# Review of TA188; Human growth hormone (somatropin) for the treatment of growth failure in children

TA188 was published in May 2010 and reviewed in July 2013.

## Decision

The decisions for this review proposal project are listed in Table 1. Briefly, the recommendations in TA188 for the technologies and indications which were appraised at that time remain relevant and do not need to be updated. The new indication for Noonan syndrome will be considered for a new single technology appraisal. The new long-acting growth hormone (somatrogon) is currently being considered for a new single technology appraisal.

Table 1 Populations, interventions, comparators and outcomes

| Population | Current status | Review outcome |
|---|---|---|
| Children with growth failure associated with any of the following conditions:<br>• growth hormone deficiency<br>• Turner syndrome<br>• Prader–Willi syndrome<br>• chronic renal insufficiency<br>• born small for gestational age with subsequent growth failure at 4 years of age or later<br>• short stature homeobox-containing gene (SHOX) deficiency. | Recommended | The guidance remains relevant, an update is not needed |

| | | |
|---|---|---|
| **Item 1 – Noonan syndrome**<br><br>Children with growth failure associated with:<br><br>• Noonan syndrome | No recommendation<br><br>(somatropin was not licensed for this indication at the time of TA188) | A new STA will be considered |
| **Item 2 – Somatrogon (long-acting growth hormone)**<br><br>Children and adolescents from 3 years of age with growth disturbance due to insufficient secretion of growth hormone' | No recommendation<br><br>(long-acting growth hormone was not licensed at the time of TA188) | A new STA will be considered<br><br>Refer to the draft scope for more information on the approach being considered for this appraisal |

## Rationale

The somatropins available at the time of TA188 were recommended for all their indications. A review was considered in 2013 and no data which would change the recommendations were identified. The current review did not identify any new clinical evidence that was likely to change the existing recommendations in TA188.

There are two items under consideration separately in this review proposal project: an extension to the marketing authorisation for one of the technologies assessed in TA188 to cover a new indication and a new long-acting growth hormone (somatrogon). An update to TA188 would involve a review of the existing recommendations alongside considering the new indication and new long-acting formulation of somatropin. Because a review of the existing recommendations is not warranted it is more appropriate to consider both the new licensed indication for somatropin and the new long-acting growth hormone as new single technology appraisals rather than within a review of TA188.

**Extension of the marketing authorisation for somatropin (Norditropin SimpleXx, Novo Nordisk): Noonan syndrome**

Noonan syndrome is a genetic condition characterised by short stature, facial dysmorphism, and a wide spectrum of congenital heart defects, and has an estimated incidence of 1 in 1,000 to 2,500 live births.[1] Currently, there is no recommendation for Noonan syndrome in TA188 – it is not included in the list of conditions associated with growth failure in TA188 for which somatropin (growth hormone) can be used. This is because 'Growth failure due to Noonan syndrome' in children is an extension to the marketing authorisation since the publication of TA188 for 1 of the 8 existing recommended somatropin analogues (Norditropin SimpleXx 5 mg/1.5 ml made by Novo Nordisk). The extension was gained in February 2020.[2] Somatropin dose differs by indication.[3] The dose of somatropin indicated in children with Noonan syndrome is 0.066 mg/kg/day however in some cases 0.033 mg/kg/day may be sufficient. The dosing for somatropin is higher end of the dose levels recommended for treating growth failure across its paediatric indications, being most similar to that used in Turner syndrome.[3,4] There are no other licensed treatments for treating restricted growth associated with Noonan syndrome apart from somatropin.

Clinical data for the use of Norditropin SimpleXx in Noonan syndrome includes:

- 2-year and 4-year study data involving children in Japan with Noonan syndrome n=51. The children were treated with either 0.033 or 0.067 mg/kg/day Norditropin SimpleXx:[4]
    - The primary endpoint was height standard deviation score (HSDS), which can be used to determine how far from the mean 'normal' or untreated height the study population's height is. Norditropin SimpleXx showed an improvement from baseline in mean HSDS at 2 years (primary endpoint) was observed with 0.033 mg/kg/day (0.84 SDS improvement) and 0.066 mg/kg/day (1.47 SDS improvement), with the higher dose levels showing greater additional improvement after 4 years.
- 4-year registry data (ANSWER program):

