicant's analyses, it is justified to introduce a risk-sharing scheme that will secure the total impact on the payer's budget due to reimbursement of the above-mentioned technology.

Comments on the proposed risk-sharing scheme
[information protected as a trade secret]

Comments on the drug programme

Not applicable.

Discussion on the solutions proposed in the rationalisation analysis

The subject of the rationalisation analysis is the identification of a mechanism, the introduction of which will result in the release of public funds in an amount corresponding to at least the increase in costs resulting from a positive decision on the reimbursement of the health technology covered in this recommendation.

The rationalisation analysis is submitted if the budget impact analysis for the entity responsible for funding indicates an increase in reimbursement costs.

[information protected as a trade secret]

Overview of recommendations issued in other countries in relation to the assessed technology

Twelve clinical recommendations related to the indication named in the application were presented. Those were issued by:

- Polish Diabetes Association (PTD 2021);
- European Society of Cardiology and European Association for the Study of Diabetes (ESC/EASD 2019);
- National Institute for Health and Care Excellence (NICE 2020);
- World Health Organisation (WHO 2020);
- American Diabetes Association (ADA 2021);
- American Association of Clinical Endocrinologists/American College of Endocrinology (AACE/ACE 2020);
- Australian Diabetes Society (ADS 2020);
- American Diabetes Association/ European Association for the Study of Diabetes (ADA/EASD 2019);
- American College of Physicians (ACP 2017/2018);
- Diabetes Canada (DC 2018);
- Scottish Intercollegiate Guidelines Network (SIGN 2017);
- International Diabetes Federation (IDF 2017).

Recommendations agree on the basic principles of type 2 diabetes treatment. The basis for improvement of health status is non-pharmacological treatment – body weight reduction, increasing physical activity. Metformin remains the primary oral first-line drug for the treatment of type 2 diabetes. All recommendations indicate that the choice of drug should take account of concomitant conditions.

In most guidelines found, GLP-1 receptor agonist is recommended for use in previously treated patients with type 2 diabetes who are obese and in patients with diagnosed cardiovascular risk.

Reimbursement recommendations

Four positive conditional recommendations – CADTH 2021, NCPE 2021, SMC 2020, ZN 2020 and one negative recommendation – HAS 2020, were found.

Positive reimbursement recommendations are for an indication narrower than the registration indication and include the use of semaglutide in a two- or three-drug therapy, or in monotherapy when metformin is not advisable. One of the recommendations - ZN 2020, referred to the use of this medical product in patients with a BMI ≥ 30 kg/m^2.

In positive recommendations, the conditions indicating the appropriateness of reimbursement relate mainly to the use of the technology applied in combination with other OADs or basal insulin, as well as in combination with metformin or other antihyperglycaemic agents and when the price is not higher than that of the existing therapies.

The negative recommendation mainly draws attention to the insufficient data concerning effectiveness of the evaluated technology (reassessment planned in 2021).

According to the information provided by the applicant, Rybelsus (semaglutide) is funded in [information protected as a trade secret] EU and EFTA countries (out of 31 indicated ones).

Legal basis for the recommendation

The recommendation was prepared based on the order of 26 July 2021 issued by the Minister of Health (ref. no.: PLR.4500.796.2021.4.JDZ, PLR.4500.797.2021.4.JDZ, PLR.4500.798.2021.4.JDZ), regarding the preparation of the President's recommendation on the assessment of Rybelsus (semaglutide) in the indication: type 2 diabetes, for patients taking at least two oral hypoglycaemic agents or basal insulin in combination with at least one oral hypoglycaemic agent, with HbA1c ≥ 8%, with obesity defined as BMI ≥ 30 kg/m^2 and with very high cardiovascular risk defined as: confirmed cardiovascular disease or damage to other organs manifested by: proteinuria or left ventricular hypertrophy, or retinopathy, or the presence of 2 or more major risk factors among the following: age ≥ 55 for men, ≥ 60 or women, dyslipidaemia, hypertension, smoking, on the basis of Art. 35 sec. 1 of the Act of 12 May 2011 on the reimbursement of drugs, foodstuffs intended for particular nutritional uses and medical devices (Dz. U. /Journal of Laws/ of 2021, item 523 as amended), having obtained Position of the Transparency Council No. 121/2021 of 18 October 2021 on the assessemnt of Rybelsus (semaglutide) in the indication: type 2 diabetes, for patients using at least two oral hypoglycaemic agents or basal insulin in combination with at least one oral hypoglycaemic agent, with HbA1c ≥ 8%, with obesity defined as BMI ≥ 30 kg/m^2 and with very high cardiovascular risk defined as: confirmed cardiovascular disease or damage to other organs manifested by: proteinuria or left ventricular hypertrophy, or retinopathy, or the presence of 2 or more major risk factors among the following: age ≥ 55 for men, ≥ 60 for women, dyslipidaemia, hypertension, smoking

References

1. Position of the Transparency Council No. 121/2021 of 18 October 2021 on the assessment of Rybelsus (semaglutide) in the indication: type 2 diabetes, for patients using at least two oral hypoglycaemic agents or basal insulin in combination with at least one oral hypoglycaemic agent, with HbA1c ≥ 8%, with obesity defined as BMI ≥ 30 kg/m^2 and with very high cardiovascular risk defined as: confirmed cardiovascular disease or damage to other organs manifested by: proteinuria or left ventricular hypertrophy, or retinopathy, or the presence of 2 or more major risk factors among the following: age ≥ 55 for men, ≥ 60 for women, dyslipidaemia, hypertension, smoking
2. Report No. OT.4230.16.2021 Application for the reimbursement of Rybelsus (semaglutide) in the indication: type 2 diabetes, for patients using at least two oral hypoglycaemic agents or basal insulin in combination with at least one oral hypoglycaemic agent, with HbA1c ≥ 8%, with obesity defined as BMI ≥ 30 kg/m^2 and with very high cardiovascular risk defined as: confirmed cardiovascular disease or damage to other organs manifested by: proteinuria or left ventricular hypertrophy, or retinopathy, or the presence of 2 or more major risk factors among the following: age ≥ 55 for men, ≥ 60 for women, dyslipidaemia, hypertension, smoking