NICE National Institute for Health and Care Excellence

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Teduglutide for treating short bowel syndrome [ID3937]

Chair's presentation

2nd Appraisal Committee A meeting
Chair: Jane Adam
Lead team: Richard Ballerand, Andy Champion, Mohit Sharma
ERG: Aberdeen HTA Group
Technical team: Emily Leckenby, Hannah Nicholas, Henry Edwards
Company: Takeda UK Ltd
12 April 2022

Draft recommendation

Recommended when it is started in children and young people aged 1 to 17
Not recommended in adults – requested further information

Issue	Analysis requested in ACD	Company response
Concomitant medications and HPN assumptions (ACD 3.21)	• Updated analyses for parenteral support costs • Updated base-case analysis for adults that aligns the concomitant medications with NHS practice	✓
Starting ages (ACD 3.13)	• Further scenario analyses considering different starting ages in the adult model, alongside justifications for the chosen starting age	✓
Placebo data from STEPS (ACD 3.8/3.11/3.13)	• Analyses that use placebo arm data from STEPS for 6 months rather than assuming a steady state for those not on teduglutide	✓

Company also:
- **Increased patient access scheme discount**
- **Provided information regarding adult carer requirement calculations (ACD 3.19)**
- **Raised the issue of inequity relating to PS demand and teduglutide (ACD 3.28/3.29)**

Abbreviations: PS; parenteral support

Disease background

- **Short bowel syndrome (SBS)** is most commonly caused by surgery which has been needed to remove abnormal small bowel
- Treatment is **parenteral support** (PS)
  - **~500** adults in England with SBS are dependent on long-term PS.[1]
  - IV delivery of nutrients and fluids,
  - ~0-14 hours overnight 2-7 days per week.
  - Self-administer at home, using a permanent intravenous tube.
  - Places a **huge burden** on patients and carers
- Long term use of PS itself is associated with **life threatening complications** such as blood infections, blood clots, and kidney and liver failure.

Teduglutide (Revestive®)

Marketing authorisation	The treatment of patients aged 1 year and above with short bowel syndrome (SBS). Patients should be stable following a period of intestinal adaptation after surgery.
Dosage	0.05 mg/kg, administered by subcutaneous injection once daily
Mechanism of action	Teduglutide is a modified analogue of the naturally occurring human glucagon-like peptide 2 (GLP-2), a peptide that promotes nutrient absorption
List price	Teduglutide 5mg vial: £521.98 Teduglutide 1.25mg vial: £260.99 Patient Access Scheme (PAS) approved by NHS England.

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[1]British Artificial Nutrition Survey report. 2016

Abbreviations: PS; parenteral support

ACD consultation responses

Comments received from:

- Company (Takeda UK)
- Clinical experts
- Patient organisations (PINNT and Short Bowel Survivor and Friends)
- Web comments

Comment Themes

- ***Uncertainties in clinical evidence***
  - Multiple real world studies showing teduglutide is effective in adults with SBS
- ***Complications of current treatment (parenteral support)***
  - PS treatment is a burden on patients and carers, difficult to manage
  - Impact of PS treatment hasn't translated into equitable access to teduglutide for all
  - Burden of complications is high in some adults
- ***Inequity of current treatment (parenteral support)***
  - High demand for PS bags, especially compounded bags
  - Prescriptions for HPN becoming increasingly complicated, resulting in multiple changes per night/multiple types of bag; higher costs than compounded bags
  - Significant equality issues in this patient group (based on age), within the UK as teduglutide is available to adults in Scotland

Abbreviations: HPN; home parenteral nutrition; PS; parenteral support

New evidence from company and ERG critique

1.Concomitant medications assumptions (ACD 3.21)

Background:

- People with SBS take numerous concomitant medications when on PS (costs saved if less PS)
- Clinical experts highlighted overestimation of concomitant medication
- *Committee requested updated analyses using more plausible costs*

Company response:

- Amended base case to reflect committee's assumptions

ERG response:

- Agreeable to company's amendments to comedication assumptions; however ERG have priced IV PPIs and ondansetron as being prescribed within secondary care setting

2. Placebo response (ACD 3.8/3.11/3.13)

Background:

- Placebo effect observed in STEPS trial; 23.1% of placebo arm reduce PS day by ≥1 day
- *Committee showed concern with disregarding placebo effect seen in STEPS*
- *Requested analysis using STEPS placebo arm data rather than assuming steady state*

Company response:

- Base case unchanged, but scenario where standard care arm has 6 months of placebo effect (not considered sustainable long term) – minor upward effect of ICER

ERG response:

- Provides additional scenario analyses using STEPS data only (rather than pooled data) for teduglutide arm, placebo effect for first 6 months in standard care arm, and a mix of both
- Third scenario represents worse case scenario for teduglutide and likely underestimates

Abbreviations: HPN; home parenteral nutrition; ICER, incremental cost-effectiveness ratio; PS; parenteral support

3. Starting age in model (ACD 3.13)

Background:
- Starting age in adult base case 50 years (average age of STEPS population)
- *Requested set of scenarios with different plausible starting ages*

Company response:
- Mean ages from real-world teduglutide studies; ranged from 46 to 54
- Base case unchanged; scenarios with starting age 40/45, lowers ICER

ERG response:
- Agrees with company's starting age and considers it appropriate to use in base case
- HES data reports higher starting age (60.2 years), so scenario provided for start age of 60

4. Number of carers (ACD 3.19)

Background:
- Committee questioned whether it was appropriate for all adults to have a caregiver

Company response:
- Adult caregiver based on UK multinational survey of 181 adults with SBS-IF
- Weighted average of 0.96 carers/adult: 21% zero carers, 62% one carer, 17% two carers
- Provided scenario considering 0.8 carers/adult; increases ICER, small impact

ERG response:
- Agrees with assumption of 1 caregiver per adult; also echoed by patient and carer groups
- Provide scenario where carer disutility and home nurse costs are removed from model

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Abbreviations: ICER, incremental cost-effectiveness ratio

Updated base case and equality issues

Company updated base case: inputs

Issue	Base case:	Scenario:
Concomitant medicine costs	Committee's preferred assumptions	• No co-medication costs • Variable PS cost
Starting age	50 (no change)	Ages 40 and 45
Placebo response	Not included (no change)	First 6-month transitions based on STEPS placebo data

Equality issues

- ACM1: Recommended for children and young people aged 1 to 17; not recommended for adults

Company ACD response

- Not equitable; no difference in clinical need for teduglutide between 17 and 18
- Compounds issues with PS capacity; need for PS outstrips available supply
- Teduglutide could ease PS supply burden – addresses inequality and unfairness in the existing distribution of PS
- **ERG**: differing recommendations in adults and children would lead to potential implication where two adult patients with equal clinical need have different access to treatments, driven by whether they developed condition as a child or as an adult
- Patient organisations and web comments also highlighted issues of inequitable access

Abbreviations: PS; parenteral support

Cost-effectiveness results

All ICERs are reported in PART 2 slides because they include confidential comparator PAS discounts