Sem-P (Semaglutide) INSTRUCTION MANUAL

سیم پی ہدایت نامہ

Wash Your Hands With Soap And Water.

اپنے ہاتھ صابن اور پانی سے دھوئیں۔

Before use check that Sem-P Solution for Injection in vial is clear and colorless.
Do not use if it is frozen, cloudy or has particles in it.

استعمال سے پہلے چیک کریں کہ سیم-پی سلوشن فار انجکشن صاف اور بے رنگ ہے۔
اگر سلوشن منجمد ہو، آلودہ ہو یا اس میں ذرات موجود ہوں تو استعمال نہ کریں۔

1

Pull off the vial's plastic protective cap. Do not remove the rubber stopper.

سیم-پی وائل سے حفاظتی کیپ ہٹادیں۔
ربڑ اسٹاپر کو نہ ہٹائیں۔

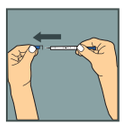
2

Take Sem-P Disposable Syringe. Remove the outer wrapping of the Syringe.

سیم-پی سرنج لیں۔ سرنج کے بیرونی کور کو ہٹادیں۔

3

Remove the Sem-P Disposable Syringe shield by pulling it off.



سیم-پی سرنج میں موجود سوئی کے حفاظتی کور کو ہٹادیں۔

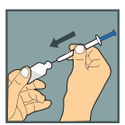
4

Hold the Sem-P Disposable Syringe in one hand with the needle pointing up. With the other hand pull down the plunger until the plunger tip reaches the line on the Sem-P Disposable Syringe indicating air volume is equivalent to the prescribed dose.

سیم-پی سرنج کو ایک ہاتھ میں سوئی کی نوک کو اوپر کی طرف رکھتے ہوئے پکڑیں۔ دوسرے ہاتھ سے پلنجر نیچے کھینچیں جب تک کہ پلنجر کی نوک سرنج میں دوا کی مطلوبہ مقدار کے مطابق لائن تک نہ پہنچ جائے۔

5

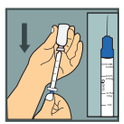
Put the needle through the rubber stopper on top of the Sem-P vial.
Inject all the air into the Sem-P vial.



سوئی کو ربڑ اسٹاپر کے ذریعے سیم-پی وائل میں ڈالیں۔ سرنج میں موجود ہوا کو سیم-پی وائل میں داخل کریں۔

6

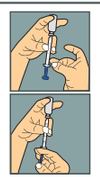
Turn the Sem-P vial upside down. Make sure that the tip of the needle is in the liquid. Slowly pull the plunger down to withdraw prescribed dose of Sem-P Solution for Injection from the vial.



سیم-پی وائل کو الٹا کریں اور اس بات کو یقینی بنائیں کہ سوئی کی نوک سلوشن میں ہے۔ وائل سے تجویز کردہ خوراک لینے کے لئے پلنجر کو آہستہ آہستہ نیچے کی طرف کھینچیں جب تک پلنجر کی نوک مطلوبہ دوا کی مقدار کی حد سے گزر نہ جائے۔

7

If there are air bubbles in the Sem-P Disposable Syringe, tap the syringe gently a few times to let any air bubbles rise to the top. Slowly push the plunger up until there is no more air in the syringe.



اگر سیم-پی سرنج میں ہوا کے بلبلے ہوں تو سرنج کو تھپتھپائیں تاکہ ہوا کے بلبلے آسانی سے اوپر آجائیں۔ پلنجر کو آہستہ آہستہ اوپر دھکیلیں جب تک سرنج میں موجود ہوا باہر نہ نکل جائے۔

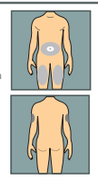
8

Once you have prescribed dose of Sem-P Solution for Injection in the syringe with no air bubbles, pull the syringe out of the rubber stopper of the vial.

