Health Technology Briefing
February 2022

Teduglutide for short bowel syndrome in infants

Company/Developer	Takeda UK Ltd

☐ New Active Substance ☒ Significant Licence Extension (SLE)

NIHRIO ID: 26498	NICE ID: Not available	UKPS ID: 664257

Licensing and Market Availability Plans

Currently in phase III/II clinical trials.

Summary

Teduglutide is in clinical development for infants aged four to twelve months with short bowel syndrome (SBS) who are dependent on parenteral support (PS). SBS is a complex disease that occurs due to the physical loss or the loss of function of a portion of the small and/or large intestine. Consequently, individuals with SBS often have a reduced ability to absorb nutrients such as fats, carbohydrates (sugars) vitamins, minerals, trace elements and fluids. Although SBS in infants is a very rare condition, SBS can incur significant illness including intestinal failure, cholestasis, sepsis, and death. However, there is a lack of approved treatments for infants with SBS.

Teduglutide is similar to human glucagon-like peptide 2 (GLP-2), a hormone made in the gut that increases absorption of nutrients from the intestine. In a phase III clinical trial, teduglutide was administered as a subcutaneous (SC) injection and was shown to be safe and effaceable. If licensed, teduglutide will offer an additional treatment option for infants aged 4-12 months with SBS.

Proposed Indication

Infants 4 to 12 months of age with short bowel syndrome (SBS) who are dependent on parenteral support (PS).[1]

Technology

Description

Teduglutide (Revestive®, Gattex®) is an analogue of naturally occurring human GLP-2 (a peptide secreted by L cells of the distal intestine in response to luminal nutrients) that is manufactured in *Escherichia coli* using recombinant DNA technology. The medicinal product 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. GLP-2 is known to increase intestinal and portal blood flow, inhibit gastric acid secretion and decrease intestinal motility. Teduglutide binds to the GLP-2 receptors located in intestinal subpopulations of enteroendocrine cells, subepithelial myofibroblasts, and enteric neurons of the submucosal and myenteric plexus. Activation of these receptors results in the local release of multiple mediators, including insulin-like growth factor-1, nitric oxide and keratinocyte growth factor.[2,3]

Teduglutide is currently in clinical development for infants with SBS. In a phase III clinical trial (NCT03571516) a subcutaneous (SC) injection of 0.05 mg/kg teduglutide was administered once daily (QD) into abdomen or into either the thigh or arm in addition to standard medical therapy for 24 weeks.[1]

Key Innovation

A phase III trial (NCT02682381) which evaluated the safety and efficacy of teduglutide in paediatric patients aged 1-17 years with SBS–associated intestinal failure (SBS-IF) showed that teduglutide was found to be generally well tolerated and resulted in clinically meaningful reductions. Both 0.025-mg/kg and 0.05-mg/kg teduglutide groups showed clinically significant reductions in parenteral support (PS) volume ($P < 0.05$ vs standard of care), PS calories, days per week and hours per day of PS infusions and increases in enteral nutrition and plasma citrulline at week 24 compared with baseline. Teduglutide has a demonstrated safety profile that is similar overall in paediatric and adult patients.[4] Therefore, it is plausible that teduglutide will result in similar outcomes for infants, and thus if licensed, will offer them an additional treatment option.

Regulatory & Development Status

In the EU and Scotland, teduglutide is indicated for the treatment of patients aged one year and above with SBS. Patients should be stable following a period of intestinal adaptation after surgery.[5,6]

Teduglutide is in phase III/II clinical development for hyperlipidemias and ileostomy – stoma.[7]

Patient Group

Disease Area and Clinical Need

SBS is a complex disease that occurs due to the physical loss or the loss of function of a portion of the small and/or large intestine. Consequently, individuals with SBS often have a reduced ability to absorb nutrients such as fats, carbohydrates (sugars), vitamins, minerals, trace elements and fluids (malabsorption). The specific symptoms and severity of SBS vary from one person to another. Diarrhoea is common, often severe and can cause dehydration, which can even be life threatening. SBS can lead to fatigue, malnutrition, unintended weight loss and additional symptoms may be due to the loss of essential vitamins and minerals.[8,9] It can incur significant morbidity including intestinal failure, cholestasis, sepsis, and death.[10]

