NATIONAL PHARMACEUTICAL REGULATORY DIVISION MINISTRY OF HEALTH MALAYSIA

TECHNICAL EVALUATION SUMMARY

PRODUCT NAME:
Ozempic 1.34mg/ml (0.25mg, 0.5mg/ dose) Solution for Injection in pre filled pen
Ozempic 1.34mg/ml (1mg/ dose) Solution for Injection in pre filled pen

ACTIVE INGREDIENT:
Semaglutide 1.34mg/ml

PRODUCT REGISTRATION HOLDER:
Novo Nordisk Pharma (Malaysia) Sdn Bhd

PRODUCT MANUFACTURER:
Novo Nordisk A/S, Denmark

APPROVAL DATE:
13 Februari 2020 (DCA 343)

1.0 BACKGROUND INFORMATION

1.1 Approved Indication

Ozempic® is indicated for the treatment of adults with insufficiently controlled type 2 diabetes mellitus as an adjunct to diet and exercise

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

For study results with respect to combinations, effects on glycaemic control and cardiovascular events, and the populations studied, see Special warnings and precautions for use, Interaction with other medicinal products and other forms of interaction and Pharmacodynamic properties.

1.2 Approved Posology

The starting dose is 0.25 mg semaglutide once weekly. After 4 weeks the dose should be increased to 0.5 mg once weekly. After at least 4 weeks with dose of 0.5 mg once weekly, the dose can be increased to 1 mg once weekly to further improve glycaemic control. Semaglutide 0.25 mg is not a maintenance dose. Weekly doses higher than 1 mg are not recommended.

When Ozempic® is added to existing metformin and/or thiazolidinedione therapy, the current dose of metformin and/or thiazolidinedione can be continued unchanged.

When Ozempic® is added to existing therapy of sulfonylurea or insulin, a reduction in the dose of sulfonylurea or insulin should be considered to reduce the risk of hypoglycaemia.

Self-monitoring of blood glucose is not needed in order to adjust the dose of Ozempic®. However, when initiating treatment with Ozempic® in combination with a sulfonylurea or insulin, blood glucose self-monitoring may become necessary to adjust the dose of the sulfonylurea or the insulin to reduce the risk of hypoglycaemia.

Missed dose
If a dose is missed, it should be administered as soon as possible and within 5 days after the missed dose. If more than 5 days have passed, the missed dose should be skipped, and the next

dose should be administered on the regularly scheduled day. In each case, patients can then resume their regular once weekly dosing schedule.

Special populations

Elderly

No dose adjustment is required based on age. Therapeutic experience in patients' ≥75 years of age is limited

Renal impairment

No dose adjustment is required for patients with mild, moderate or severe renal impairment. Experience with the use of semaglutide in patients with severe renal impairment is limited. Semaglutide is not recommended for use in patients with end-stage renal disease.

Hepatic impairment

No dose adjustment is required for patients with hepatic impairment. Experience with the use of semaglutide in patients with severe hepatic impairment is limited. Caution should be exercised when treating these patients with semaglutide

Paediatric population

The safety and efficacy of semaglutide in children and adolescents below 18 years have not yet been established. No data are available.

Method of administration

Ozempic® is to be administered once weekly at any time of the day, with or without meals.

Ozempic® is to be injected subcutaneously in the abdomen, in the thigh or in the upper arm. The injection site can be changed without dose adjustment. Ozempic® should not be administered intravenously or intramuscularly.

The day of weekly administration can be changed if necessary as long as the time between two doses is at least 3 days (>72 hours). After selecting a new dosing day, once-weekly dosing should be continued.

1.3   Method of administration

Subcutaneous injection

1.4 Pharmacological Aspects

Mechanism of action

Semaglutide is a GLP-1 analogue with 94% sequence homology to human GLP-1. Semaglutide acts as a GLP-1 receptor agonist that selectively binds to and activates the GLP-1 receptor, the target for native GLP-1.

GLP-1 is a physiological hormone that has multiple actions in glucose and appetite regulation, and in the cardiovascular system. The glucose and appetite effects are specifically mediated via GLP-1 receptors in the pancreas and the brain.

Semaglutide reduces blood glucose in a glucose dependent manner by stimulating insulin secretion and lowering glucagon secretion when blood glucose is high. The mechanism of blood glucose lowering also involves a minor delay in gastric emptying in the early postprandial phase. During hypoglycaemia, semaglutide diminishes insulin secretion and does not impair glucagon secretion.

