ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Teduglutide Viatris 5 mg powder and solvent for solution for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One vial of powder contains 5 mg of teduglutide.
After reconstitution, each vial contains 5 mg teduglutide in 0.5 ml of solution, corresponding to a concentration of 10 mg/ml.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Powder and solvent for solution for injection.

The powder is white and the solvent is clear and colourless.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Teduglutide Viatris is indicated for the treatment of patients 4 months corrected gestational age and above with Short Bowel Syndrome (SBS). Patients should be stable following a period of intestinal adaptation after surgery.

4.2 Posology and method of administration

Treatment should be initiated under the supervision of a medical professional with experience in the treatment of SBS.

Treatment should not be initiated until it is reasonable to assume that the patient is stable following a period of intestinal adaptation. Optimisation and stabilisation of intravenous fluid and nutrition support should be performed before initiation of treatment.

Clinical assessment by the physician should consider individual treatment objectives and patient preferences. Treatment should be stopped if no overall improvement of the patient condition is achieved. Efficacy and safety in all patients should be closely monitored on an ongoing basis according to clinical treatment guidelines.

Posology

Adults

The recommended dose of Teduglutide Viatris is 0.05 mg/kg body weight once daily. The injection volume per body weight is provided below in Table 1. Due to the heterogeneity of the SBS population, a carefully monitored down-titration of the daily dose may be considered for some patients to optimise tolerability of the treatment. If a dose is missed, that dose should be injected as soon as possible on that day.

Treatment effect should be evaluated after 6 months. Limited data from clinical studies have shown that some patients may take longer to respond to treatment (i.e., those who still have presence of colon-in-continuity or distal/terminal ileum); if no overall improvement is achieved after 12 months, the need for continued treatment should be reconsidered.

Continued treatment is recommended for patients who have weaned off parenteral nutrition.

Table 1 Injection volume per body weight for adults

Body weight	**5 mg strength** Volume to be injected
38-41 kg	0.20 ml
42-45 kg	0.22 ml
46-49 kg	0.24 ml
50-53 kg	0.26 ml
54-57 kg	0.28 ml
58-61 kg	0.30 ml
62-65 kg	0.32 ml
66-69 kg	0.34 ml
70-73 kg	0.36 ml
74-77 kg	0.38 ml
78-81 kg	0.40 ml
82-85 kg	0.42 ml
86-89 kg	0.44 ml
90-93 kg	0.46 ml

Paediatric population (≥ 1 year)

Treatment should be initiated under the supervision of a medical professional with experience in the treatment of paediatric SBS.

The recommended dose of Teduglutide Viatris in children and adolescents (aged 1 to 17 years) is the same as for adults (0.05 mg/kg body weight once daily). The injection volume per body weight when using the 5 mg strength vial is provided in Table 2 below. Teduglutide 1.25 mg strength vials is also available for paediatric use (patients with a body weight < 20 kg).

If a dose is missed, that dose should be injected as soon as possible on that day. A treatment period of 6 months is recommended after which treatment effect should be evaluated. In children below the age of two years, treatment should be evaluated after 12 weeks. There are no data available in paediatric patients after 6 months (see section 5.1).

Table 2 Injection volume per body weight for paediatric population (≥ 1 year)

Body weight	**5 mg strength** Volume to be injected
10-11 kg	0.05 ml
12-13 kg	0.06 ml
14-17 kg	0.08 ml
18-21 kg	0.10 ml
22-25 kg	0.12 ml
26-29 kg	0.14 ml
30-33 kg	0.16 ml
34-37 kg	0.18 ml
38-41 kg	0.20 ml
42-45 kg	0.22 ml

Body weight	**5 mg strength** Volume to be injected
46-49 kg	0.24 ml
≥50 kg	See Table 1 under “Adults” section.

Paediatric population (aged 4 months to less than 12 months)

For paediatric patients aged 4 months to less than 12 months, teduglutide 1.25 mg vials should be used. Other medicinal products with the active substance teduglutide are available for administration to paediatric patients aged 4 months to less than 12 months.

Special populations

Elderly
No dose adjustment is necessary in patients above the age of 65 years.

Renal impairment
No dose adjustment is necessary for adult or paediatric patients with mild renal impairment. In adult or paediatric patients with moderate and severe renal impairment (creatinine clearance less than 50 ml/min), and end-stage renal disease, the daily dose should be reduced by 50% (see section 5.2).

Hepatic impairment
No dose adjustment is necessary for patients with mild and moderate hepatic impairment based on a study conducted in Child-Pugh grade B subjects. Teduglutide has not been studied in patients with severe hepatic impairment (see sections 4.4 and 5.2).

Paediatric population (< 4 months)
There are currently no available data in children below 4 months corrected gestational age.

Method of administration

The reconstituted solution should be administered by subcutaneous injection once daily, alternating sites between 1 of the 4 quadrants of the abdomen. In case the injection into the abdomen is hampered by pain, scarring or hardening of the tissue, the thigh can also be used. Teduglutide Viatris should not be administered intravenously or intramuscularly.

For instructions on reconstitution of the medicinal product before administration, see section 6.6.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

Active or suspected malignancy.

Patients with a history of malignancies in the gastrointestinal tract, including the hepatobiliary system and pancreas within the last five years.

4.4 Special warnings and precautions for use

It is strongly recommended that every time Teduglutide Viatris is administered to a patient, the name and lot number of the product are recorded in order to maintain a link between the patient and the lot of the product.

Adults

Colo-rectal polyps

A colonoscopy with removal of polyps should be performed at the time of starting treatment with teduglutide. Once yearly follow-up colonoscopies (or alternate imaging) are recommended during the first 2 years of teduglutide treatment. Subsequent colonoscopies are recommended at a minimum of five-year intervals. An individual assessment whether increased frequency of surveillance is necessary should be performed based on the patient characteristics (e.g., age, underlying disease). See also section 5.1. If a polyp is found, adherence to current polyp follow-up guidelines is recommended. In case of malignancy, teduglutide therapy must be discontinued (see section 4.3).

Gastrointestinal neoplasia including hepatobiliary tract

In the rat carcinogenicity study, benign tumours were found in the small bowel and the extrahepatic bile ducts. Development of small intestinal polyps has also been observed in human SBS patients within several months after start of teduglutide treatment. Because of this, upper gastro-intestinal endoscopy or other imaging is recommended before and during the treatment with teduglutide. If a neoplasia is detected, it should be removed. In case of malignancy, teduglutide treatment must be discontinued (see sections 4.3 and 5.3).

Gallbladder and bile ducts

Cases of cholecystitis, cholangitis, and cholelithiasis have been reported in clinical studies. In case of gallbladder or bile duct-related symptoms, the need for continued teduglutide treatment should be reassessed.

Pancreatic diseases

Pancreatic adverse events such as chronic and acute pancreatitis, pancreatic duct stenosis, pancreas infection and increased blood amylase and lipase have been reported in clinical studies. In case of pancreatic adverse events, the need for continued teduglutide treatment should be reassessed.

Monitoring of small bowel, gallbladder and bile ducts, and pancreas

SBS patients are to be kept under close surveillance according to clinical treatment guidelines. This usually includes the monitoring of small bowel function, gallbladder and bile ducts, and pancreas for signs and symptoms, and, if indicated, additional laboratory investigations and appropriate imaging techniques.

Intestinal obstruction

Cases of intestinal obstruction have been reported in clinical studies. In case of recurrent intestinal obstructions, the need for continued teduglutide treatment should be reassessed.

Fluid overload and electrolyte balance

To avoid fluid overload or dehydration, careful adjustment of parenteral support is required in patients taking teduglutide. Electrolyte balance and fluid status should be carefully monitored throughout treatment, especially during initial therapeutic response and discontinuation of teduglutide treatment.

Fluid overload
Fluid overload has been observed in clinical trials. Fluid overload adverse events occurred most frequently during the first 4 weeks of therapy and decreased over time.

Due to increased fluid absorption, patients with cardiovascular disease, such as cardiac insufficiency and hypertension, should be monitored with regard to fluid overload, especially during initiation of

therapy. Patients should be advised to contact their physician in case of sudden weight gain, face swelling, swollen ankles and/or dyspnoea. In general, fluid overload can be prevented by appropriate and timely assessment of parenteral nutrition needs. This assessment should be conducted more frequently within the first months of treatment.

Congestive heart failure has been observed in clinical trials. In case of a significant deterioration of the cardiovascular disease, the need for continued treatment with teduglutide should be reassessed.

Dehydration
Patients with SBS are susceptible to dehydration that may lead to acute renal failure.
In patients receiving teduglutide, parenteral support should be reduced carefully and should not be discontinued abruptly. The patient's fluid status should be evaluated following parenteral support reduction and corresponding adjustment performed, as needed.

Concomitant medicinal products

Patients receiving oral concomitant medicinal products requiring titration or with a narrow therapeutic index should be monitored closely due to potential increased absorption (see section 4.5).