جب سرنج میں سیم-پی سلوشن فار انجکشن کی تجویز کردہ خوراک آجائے تو سرنج کو وائل سے باہر نکالیں۔

9

Choose your injection site. Sem-P Solution for Injection can be injected under the skin (subcutaneously) of your stomach area (abdomen) or thighs, and with the help of someone else, in the back of the upper arm.



انجکشن لگانے کی جگہ کا انتخاب کریں۔ سیم-پی سلوشن فار انجکشن کو پیٹ کے ارد گرد یا رانوں کی جلد یا کسی اور کی مدد سے بازو کے پچھلے اوپری حصے پر لگایا جاسکتا ہے۔

10

Gently pinch your skin and inject the needle into the skin fold at 90 degree angle.

جلد کو آہستگی سے انگوٹھے اور انگلی کی مدد سے پکڑیں اور سوئی کو جلد میں ۹۰ ڈگری کے زاویے پر داخل کریں۔

11

Inject all the Sem-P Solution for Injection from the syringe to receive a full dose. After your injection, the needle should stay under your skin for 5 seconds to make sure you receive the full dose.

سرنج میں موجود سیم-پی سلوشن فار انجکشن کی خوراک حاصل کرنے کیلئے پلنجر کو اندر دبائیں۔ انجکشن لگانے کے بعد سوئی آپ کی جلد میں کم از کم ۵ سیکنڈ تک رہنی چاہیے تاکہ یہ یقینی بنایا جاسکے کہ سرنج میں موجود تجویز کردہ خوراک آپ کے جسم میں پہنچ گئی ہے۔

12

Pull the needle out of your skin.

سوئی کو جلد سے باہر نکالیں۔

Important Instructions for Use

- Change (rotate) your injection site within the area you choose for each dose to reduce your risk of getting lipodystrophy (pits in skin or thickened skin) and localized cutaneous amyloidosis (skin with lumps) at the injection sites.
- Do not inject where the skin has pits, is thickened, or has lumps.
- Do not inject where the skin is tender, bruised, scaly or hard, or into scars or damaged skin.
- If you see blood after you take the needle out of your skin, press the injection site lightly. Do not rub the area.
- Do not share or reuse your needle or syringe.
- After opening, the vial can be used for upto 06 weeks when stored below 25°C or in refrigerator at 2°C-8°C.
- Do not freeze (if frozen, do not use the vial).
- Discard any unused solution after 06 weeks from the initial use.
- Store the vial in the outer carton before and after each use.

استعمال کے لئے اہم ہدایات

- اپنی انجکشن کی جگہ کو ہر بار تبدیل کریں تاکہ انجکشن کی جگہوں پر جلد میں گڑھے، گانٹھیں یا جلد موٹی ہونے کے خطرے کو کم کیا جاسکے۔
- جلد میں جہاں گڑھے، گانٹھیں یا جلد موٹی ہو وہاں انجکشن نہ لگائیں۔
- جہاں جلد نرم ہو، چوٹ لگی ہو، کھردری یا سخت ہو، داغ ہوں یا جلد خراب ہو وہاں انجکشن نہ لگائیں۔
- اگر جلد سے سوئی نکالنے کے بعد خون نظر آئے تو انجکشن کی جگہ کو ہلکے سے دبائیں، جگہ کو نہ رگڑیں۔
- اپنی سوئی یا سرنج کو شیئر یا دوبارہ استعمال نہ کریں۔
- وائل کو کھولنے کے بعد دوا کو ۲۵ ڈگری سینٹی گریڈ سے کم درجہ حرارت یا ریفریجریٹر میں ۲-۸ ڈگری سینٹی گریڈ درجہ حرارت پر رکھتے ہوئے ۶ ہفتوں تک استعمال کیا جاسکتا ہے۔
- دوا کو جمنے سے بچائیں (اگر دوا جم جائے تو استعمال نہ کریں)۔
- پہلے استعمال کے ۶ ہفتوں کے بعد غیر استعمال شدہ دوا کو ضائع کردیں۔
- ہر استعمال سے قبل اور بعد میں وائل کو بیرونی کارٹن میں رکھیں۔