Semaglutide reduces body weight and body fat mass through lowered energy intake, involving an overall reduced appetite. In addition, semaglutide reduces the preference for high fat foods.

GLP-1 receptors are also expressed in the heart, vasculature, immune system and kidneys. Semaglutide had a beneficial effect on plasma lipids, lowered systolic blood pressure and reduced inflammation in clinical studies. In animal studies, semaglutide attenuates the development of atherosclerosis by preventing aortic plaque progression and reducing inflammation in the plaque.

Pharmacodynamic effects

All pharmacodynamic evaluations were performed after 12 weeks of treatment (including dose escalation) at steady state with semaglutide 1 mg once weekly.

Fasting and postprandial glucose

Semaglutide reduces fasting and postprandial glucose concentrations. In patients with type 2 diabetes, treatment with semaglutide 1 mg resulted in reductions in glucose in terms of absolute change from baseline (mmol/l) and relative reduction compared to placebo (%) for fasting glucose (1.6 mmol/l; 22% reduction), 2 hour postprandial glucose (4.1 mmol/l; 37% reduction), mean 24 hour glucose concentration (1.7 mmol/l; 22% reduction) and postprandial glucose excursions over 3 meals (0.6–1.1 mmol/l) compared with placebo. Semaglutide lowered fasting glucose after the first dose.

Beta-cell function and insulin secretion

Semaglutide improves beta-cell function. Compared to placebo, semaglutide improved first- and second-phase insulin response with a 3- and 2-fold increase, respectively, and increased maximal beta-cell secretory capacity in patients with type 2 diabetes. In addition, semaglutide treatment increased fasting insulin concentrations compared to placebo.

Glucagon secretion

Semaglutide lowers the fasting and postprandial glucagon concentrations. In patients with type 2 diabetes, semaglutide resulted in the following relative reductions in glucagon compared to placebo: fasting glucagon (8–21%), postprandial glucagon response (14–15%) and mean 24 hour glucagon concentration (12%).

Glucose dependent insulin and glucagon secretion

Semaglutide lowered high blood glucose concentrations by stimulating insulin secretion and lowering glucagon secretion in a glucose dependent manner. With semaglutide, the insulin secretion rate in patients with type 2 diabetes was comparable to that of healthy subjects. During induced hypoglycemia, semaglutide compared to placebo did not alter the counter regulatory responses of increased glucagon and did not impair the decrease of C-peptide in patients with type 2 diabetes.

Gastric emptying

Semaglutide caused a minor delay of early postprandial gastric emptying, thereby reducing the rate at which glucose appears in the circulation postprandially.

Appetite, energy intake and food choice

Semaglutide compared to placebo lowered the energy intake of 3 consecutive ad libitum meals by 18–35%. This was supported by a semaglutide-induced suppression of appetite in the fasting state as well as postprandially, improved control of eating, less food cravings and a relative lower preference for high fat food.

Fasting and postprandial lipids

Semaglutide compared to placebo lowered fasting triglyceride and very low density lipoproteins (VLDL) cholesterol concentrations by 12% and 21%, respectively. The postprandial triglyceride and VLDL cholesterol response to a high fat meal was reduced by >40%.

Cardiac electrophysiology (QTc)

The effect of semaglutide on cardiac repolarization was tested in a thorough QTc trial. Semaglutide did not prolong QTc intervals at supra-therapeutic dose levels (up to 1.5 mg at steady state).

Pharmacokinetic Properties

Compared to native GLP-1, semaglutide has a prolonged half-life of around 1 week making it suitable for once weekly subcutaneous administration. The principal mechanism of protraction is albumin binding, which results in decreased renal clearance and protection from metabolic degradation. Furthermore, semaglutide is stabilized against degradation by the DPP-4 enzyme.

Absorption

Maximum concentration was reached 1 to 3 days post dose. Steady state exposure was achieved following 4–5 weeks of once weekly administration. In patients with type 2 diabetes, the mean steady state concentrations following subcutaneous administration of 0.5 mg and 1 mg semaglutide were approximately 16 nmol/l and 30 nmol/l, respectively. Semaglutide exposure increased in a dose proportional manner for doses of 0.5 mg and 1 mg. similar exposure was achieved with subcutaneous administration of semaglutide in the abdomen, thigh, or upper arm. Absolute bioavailability of subcutaneous semaglutide was 89%.