The main cause of SBS is surgery to remove a portion of the small intestine. This surgery can treat intestinal diseases, injuries, or birth defects. Some children are born with an abnormally short small intestine or with part of their bowel missing, which can cause SBS. In infants, SBS most commonly occurs following surgery to treat necrotising enterocolitis, a condition in which part of the tissue in the intestines is destroyed.[11]

In 2018 in European Union (EU), it was estimated that SBS affected approximately 0.6 in 10,000 adults. This was equivalent to a total of around 31,000 adults.[12] Approximately 80% of paediatric SBS cases develop during the neonatal period.[13] However, the exact incidence and prevalence of SBS in the general population is unknown[8] and the population likely to be eligible to receive teduglutide could not be estimated from available published sources.

Recommended Treatment Options

For the management of SBS, the National Institute for Health and Care Excellence (NICE) recommends focusing on ensuring adequate nutrition and drug absorption, thereby reducing the risk of complications resulting from these effects.[14]

For nutritional deficiencies NICE recommends:[14]

- Oral or intravenous magnesium supplementation, though administration of oral magnesium may cause diarrhoea
- Occasionally the use of oral alfacalcidol and correction of sodium depletion may be useful

Nutritional support can range from oral supplements to parenteral nutrition, depending on the severity of intestinal failure.[14]

For diarrhoea and high output stomas NICE recommends:[14]

- Antimotility drugs (such as loperamide hydrochloride, codeine phosphate and co-phenotrope)
- Colestyramine (in patients with an intact colon and less than 100 cm of ileum resected)
- Antisecretory drugs (e.g., omeprazole or octreotide)
- Growth factors (e.g., teduglutide)

Clinical Trial Information

Trial	NCT03571516; A Randomized, Open-label, 24-Week Safety, Efficacy, and Pharmacokinetic Study of Teduglutide in Infants 4 to 12 Months of Age With Short Bowel Syndrome Who Are Dependent on Parenteral Support **Phase III:** Completed **Location(s):** 3 EU countries and UK **Study completion date:** September 2020
Trial Design	Randomised, parallel assignment, open-label
Population	N=10; infants who weigh at least 5 kilograms and weight-for-length Z-score greater than -2 at screening and baseline; and are 4 to 12 months corrected gestational age at screening.
Intervention(s)	0.05 mg/kg SC injection of teduglutide into abdomen or into either the thigh or arm once a day (QD) in addition to standard medical therapy
Comparator(s)	Standard of care

Outcome(s)	Number of participants who achieved at least 20 Percent (%) reduction from baseline in weight-normalized parenteral support (PS) volume at end of treatment/early termination (EOT/ET) [time frame: baseline, EOT/ET (up to week 24) See trial record for full list of other outcomes.
Results (efficacy)	See trial record.
Results (safety)	See trial record.

Estimated Cost

Teduglutide is already marketed in the UK; a 1.25mg vial costs £7,307.70 (hospital only), and treatment with a vial of 5mg costs £14,615.39 (hospital only).[15]

Relevant Guidance

NICE Guidance

- NICE technology appraisal in development. Teduglutide for treating short bowel syndrome (GID-TA10842). Expected date of issue to be confirmed.
- NICE intervention procedure guidance. Serial transverse enteroplasty procedure (STEP) for bowel lengthening in parenteral nutrition-dependent children (IPG232). September 2007.

NHS England (Policy/Commissioning) Guidance

- NHS England. 2013/14 NHS Standard Contract Paediatric Medicine: Gastroenterology, Hepatology and Nutrition. E03/S/c.

Other Guidance

- British Society of Gastroenterology. Guidelines for management of patients with a short bowel. 2006.[16]

Additional Information

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