Getz pharma

Sem-P™ (Semaglutide)

سیمپی

Solution for Injection
2mg/1.5mL & 4mg/3mL

DESCRIPTION

Sem-P (Semaglutide) Injection, for subcutaneous use, contains Semaglutide, a human GLP-1 receptor agonist (or GLP-1 analog). The main protraction mechanism of Semaglutide is albumin binding, facilitated by modification of position 26 lysine with a hydrophilic spacer and a C18 fatty di-acid. Furthermore, Semaglutide is modified in position 8 to provide stabilization against degradation by the enzyme dipeptidyl-peptidase 4 (DPP-4). A minor modification was made in position 34 to ensure the attachment of only one fatty di-acid. Its molecular formula is $C_{187}H_{291}N_{45}O_{59}$.

QUALITATIVE AND QUANTITATIVE COMPOSITION

Sem-P (Semaglutide) Solution for Injection is available for subcutaneous administration as:

Sem-P (Semaglutide) Solution for Injection 2mg/1.5mL
Each 1.5mL vial contains:
Semaglutide… 2mg

Sem-P (Semaglutide) Solution for Injection 4mg/3mL
Each 3mL vial contains:
Semaglutide… 4mg

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 on glucose, mediated by the GLP-1 receptors. The principal mechanism of protraction resulting in the long half-life of Semaglutide 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. Semaglutide reduces blood glucose through a mechanism where it stimulates insulin secretion and lowers glucagon secretion, both in a glucose-dependent manner. Thus, when blood glucose is high, insulin secretion is stimulated and glucagon secretion is inhibited. The mechanism of blood glucose lowering also involves a minor delay in gastric emptying in the early postprandial phase.

Pharmacokinetics

Absorption
Absolute bioavailability of Semaglutide is 89%. Maximum concentration of Semaglutide is reached 1 to 3 days post dose. Similar exposure is achieved with subcutaneous administration of Semaglutide in the abdomen, thigh, or upper arm.
In patients with type 2 diabetes, Semaglutide exposure increases in a dose-proportional manner for once-weekly doses of 0.5mg and 1mg. Steady-state exposure is achieved following 4-5 weeks of once-weekly administration. In patients with type 2 diabetes, the mean population-PK estimated steady-state concentrations following once weekly subcutaneous administration of 0.5mg and 1mg Semaglutide were approximately 65.0ng/mL and 123.0ng/mL, respectively.

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

Metabolism
The primary route of elimination for Semaglutide is metabolism following proteolytic cleavage of the peptide backbone and sequential beta-oxidation of the fatty acid sidechain.

Elimination
The apparent clearance of Semaglutide in patients with type 2 diabetes is approximately 0.05L/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. The primary excretion routes of Semaglutide-related material is via the urine and feces. Approximately 3% of the dose is excreted in the urine as intact Semaglutide.

Special Population

The exposure of Semaglutide decreases with an increase in body weight. However, Semaglutide doses of 0.5mg and 1mg provide adequate systemic exposure over the body weight range of 40-198kg.

THERAPEUTIC INDICATIONS

Sem-P (Semaglutide) is indicated:
- As an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.
- To reduce the risk of major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction or non-fatal stroke) in adults with type 2 diabetes mellitus and established cardiovascular disease.
- As monotherapy when metformin is considered inappropriate due to intolerance or contraindications.
- In addition to other medicinal products for the treatment of diabetes.