Distribution

The mean volume of distribution of semaglutide following subcutaneous administration in patients with type 2 diabetes was approximately 12.5 l. Semaglutide was extensively bound to plasma albumin (>99%).

Metabolism/Biotransformation

Prior to excretion, semaglutide is extensively metabolized through proteolytic cleavage of the peptide backbone and sequential beta-oxidation of the fatty acid side chain. The enzyme neutral endopeptidase (NEP) is expected to be involved in the metabolism of semaglutide.

Elimination

In a study with a single subcutaneous dose of radiolabelled semaglutide, it was found that the primary excretion routes of semaglutide-related material were via urine and faeces; approximately 2/3 of semaglutide-related material was excreted in urine and approximately 1/3 in faeces. Approximately 3% of the dose was excreted as intact semaglutide via urine. In patients with type 2 diabetes clearance of semaglutide was approximately 0.05 l/h. With an

elimination half-life of approximately 1 week, semaglutide will be present in the circulation for about 5 weeks after the last dose.

Special population

Elderly

Age had no effect on the pharmacokinetics of semaglutide based on data from phase 3A studies including patients of 20–86 years of age.

Gender, race and ethnicity

Gender, race (White, Black or African-American, Asian) and ethnicity (Hispanic or Latino, non-Hispanic or -Latino) had no effect on the pharmacokinetics of semaglutide. \

Body weight

Body weight has an effect on the exposure of semaglutide. Higher body weight results in lower exposure; a 20% difference in body weight between individuals will result in an approximate 16% difference in exposure. Semaglutide doses of 0.5 mg and 1 mg provide adequate systemic exposure over a body weight range of 40–198 kg.

Renal impairment

Renal impairment did not impact the pharmacokinetics of semaglutide in a clinically relevant manner. This was shown with a single dose of 0.5 mg semaglutide for patients with different degrees of renal impairment (mild, moderate, severe or patients in dialysis) compared with subjects with normal renal function. This was also shown for subjects with type 2 diabetes and with renal impairment based on data from phase 3a studies, although the experience in patients with end-stage renal disease was limited.

Hepatic impairment

Hepatic impairment did not have any impact on the exposure of semaglutide. The pharmacokinetics of semaglutide were evaluated in patients with different degrees of hepatic impairment (mild, moderate, severe) compared with subjects with normal hepatic function in a study with a single-dose of 0.5 mg semaglutide.

Paediatric population

Semaglutide has not been studied in paediatric patients

2.0 SUMMARY REPORT

2.1 Quality

2.1.1 Active Substance

Semaglutide is produced using recombinant DNA technology in Saccharomyces cerevisiae followed by chemical modifications. The construction of the expression plasmid and history of the S. cerevisiae strain have been provided. The yeast strain NNY574 originates from Novo Nordisk A/S and derived from wild-type yeast strains.

Process validation activities conducted have confirmed that the manufacturing process reproducibly produces drug substance (DS) of consistent quality that meets predetermined specifications. From the stability studies conducted, the drug substance is stable when stored at -20°C ± 5°C for 60 months.

2.1.2 Finished Product

Process validation for three consecutive commercial batches for both presentations have been submitted. The results of the process validation study met the pre-defined acceptable criteria. Thus, it was concluded that the manufacturing process is able to produce the final drug product consistently.

Stability batches of finished product were placed on long-term real time studies (2 - 8°C) for 36 months. The stability data showed that Ozempic continued to meet the acceptance criteria for the monitored attributes after storage for 36 months. Thus, the proposed shelf-life of 36 months for this product is justified. The in-use stability data demonstrated that the drug product is stable for 42 days when stored at below 30°C.

Ozempic is supplied as either 1.5ml disposable pre-filled pen or a 3ml disposable pre-filled pen

The product has passed the NPRA laboratory evaluation on analytical protocol and validation.

2.2 Efficacy

The clinical development programme for Ozempic consist of nine phase 3 studies to support registration where two trials were conducted in Japanese population. The phase 3 trials assessed the efficacy and safety of once weekly SC Ozempic from monotherapy in drug naïve patients with type 2 diabetes (T2D), to combination use with one or more oral anti diabetics (OADs), as well as with basal insulin in patients with long standing T2D. Long-term effects of Ozempic on efficacy, safety and cardiovascular risk were also assessed in a dedicated pre-approval Cardiovascular Observation Trial (CVOT) in adults with T2D at high risk of cardiovascular events.