Special clinical conditions

Teduglutide has not been studied in patients with severe, clinically unstable concomitant diseases, (e.g., cardiovascular, respiratory, renal, infectious, endocrine, hepatic, or CNS), or in patients with malignancies within the last five years (see section 4.3). Caution should be exercised when prescribing teduglutide.

Hepatic impairment

Teduglutide has not been studied in patients with severe hepatic impairment. The data from use in subjects with moderate hepatic impairment do not suggest a need for restricted use.

Discontinuation of treatment

Due to the risk of dehydration, discontinuation of treatment with teduglutide should be managed carefully.

Hypersensitivity to tetracycline when changing teduglutide medicinal products

Teduglutide Viatris is produced synthetically. But teduglutide medicinal product produced in *E.coli* using recombinant DNA technology exists, and that product is contraindicated in patients with hypersensitivity to tetracycline. Patients with known hypersensitivity to tetracycline should be informed on the eventual contraindications for the alternative teduglutide medicinal product, if planning to change from Teduglutide Viatris.

Paediatric population

See also general precautions for adults under this section.

Colo-rectal polyps/Neoplasia

Prior to initiating treatment with teduglutide, faecal occult blood testing should be done for all children and adolescents. Colonoscopy/sigmoidoscopy is required if there is evidence of unexplained blood in the stool. Subsequent faecal occult blood testing should be done annually in children and adolescents while they are receiving teduglutide.
Colonoscopy/sigmoidoscopy is recommended for all children and adolescents after one year of treatment, every 5 years thereafter while on continuous treatment with teduglutide, and if they have new or unexplained gastrointestinal bleeding.

Caution is needed when administering teduglutide to persons with a known hypersensitivity to tetracycline (see section 4.3).

Excipients

This medicinal product contains less than 1 mmol sodium (23 mg) per vial, that is to say essentially 'sodium-free'.

4.5 Interaction with other medicinal products and other forms of interaction

No clinical pharmacokinetic drug-drug interaction studies have been performed. An *in vitro* study indicates that teduglutide does not inhibit cytochrome P450 drug metabolising enzymes. Based upon the pharmacodynamic effect of teduglutide, there is a potential for increased absorption of concomitant medicinal products (see section 4.4).

4.6 Fertility, pregnancy and lactation

Pregnancy

There are no data from the use of teduglutide in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity (see section 5.3). As a precautionary measure, it is preferable to avoid the use of teduglutide during pregnancy.

Breast-feeding

It is unknown whether teduglutide is excreted in human milk. In rats, mean teduglutide concentration in milk was less than 3% of the maternal plasma concentration following a single subcutaneous injection of 25 mg/kg. A risk to the breast-fed newborn/infant cannot be excluded. As a precautionary measure it is preferable to avoid the use of teduglutide during breast-feeding.

Fertility

There are no data on the effects of teduglutide on human fertility. Animal data do not indicate any impairment of fertility.

4.7 Effects on ability to drive and use machines

Teduglutide has minor influence on the ability to drive and use machines. However, cases of syncope have been reported in clinical studies (see section 4.8). Such events impact the ability to drive and use machines.

4.8 Undesirable effects

Summary of the safety profile

Adverse reactions were retrieved from 2 placebo-controlled clinical studies with teduglutide in 109 patients with SBS treated with doses of 0.05 mg/kg/day and 0.10 mg/kg/day for up to 24 weeks. Approximately 52% of the patients treated with teduglutide experienced adverse reactions (*versus* 36% of the patients given placebo). The most commonly reported adverse reactions were abdominal pain and distension (45%), respiratory tract infections (28%) (including nasopharyngitis, influenza, upper respiratory tract infection, and lower respiratory tract infection), nausea (26%), injection site reactions (26%), headache (16%), and vomiting (14%). Approximately 38% of the treated patients with a stoma experienced gastrointestinal stoma complications. The majority of these reactions were mild or moderate.

No new safety signals have been identified in patients exposed to 0.05 mg/kg/day of teduglutide for up to 30 months in a long-term open-label extension study.

Tabulated list of adverse reactions

Adverse reactions are listed below by MedDRA system organ class and by frequency. Frequencies are defined as very common (≥ 1/10); common (≥ 1/100 to < 1/10); uncommon (≥ 1/1 000 to < 1/100); rare (≥ 1/10 000 to < 1/1 000); very rare (< 1/10 000); not known (cannot be estimated from available data). Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

All adverse reactions identified in post-marketing experience are *italicised.*

Frequency **System organ class**	**Very common**	**Common**	**Uncommon**	**Not known**
Infections and infestations	Respiratory tract infection*	Influenza-like illness		
Immune system disorders				Hypersensitivity
Metabolism and nutrition disorders		Decreased appetite, Fluid overload		
Psychiatric disorders		Anxiety, Insomnia		
Nervous system disorders	Headache			
Cardiac disorders		Congestive heart, failure		
Vascular disorders			Syncope	
Respiratory, thoracic and mediastinal disorders		Cough, Dyspnoea		
Gastrointestinal disorders	Abdominal distension, Abdominal pain, Nausea, Vomiting	Colorectal polyp, Colonic stenosis, Flatulence, Intestinal obstruction, Pancreatic duct stenosis, Pancreatitis[†], Small intestinal stenosis	Small intestinal polyp[‡]	Gastric polyp
Hepatobiliary disorders		Cholecystitis, Cholecystitis acute		
General disorders and administration site conditions	Injection site reaction[§]	Oedema peripheral		Fluid retention

Frequency System organ class	Very common	Common	Uncommon	Not known
Injury, poisoning and procedural complications	Gastrointestinal stoma complication			

* Includes the following preferred terms: Nasopharyngitis, Influenza, Upper respiratory tract infection, and Lower respiratory tract infection.

† Includes the following preferred terms: Pancreatitis, *Pancreatitis acute*, and Pancreatitis chronic.

‡ Locations include duodenum, jejunum, and ileum.

§ Includes the following preferred terms: Injection site haematoma, Injection site erythema, Injection site pain, Injection site swelling and Injection site haemorrhage.

Description of selected adverse reactions

Immunogenicity

Consistent with the potentially immunogenic properties of medicinal products containing peptides, administration of teduglutide may potentially trigger the development of antibodies. Based on integrated data from two trials in adults with SBS (a 6-month randomised placebo-controlled trial, followed by a 24-month open-label trial), the development of anti-teduglutide antibodies in subjects who received subcutaneous administration of 0.05 mg/kg teduglutide once daily was 3% (2/60) at Month 3, 17% (13/77) at Month 6, 24% (16/67) at Month 12, 33% (11/33) at Month 24, and 48% (14/29) at Month 30. The antibody formation has not been associated with clinically relevant safety findings, reduced efficacy or changed pharmacokinetics of teduglutide.

Injection site reactions

Injection site reactions occurred in 26% of SBS patients treated with teduglutide, compared to 5% of patients in the placebo arm. The reactions included injection site haematoma, injection site erythema, injection site pain, injection site swelling and injection site haemorrhage (see also section 5.3). The majority of reactions were moderate in severity and no occurrences led to drug discontinuation.

C-reactive protein

Modest increases of C-reactive protein of approximately 25 mg/l have been observed within the first seven days of teduglutide treatment, which decreased continuously under ongoing daily injections.

After 24 weeks of teduglutide treatment, patients showed small overall increase in C-reactive protein of approximately 1.5 mg/l on average. These changes were neither associated with any changes in other laboratory parameters nor with any reported clinical symptoms. There were no clinically relevant mean increases of C-reactive protein from baseline following long-term treatment with teduglutide for up to 30 months.

Paediatric population

In two completed clinical trials, there were 87 paediatric subjects (aged 1 to 17 years) enrolled and exposed to teduglutide for a duration of up to 6 months. No subject discontinued the studies due to an adverse event. Overall, the safety profile of teduglutide (including type and frequency of adverse reactions, and immunogenicity) in children and adolescents (ages 1-17 years) was similar to that in adults.

In three completed clinical studies in paediatric subjects (aged 4 to < 12 months corrected gestational age), the safety profile reported in these studies was consistent with the safety profile seen in the previous paediatric studies and no new safety issues were identified.

Limited long-term safety data is available for the paediatric population. No data are available for children under 4 months of age.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

4.9 Overdose

The maximum dose of teduglutide studied during clinical development was 86 mg/day for 8 days. No unexpected systemic adverse reactions were seen (see section 4.8).

In the event of an overdose, the patient should be carefully monitored by the medical professional.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Other alimentary tract and metabolism products, various alimentary tract and metabolism products, ATC code: A16AX08.

Mechanism of action

The naturally occurring human glucagon-like peptide-2 (GLP-2) is a peptide secreted by L cells of the intestine which is known to increase intestinal and portal blood flow, inhibit gastric acid secretion, and decrease intestinal motility. Teduglutide is an analogue of GLP-2. In several nonclinical studies, teduglutide has been shown to preserve mucosal integrity by promoting repair and normal growth of the intestine through an increase of villus height and crypt depth.