DOSAGE AND ADMINISTRATION

Recommended Dosage
- Each mL contains 1.34mg of Semaglutide.
- Initiate Sem-P (Semaglutide) with a dosage of 0.25mg injected subcutaneously once weekly for 4 weeks. The 0.25mg dosage is intended for treatment initiation and is not effective for glycemic control.
- After 4 weeks on the 0.25mg dosage, increase the dosage to 0.5mg once weekly.
- If additional glycemic control is needed after at least 4 weeks on the 0.5mg dosage, the dosage may be increased to 1mg once weekly.
- If additional glycemic control is needed after at least 4 weeks on the 1mg dosage, the dosage may be increased to 2mg once weekly. The maximum recommended dosage is 2mg once weekly.
- The day of weekly administration can be changed if necessary as long as the time between two doses is at least 2 days (>48 hours).
- If a dose is missed, administer Sem-P (Semaglutide) as soon as possible within 5 days after the missed dose. If more than 5 days have passed, skip the missed dose and administer the next dose on the regularly scheduled day. In each case, patients can then resume their regular once weekly dosing schedule.

Sem-P (Semaglutide) Solution for Injection should be administered by using Sem-P Disposable Syringe that has specific markings both in mg and mL for dosing convenience and accuracy

Instructions	Dose in mg	Dose in mL	Dose Frequency
Start	0.25mg	0.188mL	Once weekly for at least 4 weeks
Increase the dose & continue	0.5mg	0.375mL	Once weekly for at least 4 weeks
Increase the dose if needed & continue	1.0mg	0.75mL	Once weekly for at least 4 weeks
Increase the dose if needed & continue	2.0mg	1.5mL	Once a week

Important Administration Instructions
- Inspect Sem-P (Semaglutide) visually before use. It should appear clear and colorless. Do not use Sem-P (Semaglutide) if particulate matter and coloration is seen.
- Administer Sem-P (Semaglutide) once weekly, on the same day each week, at any time of the day, with or without meals.
- Inject Sem-P (Semaglutide) subcutaneously to the abdomen, thigh, or upper arm. Instruct patients to use a different injection site each week when injecting in the same body region.
- When using Sem-P (Semaglutide) with insulin, instruct patients to administer as separate injections and to never mix the products. It is acceptable to inject Sem-P (Semaglutide) and insulin in the same body region, but the injections should not be adjacent to each other.
- When Semaglutide is added to existing metformin and/or thiazolidinedione therapy or to a sodium-glucose cotransporter 2 (SGLT2) inhibitor, the current dose of metformin and/or thiazolidinedione or SGLT2 inhibitor can be continued unchanged.
- When Semaglutide 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 hypoglycemia.
- Self-monitoring of blood glucose is not needed in order to adjust the dose of Semaglutide. Blood glucose self-monitoring is necessary to adjust the dose of sulfonylurea and insulin, particularly when Semaglutide is started and insulin is reduced. A stepwise approach to insulin reduction is recommended.

Special Population
Patients with hepatic or renal impairment
No dose adjustment is required for patients with hepatic or renal impairment.

Pediatric population
Safety and efficacy of Sem-P (Semaglutide) have not been established in pediatric patients (younger than 18 years).

ADVERSE REACTIONS

Very Common: Hypoglycemia when used with insulin or sulfonylurea, nausea and diarrhea.

Common: Hypoglycemia when used with other oral antidiabetics (OAD), decreased appetite, dizziness, diabetic retinopathy complications, vomiting, abdominal pain, abdominal distension, constipation, dyspepsia, gastritis, gastroesophageal reflux disease, eructation, flatulence, cholelithiasis, fatigue, increased lipase, increased amylase and weight decreased.

Uncommon: Hypersensitivity, dysgeusia, increased heart rate, acute pancreatitis, delayed gastric emptying and injection site reactions.

Rare: Anaphylactic reaction, intestinal obstruction and angioedema.

"To report SUSPECTED ADVERSE REACTIONS to Getz Pharma's Pharmacovigilance Section, please contact at dsafety@getzpharma.com or +92-21-38636363"

CONTRAINDICATIONS

Semaglutide is contraindicated in patients with:
- Hypersensitivity to active substance and to any of the excipient of the product.
- A personal or family history of medullary thyroid carcinoma (MTC) or in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2).