Table 1: Summary of Clinical Studies Conducted

Study Type & Design (N)	Objective (s) of the Study	Results of Primary Endpoint
SUSTAIN 1 *Sorli.C et.al.* Efficacy and safety of once weekly semaglutide monotherapy versus placebo in patients with type 2 diabetes (SUSTAIN 1): a double blind, randomized, placebo-controlled, parallel-group, multinational, multicenter phase 3a trial. **January 2017 Vol 5 Lancet Diabetes Endocrinol 251-260** (N=388)	To demonstrate superiority of once-weekly dosing of two dose levels of semaglutide versus placebo on glycemic control after 30 weeks of treatment in drug-naïve subjects with T2D	• At week 30, mean baseline HbA1c significantly decreased by 1·45% (95% CI: −1·65 to −1·26) with 0·5 mg semaglutide (estimated treatment difference vs placebo −1·43% (95% CI: −1·71 to −1·15; p<0·0001), significantly decreased by 1·55% (95% CI : −1·74 to −1·36) with 1·0 mg semaglutide (estimated treatment difference vs placebo −1·53%, (95% CI: −1·81 to −1·25; p<0·0001), and non-significantly decreased by 0·02% (95% CI : −0.23 to 0·18) with placebo. • Superiority for change in HbA1c was claimed if the upper limit of the 2-sided 95% CI for the estimated difference was below 0% • Bodyweight significantly decreased by 3.73kg (95% CI: -4.54 to -2.91) with 0.5mg semaglutide and significantly decreased by 4.53kg (-5.34 to -3.72) with 1mg semaglutide versus a decrease of 0.98kg with placebo (-1.82 to -0.13). **Conclusion:** Semaglutide monotherapy at doses of 0.5mg or 1mg with T2D naïve patients was associated with better glycemic control and better body weight reduction.
SUSTAIN 2 *Ahren.B., et.al* Efficacy and safety of once weekly semaglutide versus once daily sitagliptin as an add on	To compare the effect of once-weekly dosing of two dose levels of semaglutide versus **sitagliptin** 100	• At week 56, the mean HbA1c significantly decreased with semaglutide 0.5mg and 1mg by 1.3% and 1.6% respectively versus 0.5% with sitagliptin. The estimated treatment difference versus sitagliptin was -0.77% (95% CI: -0.92 to -0.62) with semaglutide

to metformin, thiazolidinedione, or both, in patients with type 2 diabetes (SUSTAIN 2): A 56 week, double blind, phase 3a, randomized trial., 2017 Vol 6 *Lancet Diabetes Endocrinol* pg 314-54 (N- 1231)	mg once-daily on glycaemic control after 56 weeks of treatment	0.5mg and -1.06% (95% CI: -1.21 to -0.91) with semaglutide 1mg. (p<0·0001) • Non-inferiority of HbA1c was confirmed if the upper boundary of the two-sided 95% CI of the estimated treatment difference was below 0.3%, and HbA1c superiority were confirmed if below 0%. • Bodyweight reduced by 4·3 kg with semaglutide 0·5 mg, 6·1 kg with semaglutide 1·0 mg,1·9 kg with sitagliptin (estimated treatment difference vs sitagliptin –2·35 kg [95% CI –3·06 to –1·63] with semaglutide 0·5 mg & –4·20 kg [–4·91 to –3·49] with semaglutide 1·0 mg; p< 0.0001) **Conclusion:** Semaglutide 0.5 mg and 1.0 mg administered once weekly significantly improved glycaemic control & bosy weight reduction compared to sitagliptin in patients with type 2 diabetes as add-on to metformin and/or thiazolidinediones.
SUSTAIN 3 *Ahmann.A.J., et.al.,* Efficacy and Safety of Once-Weekly Semaglutide Versus Exenatide ER in Subjects With Type 2 Diabetes (SUSTAIN 3): A 56-Week, Open-Label, Randomized Clinical Trial. 2018 Vol 41 *Diabetes Care* pg 258-266 (N=844)	To compare the efficacy and safety of once weekly semaglutide 1mg subcutaneous with **exenatide** extended release (ER) 2mg subcutaneous in subjects with type 2 diabetes.	• At week 56, patients with a mean baseline HbA_{1c} of 8.3% achieved a superior HbA_{1c} reduction of 1.5% when treated with 1.0 mg semaglutide vs 0.9% with 2.0 mg exenatide ER (p<0.0001), as add-on to one or two oral antidiabetics (metformin, sulfonylurea or thiazolidinediones) [Estimated treatment difference vs exenatide -0.62%; 95%CI:-0.80, -0.44 [-6.78mmol/mol; 95% CI-8.70, -4.86]. • Superiority for change in either HbA1c required an upper limit of the two-sided 95% CI for the estimated difference below 0%. • Semaglutide 1.0 mg [-5.59 kg (-5.93%)] was superior to exenatide ER 2.0 mg [(-1.85 kg (-1.79%)] on change from baseline at week 56 in body weight; the estimated treatment difference was -3.78 kg [-4.58;-2.98]; 95%CI (-4.19% [-5.02;- 3.36]95%CI).