Pharmacodynamic effects

Similar to GLP-2, teduglutide is 33 amino acids in length with an amino acid substitution of alanine by glycine at the second position of the N-terminus. The single amino acid substitution relative to naturally occurring GLP-2 results in resistance to *in vivo* degradation by the enzyme dipeptidyl peptidase-IV (DPP-IV), resulting in an extended half-life. Teduglutide increases villus height and crypt depth of the intestinal epithelium.

Based on the findings derived from pre-clinical studies (see sections 4.4 and 5.3) and the proposed mechanism of action with the trophic effects on intestinal mucosa, there appears to be a risk for the promotion of small intestinal and/or colonic neoplasia. The clinical studies conducted could neither exclude nor confirm such an increased risk. Several cases of benign colorectal polyps occurred during the course of the trials, however, the frequency was not increased compared to placebo-treated patients. In addition to the need for a colonoscopy with removal of polyps by the time of the initiation of the treatment (see section 4.4.), every patient should be assessed for the need of an enhanced surveillance schedule based on the patient characteristics (e.g., age and underlying disease, previous occurrence of polyps etc.).

Clinical efficacy

Paediatric population

The European Medicines Agency has deferred the obligation to submit the results of studies with the reference medicinal product containing teduglutide in one or more subsets of the paediatric population in the treatment of SBS (see section 4.2 for information on paediatric use).

Paediatric population 4 months to less than 12 months of age

The efficacy data presented are derived from 1 controlled and 1 un-controlled core studies for a 28-week duration, and 2 extension studies for up to 9 cycles (24 weeks per cycle) of teduglutide treatment. These studies included infants 4 months to < 12 months corrected gestational age: 10 infants (2 infants aged 4 to < 6 months, 8 aged 6 to < 12 months) in the controlled study (5 in teduglutide treatment arm and 5 in standard of care arm), 2 infants in the un-controlled study (both treated). From the core controlled study, 6 of the 10 infants completed the study, and continued in the extension study (5 treated and 1 non-treated). From the core uncontrolled study, 2 infants completed the study and continued in the second extension study (both treated). The infants in these studies were treated with teduglutide 0.05 mg/kg/day. Despite the limited sample size in the core and extension studies, clinically meaningful numerical reductions in the requirement for parenteral support were observed.

The controlled core study
Complete weaning:

No subject achieved enteral autonomy, i.e., complete weaning off PS during either core or extension studies.

Reduction in parenteral nutrition volume:

In the controlled core study, based on subject diary data, 3 (60.0%) subjects enrolled in the TED arm and 1 (20.0%) subject in the SOC arm experienced at least 20% reduction in PS volume at end of treatment (EOT) from baseline (2 subjects in the SOC arm had missing data). In the TED arm, the mean change in PS volume at EOT from baseline was -21.5±28.91 ml/kg/day (-24.8%). In the SOC arm, the mean change in PS volume at EOT from baseline was -9.5±7.50 ml/kg/day (-16.8%).

Reduction in parenteral nutrition calories:

In the controlled core study, based on subject diary data, the mean percentage change in PS caloric intake at EOT from baseline was -27.0±29.47% for subjects in the TED arm and -13.7±21.87% in the SOC arm.

Reduction in infusion time:

In the controlled core study, in the TED arm, the change in diary PS infusion time at EOT from baseline was -3.1±3.31 hours/day (-28.9%) and -1.9±2.01 days/week (-28.5%). In the SOC arm, the change in diary PS infusion time at EOT from baseline was -0.3±0.63 hours/day (-1.9%) and no change was observed on the days per week of PS infusion time.

The un-controlled core study
Complete weaning:

No infant subjects reached complete weaning.

Reduction in parenteral nutrition volume:

Among the 2 infants included in and completed the study, a ≥20% reduction in PS volume was recorded in 1 infant during the teduglutide treatment. The mean change in PS volume at EOT from baseline was -26.2±13.61 ml/kg/day (-26.7%).

Reduction in parenteral nutrition calories:

In infants, the mean change in PS caloric intake at EOT from baseline was -13.8±3.17 kcal/kg/day (-25.7%).

Reduction in infusion time:

There was no change in daily PS usage hours in the 2 infants during the study.

Paediatric population between 1 and 17 years of age

The efficacy data presented are derived from 2 controlled studies in paediatric patients up to 24 weeks duration. These studies included 101 patients in the following age groups: 5 patients 1-2 years, 56 patients 2 to < 6 years, 32 patients 6 to < 12 years, 7 patients 12 to < 17 years, and 1 patient 17 to < 18 years. Despite the limited sample size, which did not allow meaningful statistical comparisons, clinically meaningful, numerical reductions in the requirement for parenteral support were observed across all age groups.

Teduglutide was studied in a 12-week, open-label, clinical study in 42 paediatric subjects aged 1 year through 14 years with SBS who were dependent on parenteral nutrition. The objectives of the study were to evaluate safety, tolerability, and efficacy of teduglutide compared to standard of care. Three (3) doses of teduglutide, 0.0125 mg/kg/day (n=8), 0.025 mg/kg/day (n=14), and 0.05 mg/kg/day (n=15), were investigated for 12 weeks. Five (5) subjects were enrolled in a standard of care cohort.

Complete weaning
Three subjects (3/15, 20%) on the recommended teduglutide dose were weaned off parenteral nutrition by Week 12. After a 4-week washout period, two of these patients had reinitiated parenteral nutrition support.

Reduction in parenteral nutrition volume
The mean change in parenteral nutrition volume from baseline at Week 12 in the ITT population, based on physician-prescribed data, was -2.57 (±3.56) l/week, correlating to a -39.11% (±40.79) mean decrease, compared to 0.43 (±0.75) l/week, correlating to a 7.38% (±12.76) increase in the standard of care cohort. At Week 16 (4 weeks following the end of treatment) parenteral nutrition volume reductions were still evident but less than observed at Week 12 when subjects were still on teduglutide (mean decrease of -31.80% (±39.26) compared to a 3.92% (±16.62) increase in the standard of care group).

Reduction in parenteral nutrition calories
At Week 12, there was a -35.11% (±53.04) mean change from baseline in parenteral nutrition calorie consumption in the ITT population based on physician-prescribed data. The corresponding change in the standard of care cohort was 4.31% (±5.36). At Week 16, the parenteral nutrition calories consumption continued to decrease with percentage mean changes from baseline of -39.15% (±39.08) compared to -0.87% (±9.25) for the standard of care cohort.

Increases in enteral nutrition volume and enteral calories
Based on prescribed data, the mean percentage change from baseline at Week 12 in enteral volume, in the ITT population, was 25.82% (±41.59) compared to 53.65% (±57.01) in the standard of care cohort. The corresponding increase in enteral calories was 58.80% (±64.20), compared to 57.02% (±55.25) in the standard of care cohort.

Reduction in infusion time
The mean decrease from baseline at Week 12 in the number of days/week on parenteral nutrition, in the ITT population based on physician-prescribed data, was -1.36 (±2.37) days/week corresponding to a percentage decrease of -24.49% (±42.46). There was no change from baseline in the standard of care cohort. Four subjects (26.7%) on the recommended teduglutide dose achieved at least a three-day reduction in parenteral nutrition needs.

At Week 12, based on subject diary data, subjects showed mean percentage reductions of 35.55% (±35.23) hours per day compared to baseline, which corresponded to reductions in the hours/day of parenteral nutrition usage of -4.18 (±4.08), while subjects in the standard of care cohort showed minimal change in this parameter at the same time point.

An additional 24-week, randomised, double-blind, multicentre study was conducted in 59 paediatric subjects aged 1 year through 17 years who were dependent on parenteral support. The objective was to evaluate safety/tolerability, pharmacokinetics and efficacy of teduglutide. Two doses of teduglutide were studied: 0.025 mg/kg/day (n=24) and 0.05 mg/kg/day (n=26); 9 subjects were enrolled in a standard of care (SOC) arm. Randomisation was stratified by age across dose groups. Results below correspond to the ITT population at the recommended dose of 0.05 mg/kg/day.

Complete weaning
Three (3) paediatric subjects in the 0.05 mg/kg group achieved the additional endpoint of enteral autonomy by week 24.

Reduction in parenteral nutrition volume
Based on subject diary data, 18 (69.2%) subjects in the 0.05 mg/kg/day group achieved the primary endpoint of ≥ 20% reduction in PN/IV volume at end of treatment, compared to baseline; in the SOC arm, 1 (11.1%) subject achieved this endpoint.
The mean change in parenteral nutrition volume from baseline at Week 24, based on subject diary data, was -23.30 (±17.50) ml/kg/day, corresponding to -41.57% (±28.90); the mean change in the SOC arm was -6.03 (±4.5) ml/kg/day (corresponding to a -10.21% [±13.59]).