PRECAUTIONS

WARNING: RISK OF THYROID C-CELL TUMORS
- In rodents, Semaglutide causes dose-dependent and treatment-duration-dependent thyroid C-cell tumors at clinically relevant exposures. It is unknown whether Semaglutide causes thyroid C-cell tumors, including medullary thyroid carcinoma (MTC), in humans as human relevance of Semaglutide-induced rodent thyroid C-cell tumors has not been determined.
- Semaglutide is contraindicated in patients with a personal or family history of MTC or in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2). Counsel patients regarding the potential risk for MTC with the use of Semaglutide and inform them of symptoms of thyroid tumors (e.g. a mass in the neck, dysphagia, dyspnea, persistent hoarseness). Routine monitoring of serum calcitonin or using thyroid ultrasound is of uncertain value for early detection of MTC in patients treated with Semaglutide.

General
Semaglutide should not be used in patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis. Semaglutide is not a substitute for insulin. Diabetic ketoacidosis has been reported in insulin-dependent patients whom had rapid discontinuation or dose reduction of insulin when treatment with a GLP-1 receptor agonist is started.

Risk of Thyroid C-Cell Tumors
Semaglutide is contraindicated in patients with a personal or family history of MTC or in patients with MEN 2. Counsel patients regarding the potential risk for MTC with the use of Semaglutide and inform them of symptoms of thyroid tumors (e.g. a mass in the neck, dysphagia, dyspnea, persistent hoarseness). If serum calcitonin is measured and found to be elevated, the patient should be further evaluated. Patients with thyroid nodules noted on physical examination or neck imaging should also be further evaluated.

Pancreatitis
After initiation of Semaglutide, observe patients carefully for signs and symptoms of pancreatitis (including persistent severe abdominal pain, sometimes radiating to the back and which may or may not be accompanied by vomiting). If pancreatitis is suspected, Semaglutide should be discontinued and appropriate management initiated; if confirmed, Semaglutide should not be restarted.

Hypoglycemia with Concomitant Use of Insulin Secretagogues or Insulin
Patients receiving Semaglutide in combination with an insulin secretagogue (e.g., sulfonylurea) or insulin may have an increased risk of hypoglycemia, including severe hypoglycemia. The risk of hypoglycemia is increased when Semaglutide is used in combination with insulin secretagogues (e.g., sulfonylureas) or insulin. Patients may require a lower dose of the secretagogue or insulin to reduce the risk of hypoglycemia.

Acute Kidney Injury
There have been postmarketing reports of acute kidney injury and worsening of chronic renal failure, which may sometimes require hemodialysis, in patients treated with GLP-1 receptor agonists. A majority of the reported events occurred in patients who had experienced nausea, vomiting, diarrhea, or dehydration. Monitor renal function when initiating or escalating doses of Semaglutide in patients reporting severe adverse gastrointestinal reactions.

Hypersensitivity
Serious hypersensitivity reactions (e.g., anaphylaxis, angioedema) have been reported with GLP-1 receptor agonists. If hypersensitivity reactions occur, discontinue use of Semaglutide; treat promptly per standard of care, and monitor until signs and symptoms resolve. Do not use in patients with a previous hypersensitivity to Semaglutide. Anaphylaxis and angioedema have been reported with other GLP-1 receptor agonists. Use caution in a patient with a history of angioedema or anaphylaxis with another GLP-1 receptor agonist because it is unknown whether such patients will be predisposed to anaphylaxis with Semaglutide.

Acute Gallbladder Disease
Acute events of gallbladder disease such as cholelithiasis or cholecystitis have been reported. If cholelithiasis is suspected, gallbladder studies and appropriate clinical follow-up are indicated.

Aspiration in association with general anesthesia or deep sedation
Cases of pulmonary aspiration have been reported in patients receiving GLP-1 receptor agonists undergoing general anesthesia or deep sedation. Therefore, the increased risk of residual gastric content due to delayed gastric emptying should be considered prior to performing procedures with general anesthesia or deep sedation.