		Conclusion: Semaglutide 1.0 mg produced a larger HbA1c and body weight reduction than exenatide 2.0 mg, of 1.5% versus 0.9% over 56 weeks
SUSTAIN 4 *Aroda.R.V. et.al.* Efficacy and safety of once-weekly semaglutide versus once-daily insulin glargine as add-on to metformin (with or without sulfonylureas) in insulin-naive patients with type 2 diabetes (SUSTAIN 4): a randomized, open-label, parallel-group, multicentre, multinational, phase 3a trial. 2017 Vol 5 *Lancet Diabetes Endocrinol* pg 355–66 (N= 1089)	To compare the effect of once-weekly dosing of two dose levels of semaglutide versus **insulin glargine** once-daily on glycaemic control after 30 weeks of treatment in insulin-naïve subjects with type 2 diabetes.	• By week 30, mean HbA1c decreased by 1.21% (95% CI: 1.10 -1.31) with semaglutide 0.5mg & 1.64% (95% CI: 1.54-1.74) with semaglutide 1mg versus 0.83% (95% CI: 0.73 -0.93) for insulin glargine (p < 0.0001 for both). The estimated treatment difference was -0.38% [95%CI: -0.52; -0.24] with semaglutide 0.5 mg and -0.81% [95% CI: -0.96; -0.67] for semaglutide 1.0 mg. • Non-inferiority was concluded if the upper limit of the two-sided 95% confidence interval for the estimated difference in HbA1c between semaglutide and insulin glargine was less than 0.3%. Superiority for change in HbA1c was concluded if the upper limit of the 2-sided 95% confidence interval for the estimated difference is below 0%. • Semaglutide 0.5mg & 1mg achieved weight losses of 3·47 kg (95% CI 3·00–3·93) and 5·17 kg (4·71–5·66), respectively, versus a weight gain of 1·15 kg (0·70–1·61) with insulin glargine; estimated treatment difference versus insulin glargine –4·62 kg (95% CI –5·27 to –3·96) with 0·5 mg semaglutide and –6·33 kg (–6·99 to –5·67) with 1·0 mg semaglutide (both p< 0.0001) **Conclusion**: Insulin naïve patients on semaglutide achieved significantly larger HbA1c reductions than insulin.
SUSTAIN 5 **Rodbard.H.W., et.al.,** Semaglutide added to Basal Insulin in Type 2 Diabetes (SUSTAIN 5): a Randomized controlled trial, June 2018, Vol 103, No 6. *J Clin Endocrinol Metab*, **June 2018, pg 2291-2301**	To demonstrate the superiority of semaglutide vs placebo on glycaemic control as an add on to **basal insulin** in patients with T2D	• At week 30, mean HbA1c reductions with semaglutide 0.5mg and 1.0mg were 1.4% and 1.8% versus 0.1% with placebo. [Estimated treatment differences (ETD) vs placebo, -1.35% (95%CI: -1.61 to -1.10) and ETD, -1.75%, (95%CI: -2.01 to -1.50)] (p< 0.001 both)]. • Mean body weight decreased with semaglutide 0.5mg and 1.0mg vs placebo by 3.7, 6.4 and 1.4kg