Reduction in infusion time
At week 24, there was a decrease in the infusion time of -3.03 (±3.84) hours/day in the 0.05 mg/kg/day arm, corresponding to a percentage change of -26.09% (±36.14). The change from baseline in the SOC cohort was -0.21 (±0.69) hours/day (-1.75% [±5.89]).

The mean decrease from baseline at Week 24 in the number of days/week on parenteral nutrition, based on subject diary data, was -1.34 (±2.24) days/week corresponding to a percentage decrease of -21.33% (±34.09). There was no reduction in PN/IV infusion days per week in the SOC arm.

Clinical efficacy in adults

Teduglutide was studied in 17 patients with SBS allocated to five treatment groups using doses of 0.03, 0.10 or 0.15 mg/kg teduglutide once daily, or 0.05 or 0.075 mg/kg bid in a 21-day open-label, multicenter, dose-ranging study. Treatment resulted in enhanced gastrointestinal fluid absorption of approximately 750-1 000 ml/day with improvements in the absorption of macronutrients and electrolytes, decreased stomal or faecal fluid and macronutrients excretion, and enhanced key structural and functional adaptations in the intestinal mucosa. Structural adaptations were transient in nature and returned to baseline levels within three weeks of discontinuing the treatment.
In the pivotal phase 3 double-blind, placebo-controlled study in patients with SBS, who required parenteral nutrition, 43 patients were randomised to a 0.05 mg/kg/day dose of teduglutide and 43 patients to placebo for up to 24 weeks.

The proportion of teduglutide-treated subjects achieving a 20% to 100% reduction of parenteral nutrition at Week 20 and 24 was statistically significantly different from placebo (27 out of 43 subjects, 62.8% *versus* 13 out of 43 patients, 30.2%, p=0.002). Treatment with teduglutide resulted in a 4.4 l/week reduction in parenteral nutrition requirements (from a pre-treatment baseline of 12.9

litres) *versus* 2.3 l/week (from a pre-treatment baseline of 13.2 litres) for placebo at 24 weeks. Twenty-one (21) patients treated with teduglutide (48.8%) *versus* 9 on placebo (20.9%) achieved at least a one day reduction in parenteral nutrition administration (p=0.008).

Ninety-seven percent (97%) of patients (37 out of 39 patients treated with teduglutide) that completed the placebo-controlled study entered a long-term extension study where all patients received 0.05 mg/kg of teduglutide daily for up to an additional 2 years. In total 88 patients participated in this extension study, thereof 39 treated with placebo and 12 enrolled, but not randomised, in the previous study; 65 of 88 patients completed the extension study. There continued to be evidence of increased response to treatment for up 2.5 years in all groups exposed to teduglutide in terms of parenteral nutrition volume reduction, gaining additional days off parenteral nutrition per week, and achieving weaning of parenteral support.

Thirty (30) of the 43 teduglutide-treated patients from the pivotal study who entered the extension study completed a total of 30 months of treatment. Of these, 28 patients (93%) achieved a 20% or greater reduction of parenteral support. Of responders in the pivotal study who completed the extension study, 21 out of 22 (96%) sustained their response to teduglutide after an additional 2 years of continuous treatment.

The mean reduction in parenteral nutrition (n=30) was 7.55 l/week (a 65.6% reduction from baseline). Ten (10) subjects were weaned off their parenteral support while on teduglutide treatment for 30 months. Subjects were maintained on teduglutide even if no longer requiring parenteral nutrition. These 10 subjects had required parenteral nutrition support for 1.2 to 15.5 years, and prior to treatment with teduglutide had required between 3.5 l/week and 13.4 l/week of parenteral nutrition support. At the end of study, 21 (70%), 18 (60%) and 18 (60%) of the 30 completers achieved a reduction of 1, 2, or 3 days per week in parenteral support, respectively.

Of the 39 placebo subjects, 29 completed 24 months of treatment with teduglutide. The mean reduction in parenteral nutrition was 3.11 l/week (an additional 28.3% reduction). Sixteen (16, 55.2%) of the 29 completers achieved a 20% or greater reduction of parenteral nutrition. At the end of study, 14 (48.3%), 7 (24.1%) and 5 (17.2%) patients achieved a reduction of 1, 2, or 3 days per week in parenteral nutrition, respectively. Two (2) subjects were weaned off their parenteral support while on teduglutide.

Of the 12 subjects not randomised in the pivotal study, 6 completed 24 months of treatment with teduglutide. The mean reduction in parenteral nutrition was 4.0 l/week (39.4% reduction from baseline – the start of the extension study) and 4 of the 6 completers (66.7%) achieved a 20% or greater reduction in parenteral support. At the end of study, 3 (50%), 2 (33%) and 2 (33%) achieved a reduction of 1, 2, or 3 days per week in parenteral nutrition, respectively. One subject was weaned off their parenteral support while on teduglutide.

In another phase 3 double-blind, placebo-controlled study in patients with SBS, who required parenteral nutrition, patients received a 0.05 mg/kg/day dose (n=35), a 0.10 mg/kg/day dose (n=32) of teduglutide or placebo (n=16) for up to 24 weeks.

The primary efficacy analysis of the study results showed no statistically significant difference between the group on teduglutide 0.10 mg/kg/day and the placebo group, while the proportion of subjects receiving the recommended teduglutide dose of 0.05 mg/kg/day achieving at least a 20% reduction of parenteral nutrition at Week 20 and 24 was statistically significantly different *versus* placebo (46% *versus* 6.3%, $p< 0.01$). Treatment with teduglutide resulted in a 2.5 l/week reduction in parenteral nutrition requirements (from a pre-treatment baseline of 9.6 litres) *versus* 0.9 l/week (from a pre-treatment baseline of 10.7 litres) for placebo at 24 weeks.

Teduglutide treatment induced expansion of the absorptive epithelium by significantly increasing villus height in the small intestine.

Sixty-five (65) patients entered a follow-up SBS study for up to an additional 28 weeks of treatment. Patients on teduglutide maintained their previous dose assignment throughout the extension phase, while placebo patients were randomised to active treatment, either 0.05 or 0.10 mg/kg/day.

Of the patients who achieved at least a 20% reduction of parenteral nutrition at Weeks 20 and 24 in the initial study, 75% sustained this response on teduglutide after up to 1 year of continuous treatment.

The mean reduction of weekly parenteral nutrition volume was 4.9 l/week (52% reduction from baseline) after one year of continuous teduglutide treatment.

Two (2) patients on the recommended teduglutide dose were weaned off parenteral nutrition by Week 24. One additional patient in the follow-up study was weaned off parenteral nutrition.

5.2 Pharmacokinetic properties

Absorption

Teduglutide was rapidly absorbed from subcutaneous injection sites with maximum plasma levels occurring approximately 3-5 hours after dose administration at all dose levels. The absolute bioavailability of subcutaneous teduglutide is high (88%). No accumulation of teduglutide was observed following repeated subcutaneous administration.

Distribution

Following subcutaneous administration, teduglutide has an apparent volume of distribution of 26 litres in patients with SBS.

Biotransformation

The metabolism of teduglutide is not fully known. Since teduglutide is a peptide it is likely that it follows the principal mechanism for peptide metabolism.

Elimination

Teduglutide has a terminal elimination half-life of approximately 2 hours. Following intravenous administration teduglutide plasma clearance was approximately 127 ml/hr/kg which is equivalent to the glomerular filtration rate (GFR). Renal elimination was confirmed in a study investigating pharmacokinetics in subjects with renal impairment. No accumulation of teduglutide was observed following repeated subcutaneous administrations.

Dose linearity

The rate and extent of absorption of teduglutide is dose-proportional at single and repeated subcutaneous doses up to 20 mg.

Pharmacokinetics in subpopulations

Paediatric population

Following subcutaneous administration, similar C_{max} of teduglutide driving the efficacy responses, across age groups (4 months corrected by gestational age to 17 years) was demonstrated by population pharmacokinetics modelling based on PK samples collected in the population following SC 0.05 mg/kg daily dose. However, lower exposure (AUC) and shorter half-life were seen in paediatric patients 4 months to 17 years of age, as compared with adults. The pharmacokinetic profile of teduglutide in this paediatric population, as evaluated by clearance and volume of distribution, was different from that observed in adults after correcting for body weights. Specifically, clearance

decreases with increasing age from 4 months to adults. No data are available for paediatric patients with moderate to severe renal impairment and end-stage renal disease (ESRD).

Gender

No clinically relevant gender differences were observed in clinical studies.

Elderly

In a phase 1 study no difference in pharmacokinetics of teduglutide could be detected between healthy subjects younger than 65 years *versus* older than 65 years. Experience in subjects 75 years and above is limited.

Hepatic impairment

In a phase 1 study the effect of hepatic impairment on the pharmacokinetics of teduglutide following subcutaneous administration of 20 mg teduglutide was investigated. The maximum exposure and the overall extent of exposure to teduglutide following single 20 mg subcutaneous doses were lower (10-15%) in subjects with moderate hepatic impairment relative to those in healthy matched controls.