Gastrointestinal effects
Use of GLP-1 receptor agonists may be associated with gastrointestinal adverse reactions. This should be considered when treating patients, with impaired renal function as nausea, vomiting, and diarrhea may cause dehydration which could cause a deterioration of renal function.

Diabetic Retinopathy
In patients with diabetic retinopathy treated with insulin and Semaglutide, an increased risk of developing diabetic retinopathy complications has been observed. Caution should be exercised when using Semaglutide in patients with diabetic retinopathy treated with insulin. Patients with a history of diabetic retinopathy should be monitored for worsening and treated according to clinical guidelines.

Heart Failure
There is no therapeutic experience in patients with congestive heart failure therefore, use of Semaglutide is not recommended in these patients.

Use in 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.

Use in renal impairment
Experience with the use of Semaglutide in patients with severe (CrCL<30 ml/min) renal impairment is limited. Semaglutide is not recommended for use in patients with end-stage renal disease.

Effects on ability to drive and use machines
Semaglutide has no or negligible influence on the ability to drive or use machines. When it is used in combination with a sulfonylurea or insulin, patients should be advised to take precautions to avoid hypoglycemia while driving and using machines.

Pregnancy

Semaglutide should not be used during pregnancy. Women of childbearing potential are recommended to use contraception when treated with Semaglutide. If a patient wishes to become pregnant, or pregnancy occurs, Semaglutide should be discontinued. Semaglutide should be discontinued at least 2 months before a planned pregnancy due to the long half-life.

Nursing Mothers

Semaglutide was excreted in milk. As a risk to a breast-fed child cannot be excluded, Semaglutide should not be used during breast-feeding.

DRUG INTERACTIONS

Concomitant Use with an Insulin Secretagogue (e.g., Sulfonylurea) or with Insulin
Semaglutide stimulates insulin release in the presence of elevated blood glucose concentrations. Patients receiving Semaglutide in combination with an insulin secretagogue (e.g., sulfonylurea) or insulin may have an increased risk of hypoglycemia, including severe hypoglycemia. When initiating Semaglutide, consider reducing the dose of concomitantly administered insulin secretagogue (such as sulfonylureas) or insulin to reduce the risk of hypoglycemia.

Oral Medications
Semaglutide delays gastric emptying and has the potential to impact the rate of absorption of concomitantly administered oral medicinal products. Semaglutide should be used with caution in patients receiving oral medicinal products that require rapid gastrointestinal absorption.

Warfarin and other coumarin derivatives
Cases of decreased INR have been reported during concomitant use of acenocoumarol and Semaglutide. Upon initiation of Semaglutide treatment in patients on warfarin or other coumarin derivatives, frequent monitoring of INR is recommended.

OVERDOSAGE

Overdoses of up to 4mg in a single dose, and up to 4mg in a week have been reported in clinical trials. The most commonly reported adverse reaction was nausea. All patients recovered without complications. There is no specific antidote for overdose with Semaglutide. In the event of overdose, appropriate supportive treatment should be initiated according to the patient's clinical signs and symptoms. A prolonged period of observation and treatment for these symptoms may be necessary, taking into account the long half-life of Semaglutide of approximately 1 week.

STORAGE

Store in refrigerator at 2°C-8°C.
Protect from excessive heat and sunlight.
Do not freeze.
After opening, the vial can be used for upto 06 weeks when stored below 25°C or in refrigerator at 2°C-8°C.
Store the vial in the outer carton before and after each use.

The expiration date refers to the product correctly stored at the required conditions.

HOW SUPPLIED

Sem-P (Semaglutide) Solution for Injection 2mg/1.5mL is available in pack of 1's.
Sem-P (Semaglutide) Solution for Injection 4mg/3mL is available in pack of 1's.

Keep out of reach of children.

To be sold on prescription of a registered medical practitioner only.

Please read the contents carefully before use.
This package insert is continually updated from time to time.

Manufactured by:

Getz pharma (PVT) LIMITED
www.getzpharma.com
29-30/27, K.I.A., Karachi, Pakistan

PAK-200020950