(N= 397)		• [ETD for semaglutide 0.5mg and 1.0mg vs placebo -2.31; 95%CI: -3.33 to -1.29 and ETD, -5.06; 95%CI: -6.08 to -4.04] • The trial was designed to establish superiority for both doses of semaglutide vs pooled placebo for the change in HbA1c & body weight at week 30 with a one sided α of 2.5% assuming estimated treatment differences vs placebo of 0.45% & 2.25kg for each semaglutide dose levels and SDs of 1.1% & 4.0kg. **Conclusion:** Semaglutide provided superior glycemic control & weight reduction compared with placebo in patients with T2D receiving basal insulin therapy.
SUSTAIN 6 (CVOT) *Marso.S.P.et.al.* Semaglutide and Cardiovascular Outcomes in Patients with Type 2 Diabetes (SUSTAIN 6).2016 *New England Journal of Medicine (NJEM)* (N=3297)	To assess the non-inferiority of semaglutide as compared with placebo in terms of **cardiovascular** safety in patients with type 2 diabetes	• At week 104, The composite primary outcome occurred in 108 of 1648 (6.6%) patients in the semaglutide group and 146 of 1649 (8.9%) in the placebo group (hazard ratio, 0.74; 95% CI: 0.58 to 0.95; p< 0.001) *The primary composite outcome was the first occurrence of death from cardiovascular causes, nonfatal myocardial infarction or nonfatal stroke. • Non-inferiority for the primary outcome was confirmed if the upper boundary of the two-sided 95% confidence interval of the HR was below the non inferiority margin 1.80 **Conclusion:** Semaglutide treated patients had a significant 26% lower risk of the primary composite outcome compared with those receiving placebo.
SUSTAIN 7 *Pratley.R.E. et.al.* Semaglutide versus dulaglutide once weekly in patients with type 2 diabetes (SUSTAIN 7): a randomized, open label, phase 3b trial. 2018 *Lancet Diabetes Endocrinol.*	To compare the efficacy and safety of semaglutide and **dulaglutide** at low doses (semaglutide 0.5mg vs dulaglutide 0.75mg) and high doses (Semaglutide 1.0mg vs dulaglutide 1.5mg)when given	• At week 40, the mean percentage HbA1c was reduced by 1·5 (SE 0.06) percentage points from baseline with semaglutide 0·5 mg versus 1·1 (SE 0·05) percentage points with dulaglutide 0·75 mg. Estimated treatment differences (95% CI: -0.40 (-0.55 to -0.25) p< 0.0001) • For both dose levels, HbA1c non-inferiority margin was set as 0·4%. • Mean bodyweight was reduced at week 40 by 4·6 kg

(N= 1201)	once a week to patients with type 2 diabetes inadequately controlled with metformin monotherapy.	with semaglutide 0·5 mg versus 2·3 kg with dulaglutide 0·75 mg (treatment difference −2·26 [95% CI −3·02 to −1·51]; p<0·0001 **Conclusion**: The study demonstrated significant differences in HbA1c & body weight reductions favouring semaglutide at both low and high doses compared with dulaglutide.

2.3   Safety

- Most safety issues identified were among commonly reported adverse events or serious adverse events that have previously been seen for other GLP-1 receptor agonists.
- The most commonly reported adverse events with both doses of semaglutide were gastrointestinal (GI) disorders, which are known common side effects of GLP-1 receptor agonists. The proportion of patients with GI AEs as well as the rate of events increased with semaglutide dose.
- One new safety finding emerged from SUSTAIN 6 (CVOT) which was an increased risk of diabetic retinopathy complications with semaglutide (3.0%) versus placebo (1.8%) [HR 1.76, 95% CI: 1.11, 2.78]. The majority of these subjects had pre-existing diabetes retinopathy, long duration of diabetes at baseline, high baseline HbA1c and insulin use. This information has been documented in the package insert.
- Semaglutide does not increase the risk of hypoglycaemia unless combined with either sulphonyureas or insulin.
- The proportion of patients that tested positive for anti-semaglutide antibodies at any time point post baseline was low and appeared to be transient. None of the anti-drug antibodies have neutralizing effect and hence bring no clinical significance.

3.0   CONCLUSION

Drug Control Authority (DCA) on the 343rd meeting on 13th February 2020 has decided to approve the registration of this product with the following indication:

Ozempic® is indicated for the treatment of adults with insufficiently controlled type 2 diabetes mellitus as an adjunct to diet and exercise
- as monotherapy when metformin is considered inappropriate due to intolerance or contraindications
- in addition to other medicinal products for the treatment of diabetes.

For study results with respect to combinations, effects on glycaemic control and cardiovascular events, and the populations studied, see Special warnings and precautions for use, Interaction with other medicinal products and other forms of interaction and Pharmacodynamic properties.