Renal impairment

In a phase 1 study, the effect of renal impairment on the pharmacokinetics of teduglutide following subcutaneous administration of 10 mg teduglutide was investigated. With progressive renal impairment up to and including end-stage renal disease the primary pharmacokinetic parameters of teduglutide increased up to a factor of 2.6 (AUC_{inf}) and 2.1 (C_{max}) compared to healthy subjects.

5.3 Preclinical safety data

Hyperplasia in the gall bladder, hepatic biliary ducts, and pancreatic ducts were observed in subchronic and chronic toxicology studies. These observations were potentially associated with the expected intended pharmacology of teduglutide and were to a varying degree reversible within an 8-13 week recovery period following chronic administration.

Injection site reactions

In pre-clinical studies, severe granulomatous inflammations were found associated with the injection sites.

Carcinogenicity / mutagenicity

Teduglutide was negative when tested in the standard battery of tests for genotoxicity.

In a rat carcinogenicity study, treatment related benign neoplasms included tumours of the bile duct epithelium in males exposed to teduglutide plasma levels approximately 32- and 155-fold higher than obtained in patients administered the recommended daily dose (incidence of 1 out of 44 and 4 out of 48, respectively). Adenomas of the jejunal mucosa were observed in 1 out of 50 males and 5 out of 50 males exposed to teduglutide plasma levels approximately 10- and 155-fold higher than obtained in patients administered the recommended daily dose. In addition, a jejunal adenocarcinoma was observed in a male rat administered the lowest dose tested (animal:human plasma exposure margin of approximately 10-fold).

Reproductive and developmental toxicity

Reproductive and developmental toxicity studies evaluating teduglutide have been carried out in rats and rabbits at doses of 0, 2, 10 and 50 mg/kg/day subcutaneously. Teduglutide was not associated with

effects on reproductive performance, *in utero* or developmental parameters measured in studies to investigate fertility, embryo-foetal development and pre- and post-natal development. Pharmacokinetic data demonstrated that the teduglutide exposure of foetal rabbits and suckling rat pups was very low.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Powder

Mannitol
Sodium dihydrogen phosphate monohydrate
Disodium hydrogen phosphate heptahydrate
L-Histidine

Solvent

Water for injections

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

Unopened powder vial

18 months

Unopened solvent vial

4 years

Reconstituted product

Chemical and physical stability has been demonstrated for 3 hours at 20-25 °C.

From a microbiological point of view, unless the method of reconstitution precludes the risk of microbial contamination, the solution should be used immediately.

If not used immediately, in-use storage times and conditions are the responsibility of the user and would normally not be longer than 24 hours at 2 to 8 °C, unless reconstitution has taken place in controlled and validated aseptic conditions.

6.4 Special precautions for storage

Powder

Store in a refrigerator (2 °C – 8 °C).

Do not freeze.

Solvent

The solvent (sterile water for Injections) does not require any special storage conditions.

For storage conditions after reconstitution of the medicinal product, see section 6.3.

6.5 Nature and contents of container

Powder

Vial (Type I glass) with a grey rubber stopper (bromobutyl) and an aluminium flip-flop seal with a blue polypropylene disc, containing 5 mg teduglutide.

Solvent

Pre-filled syringe (Type I glass) with a plunger stopper (bromobutyl) and a plastic rigid tip cap, containing 0.5 ml of solvent.

Pack sizes

28 vials of powder with 28 pre-filled syringes of solvent.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Determination of the number of vials needed for administration of one dose must be based on the individual patient's weight and the recommended dose of 0.05 mg/kg/day. The physician should at each visit weigh the patient, determine the daily dose to be administered until next visit and inform the patient accordingly.

Tables with the injection volumes based on the recommended dose per body weight for both adults and paediatric patients are provided in section 4.2.

The pre-filled syringe must be assembled with a reconstitution needle.

The powder in the vial must then be dissolved by adding all the solvent from the pre-filled syringe.

The vial should not be shaken, but can be rolled between the palms and gently turned upside-down once. Once a clear colourless solution is formed in the vial, the solution should be sucked up into a 1 ml injection syringe (or 0.5 ml or smaller injection syringe for paediatric use) with scale intervals of 0.02 ml or smaller (not included in the pack).

If two vials are needed, the procedure for the second vial must be repeated and the additional solution sucked up into the injection syringe containing the solution from the first vial. Any volume exceeding the prescribed dose in ml must be expelled and discarded.

The solution must be injected subcutaneously into a cleaned area on the abdomen, or if this is not possible, on the thigh (see section 4.2 Method of administration) using a thin needle for subcutaneous injection.

Detailed instructions on the preparation and injection of Teduglutide Viatris are provided in the package leaflet.

The solution must not be used if it is cloudy or contains particulate matter.

For single use only.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

All needles and syringes should be disposed of in a sharps disposal container.

7. MARKETING AUTHORISATION HOLDER

Viatris Limited
Damastown Industrial Park
Mulhuddart, Dublin 15
DUBLIN
Ireland

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/25/2005/001

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation:

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency https://www.ema.europa.eu.

ANNEX II

A. MANUFACTURERS RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

A. MANUFACTURERS RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturers responsible for batch release

Pharmadox Healthcare Ltd,
KW20A Kordin Industrial Park, Paola,
PLA3000
Malta

Mylan Germany GmbH,
Benzstrasse 1
61352 Bad Homburg v. d. Hohe
Germany

The printed package leaflet of the medicinal product must state the name and address of the manufacturer responsible for the release of the concerned batch.

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to restricted medical prescription (see Annex I: Summary of Product Characteristics, section 4.2).

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

- **Periodic safety update reports (PSURs)**

The requirements for submission of PSURs for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

- **Risk management plan (RMP)**

The marketing authorisation holder (MAH) shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the marketing authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:
- At the request of the European Medicines Agency;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

Carton

1. NAME OF THE MEDICINAL PRODUCT

Teduglutide Viatris 5 mg powder and solvent for solution for injection
teduglutide

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One vial of powder contains 5 mg of teduglutide. After reconstitution, each vial contains 5 mg of teduglutide in 0.5 ml of solution, corresponding to a concentration of 10 mg/ml.

3. LIST OF EXCIPIENTS

Powder: Mannitol, sodium dihydrogen phosphate monohydrate, disodium hydrogen phosphate heptahydrate and L-Histidine.
Solvent: Water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Powder and solvent for solution for injection
28 vials of powder containing 5 mg teduglutide
28 pre-filled syringes containing 0.5 ml of solvent

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use.
Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator (2 °C – 8 °C).
Do not freeze.
After reconstitution, the solution should be used immediately.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Viatris Limited
Damastown Industrial Park
Mulhuddart, Dublin 15
DUBLIN
Ireland

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/25/2005/001

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Teduglutide Viatris

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

Vial label

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Teduglutide Viatris 5 mg powder for solution for injection
teduglutide
Subcutaneous use

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

5 mg

6. OTHER

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

Solvent – Pre-filled syringe label

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Solvent for Teduglutide Viatris
Subcutaneous use

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

0.5 ml

6. OTHER

For reconstitution.

B. PACKAGE LEAFLET

Package leaflet: Information for the patient

Teduglutide Viatris 5 mg powder and solvent for solution for injection
teduglutide

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Teduglutide Viatris is and what it is used for

Teduglutide Viatris contains the active substance teduglutide. It improves the absorption of nutrients and fluid from your remaining gastrointestinal tract (gut).

Teduglutide Viatris is used to treat adults, children and adolescents (aged 4 months and above) with Short Bowel Syndrome. Short Bowel Syndrome is a disorder arising from an inability to absorb food nutrients and fluid across the gut. It is often caused by surgical removal of all or part of the small intestine.

2. What you need to know before you use Teduglutide Viatris

Do not use Teduglutide Viatris
- if you are allergic to teduglutide or any of the other ingredients of this medicine (listed in section 6) or trace residues of tetracycline.
- if you have or are suspected to have cancer.
- if you have had cancer in the gastrointestinal tract, including liver, gallbladder or bile ducts, and pancreas within the last five years.

Warnings and precautions
Talk to your doctor before using Teduglutide Viatris:
- if you have severely decreased liver function. Your doctor will consider this when prescribing this medicine.
- if you suffer from certain cardiovascular diseases (affecting the heart and/or blood vessels) such as high blood pressure (hypertension) or have a weak heart (cardiac insufficiency). The signs and symptoms include sudden weight gain, face swelling, swollen ankles and/or shortness of breath.
- if you have other severe diseases that are not well controlled. Your doctor will consider this when prescribing this medicine.
- if you have decreased kidney function. Your doctor may need to give you a lower dose of this medicine.

When starting and while getting treated with Teduglutide Viatris, your doctor may adjust the amount of intravenous fluids or nutrition you receive.

Medical check-ups before and during treatment with Teduglutide Viatris
Before you start treatment with this medicine, your doctor will need to perform a colonoscopy (a procedure to see inside your colon and rectum) to check for the presence of polyps (small abnormal growths) and remove them. It is recommended that your doctor performs these examinations once a year during the first 2 years after starting treatment, and then at a minimum of five-year intervals. If polyps are found either before or during your treatment with Teduglutide Viatris, your doctor will decide whether you should continue using this medicine. Teduglutide Viatris should not be used if a cancer is detected during your colonoscopy. The doctor will monitor your body fluids and electrolytes as an imbalance may cause fluid overload or dehydration.

Your doctor will take special care and monitor your small bowel function and monitor for signs and symptoms indicating problems with your gallbladder, bile ducts and pancreas.

Children and adolescents

Medical check-ups before and during treatment with Teduglutide Viatris
Before you start treatment with this medicine, you will need to have a test done to see if there is blood in the stool. You will also have a colonoscopy done (a procedure to see inside your colon and rectum to check for the presence of polyps (small abnormal growths) and have them removed) if you have unexplained blood in your bowel movements (stools). If polyps are found before your treatment with Teduglutide Viatris, your doctor will decide whether you should use this medicine. Teduglutide Viatris should not be used if a cancer is detected during your colonoscopy. Your doctor will perform further colonoscopies if you continue treatment with Teduglutide Viatris. The doctor will monitor your child's body fluids and electrolytes as an imbalance may cause fluid overload or dehydration.

Children aged below 1 year and above 4 months
Teduglutide Viatris should not be used in children aged below 1 year and above 4 months. Your child's doctor may prescribe a lower strength medicine containing teduglutide which can be more accurately dosed.

Children aged below 4 months
Teduglutide should not be used in children under 4 months of age. This is because there is limited experience with teduglutide in this age group.

Other medicines and Teduglutide Viatris
Tell your doctor, pharmacist or nurse if you are using, have recently used or might use any other medicines.

Teduglutide Viatris may affect how other medicines are absorbed from the gut and therefore how well they work. Your doctor may have to change your dose of other medicines.

Pregnancy and breast-feeding
If you are pregnant or breast-feeding, the use of Teduglutide Viatris is not recommended.
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor, pharmacist or nurse for advice before using this medicine.

Driving and using machines
This medicine may cause you to feel dizzy. If this happens to you, do not drive or use machines until you feel better.

Teduglutide Viatris contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per vial, that is to say essentially 'sodium-free'.

3. How to use Teduglutide Viatris

Always use this medicine exactly as your doctor has told you. Check with your doctor, pharmacist or nurse if you are not sure.

Dose
The recommended daily dose is 0.05 mg per kg body weight. The dose will be given in millilitres (ml) of solution.

Your doctor will choose the dose that is right for you depending on your body weight. Your doctor will tell you which dose to inject. If you are not sure, ask your doctor, pharmacist or nurse.

Use in children and adolescents
Teduglutide Viatris can be used in children and adolescents (aged 4 months and above). Use this medicine exactly as your doctor has told you.

How to use Teduglutide Viatris
Teduglutide Viatris is injected under the skin (subcutaneously) once daily. The injection can be self-administered or given by another person, for example your doctor, his/her assistant or your home nurse. If you, or your carer, are injecting the medicine, you or your carer must receive adequate training by your doctor or nurse. You will find detailed instructions for injections at the end of this leaflet.

It is strongly recommended that every time you or your child receive a dose of Teduglutide Viatris, the name and lot number of the product are recorded in order to maintain a record of the lots used.

If you use more Teduglutide Viatris than you should
If you inject more Teduglutide Viatris than you are told to by your doctor, you should contact your doctor, pharmacist or nurse.

If you forget to use Teduglutide Viatris
If you forget to inject this medicine (or cannot inject it at your usual time), use it as soon as possible on that day. Never use more than one injection in the same day. Do not inject a double dose to make up for a forgotten dose.

If you stop using Teduglutide Viatris
Keep using this medicine for as long as your doctor prescribes it for you. Do not stop using this medicine without consulting your doctor, as a sudden stop can cause changes in your fluid balance.

If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Seek immediate medical attention if any of the following side effects occur:

Common (may affect up to 1 in 10 people):
- Congestive heart failure. Contact your doctor if you experience tiredness, shortness of breath or swelling of ankles or legs or face swelling.
- Inflammation of the pancreas (pancreatitis). Contact your doctor or the emergency unit if you experience severe stomach ache and fever.
- Intestinal obstruction (blockage of the bowel). Contact your doctor or the emergency unit if you experience severe stomach ache, vomiting and constipation.

- Reduced flow of bile from the gallbladder and/or inflammation of the gallbladder. Contact your doctor or the emergency unit if you experience yellowing of the skin and the whites in the eyes, itching, dark urine and light-coloured stools or pain in the upper right side or middle of the stomach area.

Uncommon (may affect up to 1 in 100 people):
- Fainting. If heart rate and breathing is normal and you awaken fast, speak to your doctor. In other cases, seek help as soon as possible.

Other side effects include:

Very common (may affect more than 1 in 10 people):
- Respiratory tract infection (any infection of the sinuses, throat, airways or lungs)
- Headache
- Stomach pain, bloated stomach, feeling sick (nausea), swelling of stoma (an artificial opening for waste removal), vomiting
- Reddening, pain or swelling at the site of the injection

Common (may affect up to 1 in 10 people):
- Flu (influenza) or flu-like symptoms
- Decreased appetite
- Swelling of hands and/or feet
- Problems sleeping, anxiety
- Cough, shortness of breath
- Polyps (small abnormal growths) in your large bowel
- Passing gas (flatulence)
- Narrowing or blockage of your pancreatic duct, which may cause inflammation of the pancreas
- Inflammation of the gallbladder

Uncommon (may affect up to 1 in 100 people)
- Polyps (small abnormal growths) in your small bowel

Not known (frequency cannot be estimated from the available data):
- Allergic reaction (hypersensitivity)
- Fluid retention
- Polyps (small abnormal growths) in your stomach

Use in children and adolescents
In general, the side effects in children and adolescents are similar to those seen in adults.

There is limited experience in children under 4 months of age.

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Teduglutide Viatris

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton, vial and the pre-filled syringe after EXP. The expiry date refers to the last day of that month.

Powder
Store in a refrigerator (2 °C – 8 °C).

Do not freeze.

Solvent
This does not require any special storage conditions.

After reconstitution, from a microbiological point of view, the solution should be used immediately. However, chemical and physical stability has been demonstrated for 3 hours at 20-25 °C.

Do not use this medicine if you notice that the solution is cloudy or contains particulate matter.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

Dispose of all needles and syringes in a sharps disposal container.

6. Contents of the pack and other information

What Teduglutide Viatris contains
- The active substance is teduglutide. One vial of powder contains 5 mg of teduglutide. After reconstitution, each vial contains 5 mg teduglutide in 0.5 ml of solution, corresponding to a concentration of 10 mg/ml.
- The other ingredients are mannitol, sodium dihydrogen phosphate monohydrate, disodium hydrogen phosphate heptahydrate and L-Histidine.
- The solvent contains water for injections.

What Teduglutide Viatris looks like and contents of the pack
Teduglutide Viatris is a powder and solvent for solution for injection (5 mg teduglutide in vial, 0.5 ml solvent in pre-filled syringe).

The powder is white and the solvent is clear and colourless.

Teduglutide Viatris is available in packs of 28 vials of powder with 28 pre-filled syringes.

Marketing Authorisation Holder
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Mulhuddart, Dublin 15,
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Ireland

Manufacturer
Pharmadox Healthcare Ltd,
KW20A Kordin Industrial Park, Paola,
PLA3000
Malta

Mylan Germany GmbH,
Benzstrasse 1
61352 Bad Homburg v. d. Hohe
Germany

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

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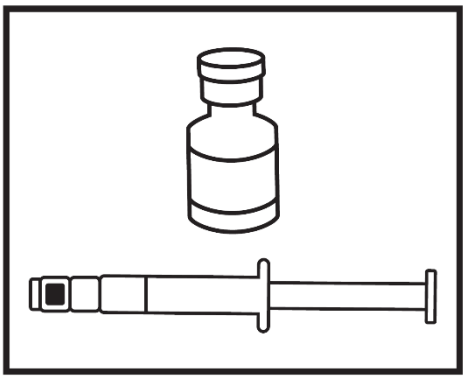
Detailed information on this medicine is available on the European Medicines Agency web site: https://www.ema.europa.eu.

Instructions for preparing and injecting Teduglutide Viatris

Important information:

- Read the Package Leaflet before using Teduglutide Viatris.
- Teduglutide Viatris is for injection under the skin (subcutaneous injection).
- Do not inject Teduglutide Viatris into a vein (intravenously) or muscle (intramuscularly).
- Keep Teduglutide Viatris out of the sight and reach of children.
- Do not use Teduglutide Viatris after the expiry date which is stated on the carton, the vial and the pre-filled syringe. The expiry date refers to the last day of that month.
- Store in a refrigerator (2 °C – 8 °C).
- Do not freeze.
- After reconstitution, from a microbiological point of view, the solution should be used immediately. However, chemical and physical stability has been demonstrated for 3 hours at 20-25 ºC.
- Do not use Teduglutide Viatris if you notice that the solution is cloudy or contains particulate matter.
- Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.
- Dispose of all needles and syringes in a sharps disposal container.



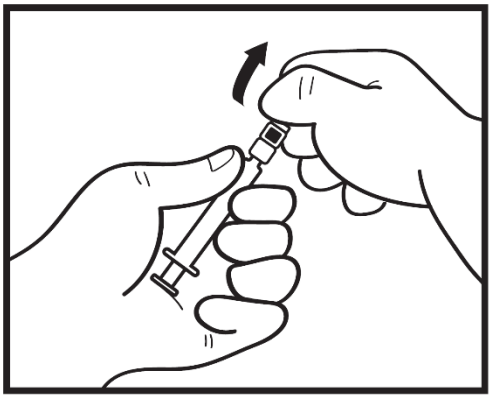
Materials provided in the pack:
- 28 vials with 5 mg teduglutide as a powder
- 28 pre-filled syringes with solvent

Materials needed but not included in the pack:
- Reconstitution needles (size 22G, length 1½" (0.7 x 40 mm))
- 0.5 or 1 ml injection syringes (with scale intervals of 0.02 ml or smaller). ***For children, a 0.5 ml (or smaller) injection syringe may be used***
- Thin injection needles for subcutaneous injection (e.g., size 26G, length 5/8" (0.45 x 16 mm), or smaller needles for children, as appropriate)
- Alcohol wipes
- Alcohol swabs
- A puncture-proof container for safe disposal of the used syringes and needles

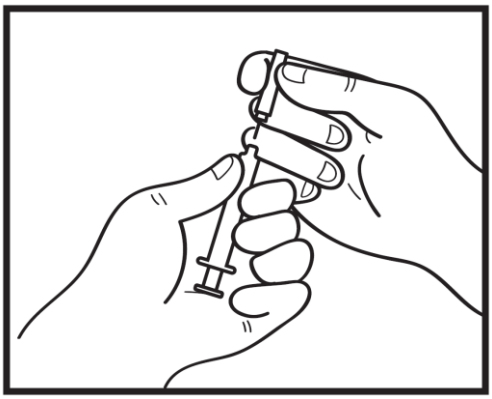
NOTE: Before you start, make sure you have a clean work surface and that you have washed your hands before proceeding.

1. Assemble the pre-filled syringe

Once you have all the materials ready, you need to assemble the pre-filled syringe. The following procedure shows how you do this.



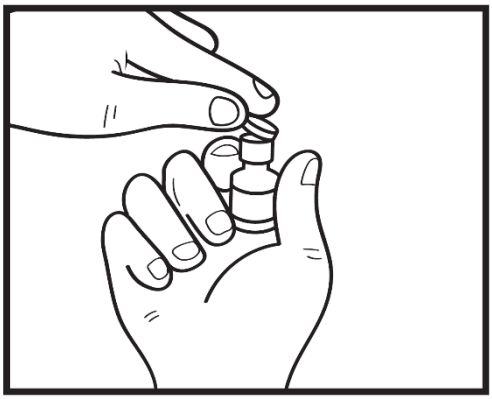
1.1 Take the pre-filled syringe with the solvent and flip off the top part of the white plastic cap on the pre-filled syringe so that it is ready for the reconstitution needle to be attached.



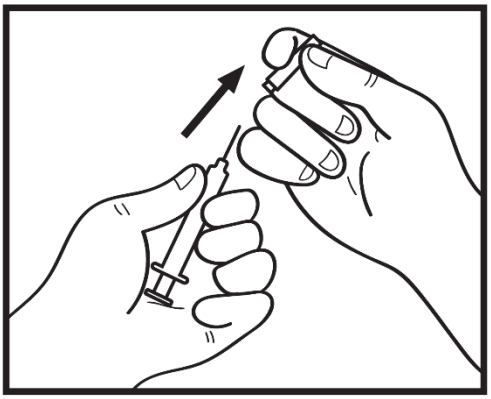
1.2 Attach the reconstitution needle (22G, 1½" (0.7 x 40 mm)) to the assembled pre-filled syringe by screwing it on in a clockwise direction.

2. Dissolve the powder

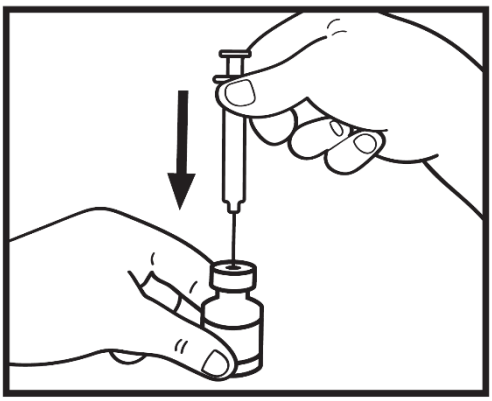
Now you are ready to dissolve the powder with the solvent.



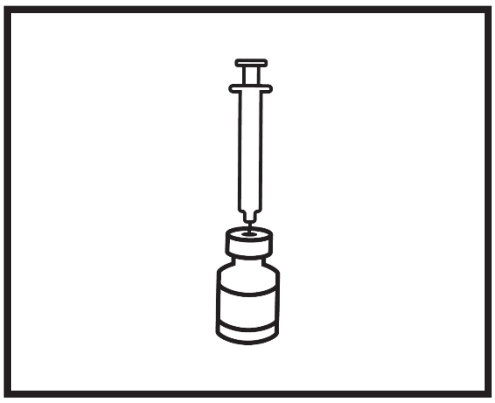
2.1 Remove the blue flip-off button from the powder vial, wipe the top with an alcohol wipe and allow to dry. Do not touch the top of the vial.



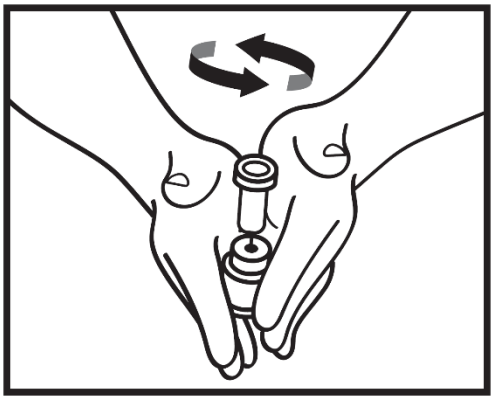
2.2 Uncap the reconstitution needle on the assembled pre-filled syringe with solvent without touching the tip of the needle.



2.3 Taking the powder vial, insert the reconstitution needle attached to the assembled pre-filled syringe into the centre of the rubber stopper and gently push the plunger all the way down to inject all the solvent into the vial.

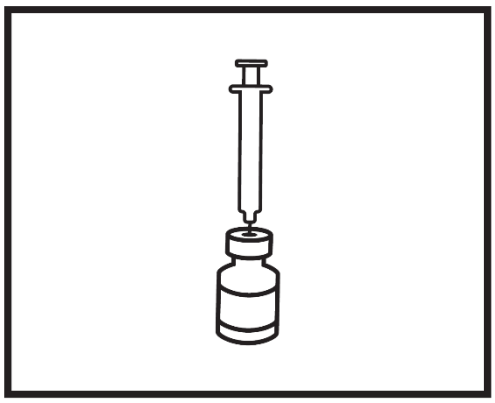


2.4 Leave the reconstitution needle and empty syringe in the vial. Let the vial rest for approximately 30 seconds.



2.5 Gently roll the vial between your palms for about 15 seconds. Then gently turn the vial upside-down once with the reconstitution needle and empty syringe still in the vial.

NOTE: Do not shake the vial. Shaking the vial may produce foam, which makes it difficult to extract the solution from the vial.



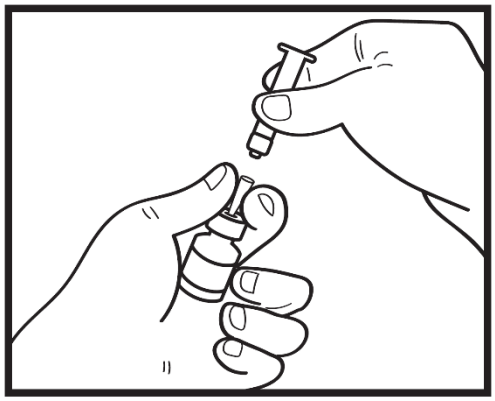
2.6 Let the vial rest for about two minutes.

2.7 Observe the vial for any undissolved powder. If any powder remains, repeat steps 2.5 and 2.6. Do not shake the vial. If there is still some undissolved powder, discard the vial and start the preparation again from the beginning with a new vial.

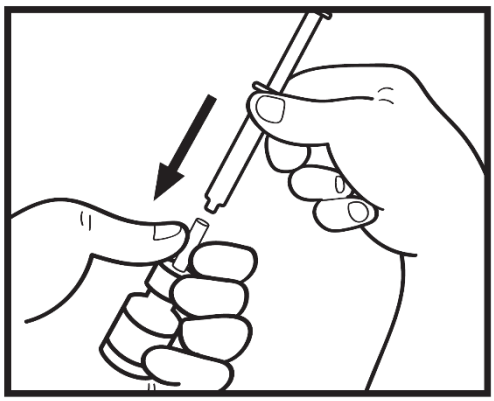
NOTE: The final solution should be clear. If the solution is cloudy or contains particulate matter, do not inject it.

NOTE: Once prepared, the solution should be used immediately. It should be kept below 20-25°C and maximum storage time is 3 hours.

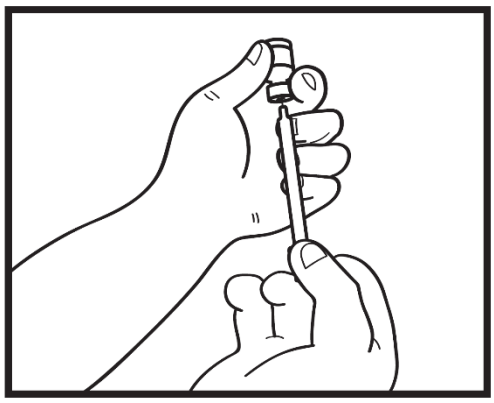
3. Prepare the injection syringe



3.1 Remove the reconstitution syringe from the reconstitution needle which is still in the vial and discard the reconstitution syringe.

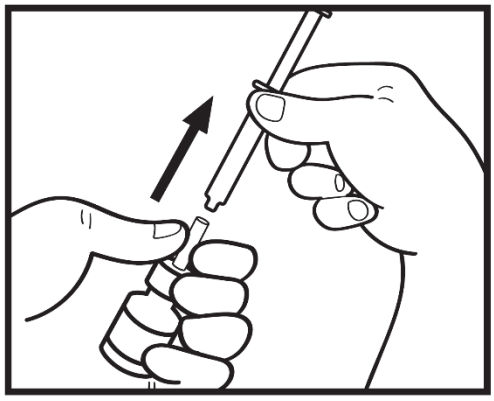


3.2 Take the injection syringe and attach it to the reconstitution needle which is still in the vial.

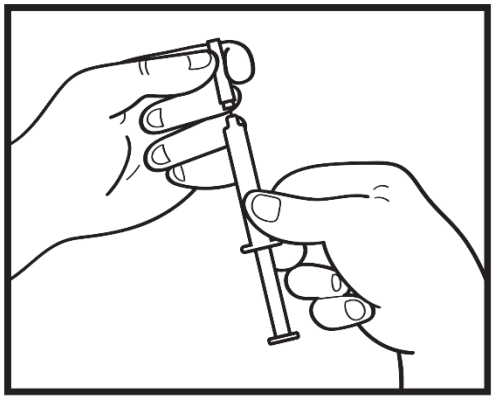


3.3 Turn the vial upside down, slide the tip of the reconstitution needle close to the stopper and allow all the medicine to fill the syringe by pulling the plunger back gently.

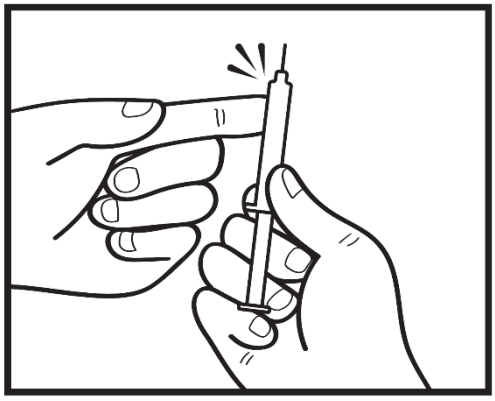
NOTE: If your doctor has told you that you need two vials, prepare a second pre-filled syringe with solvent and a second powder vial as shown in the main steps 1 and 2. Withdraw the solution from the second vial into the same injection syringe by repeating step 3.



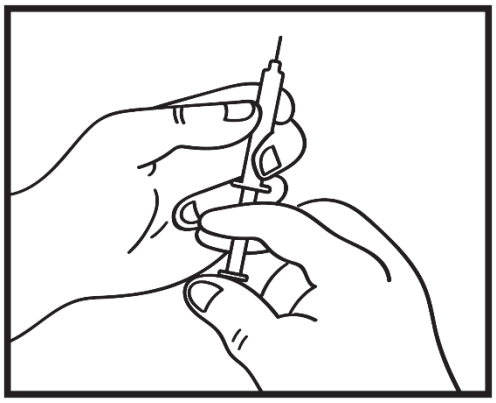
3.4 Remove the injection syringe from reconstitution needle leaving the needle in the vial. Discard the vial and reconstitution needle together into the sharps disposal container.



3.5 Take the injection needle, but do not remove the plastic needle cap. Attach the needle to the injection syringe containing the medicine.

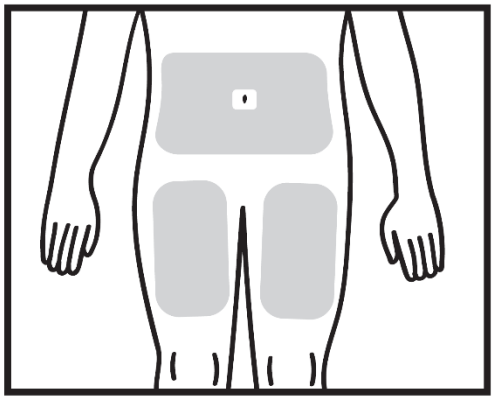


3.6 Check for air bubbles. If air bubbles are present, gently tap the syringe until they rise to the top. Then gently push up the plunger to expel the air.



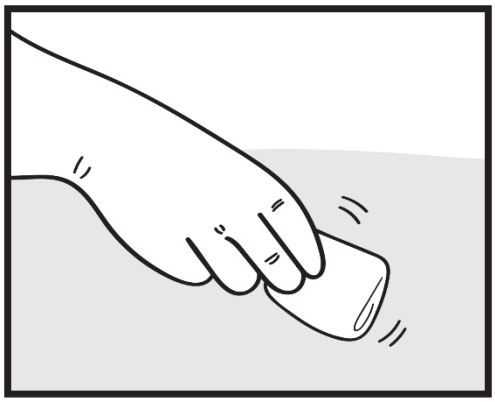
3.7 Your dose in ml has been calculated by the doctor. Expel any excessive volume from the syringe with the needle cap still on until your dose is reached.

4. Inject the solution

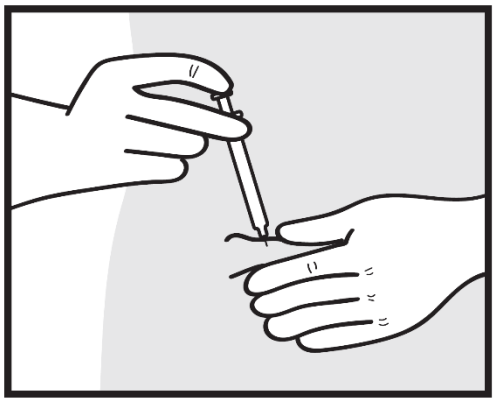


4.1 Find an area on your belly, or if you have pain or hardening of the tissue on your belly, on your thigh where it is easy for you to give the injection (see the diagram).

NOTE: Do not use the same area each day for each injection - rotate sites (use upper, lower, and left and right side of your belly) to avoid discomfort. Avoid areas that are inflamed, swollen, scarred or covered by a mole, birthmark or other lesion.



4.2 Clean the intended site of injection on your skin with an alcohol swab, using a circular motion, working outwards. Allow the area to air-dry.



4.3 Remove the plastic cap from the needle of the prepared injection syringe. Gently grasp the cleaned skin at the injection site with one hand. With the other hand, hold the syringe as you would with a pencil. Bend your wrist back and quickly insert the needle at a 45° angle.

4.4 Pull back the plunger slightly. If you see any blood in the syringe, withdraw the needle and replace the needle on the injection syringe with a clean one of the same size. You can still use the medicine that is already in the syringe. Try to inject in another place in the cleaned skin area.

4.5 Inject the medicine slowly by pushing steadily on the plunger until all the medicine is injected and the syringe is empty.

4.6 Pull the needle straight out of the skin and discard the needle and syringe together into the sharps disposal container. A small amount of bleeding may occur. If necessary, press gently on the injection site with an alcohol swab or 2x2 gauze until any bleeding has stopped.

4.7 Dispose all needles and syringes in a sharps disposal container or hard-walled container (for example, a detergent bottle with a lid). This container must be puncture proof (top and sides). If you need a sharps disposal container, please contact your doctor.