- mean HSDS improved from baseline by 1.33 SDS at year 4 in children with Noonan syndrome treated with Norditropin.[5]

Somatropin is recommended for Turner syndrome in TA188. Analyses of the ANSWER data showed that Noonan syndrome and Turner syndrome responded well and similarly over 4 years of growth hormone treatment, with improvement in HSDS of 1.48 cm (± 0.10) for Noonan syndrome and 1.79 cm (± 0.04) for Turner syndrome.[6] If a new STA of somatropin for treating Noonan Syndrome were to be carried out, it is anticipated that the committee's preferred modelling approach in TA188 would also be applicable to Noonan syndrome.

Somatropin for treating Noonan syndrome is currently funded via Clinical Commissioning Groups (CCGs) or NHS England specialised services. NICE received a letter from the British Society for Paediatric Endocrinology and Diabetes in March 2021 noting that the society has 'been receiving an increasing number of queries about this and some CCGs are refusing to fund somatropin for Noonan syndrome despite the licence on the grounds that it is not recommended in the NICE guidance'. The NHS England drugs list states: 'NHS England is the responsible commissioner when somatropin analogues (growth hormone) are prescribed in specialist centres for indications falling outside NICE guidance'.[7] NHS England have confirmed that the policy supported access to somatropin as an off-label option, but now somatropin is licenced for Noonan syndrome it considers a NICE review of all licensed indications and technologies for growth failure to be warranted. NHS England have further confirmed that there is no planned clinical commissioning policy in its work programme for Noonan syndrome.

## Summary of new evidence and implications for review

### *Has there been any change to the price of the technology(ies) since the guidance was published?*

**Noonan syndrome:** In TA188, Norditropin SimpleXx was considered at a price of £21.39 per mg. The BNF price for October 2021 is equivalent to £21.27 per mg (full details of prices in Appendix C).

### *Are there any existing or proposed changes to the marketing authorisation that would affect the existing guidance?*

**Noonan syndrome:** 'Growth failure due to Noonan syndrome' in the paediatric population is a new marketing authorisation for 1 of the 8 existing somatropin drugs (Norditropin SimpleXx 5 mg/1.5 ml by Novo Nordisk). This is a new indication not covered by TA188 and does not affect existing recommendations in TA188.

### *Were any uncertainties identified in the original guidance? Is there any new evidence that might address this?*

TA188 noted some uncertainties in relation to the population with Prada-Willi syndrome (section 4.2.17, 4.3.8, 4.3.13); this population is different in the key outcomes measured compared with all the other conditions leading to growth failure considered by the guidance. The uncertainty in TA188 does not appear directly relevant to this review proposal project, and there is no new evidence that addresses the uncertainty in TA188 in the updated search. However, the modelling assumptions in TA188 and the uncertainty around health-related quality of life, utilities and ICERs, are applicable to Noonan syndrome.

### *Are there any related pieces of NICE guidance relevant to this appraisal? If so, what implications might this have for the existing guidance?*

The new marketing authorisation for Noonan syndrome is for a paediatric population only. As the treatment is given until epiphyseal closure in the development of children and young people, it is not expected to be relevant to adults as they will have passed this stage of development.

### *Additional comments*

The search strategy from the Review Proposal Project completed in May 2013 was adapted for the Cochrane Library, Medline, Medline In-Process and Embase. References from March 2013 to October 2021 were reviewed. Additional searches of clinical trials registries and other sources were also carried out. The results of the literature search are discussed in the 'Summary of evidence and implications for review' section above. See Appendix C for further details of ongoing and unpublished studies.

## Equality issues

TA188 considered uncertainty in the ICER for somatropin in the population with Prada-Willi syndrome (range £32,500 to £54,800, markedly higher than for the other populations with growth hormones deficiency, which were <£20,000 to £30,000). Noting that 'the Committee did not consider that a change in the recommendation made in NICE TA42 [preceded TA188] for the use of somatropin in this disabled and socially marginalised group of children was justified, particularly in light of duties under disability discrimination legislation to have due regard to the need to promote equality of opportunity for disabled people, and to take account of their disabilities.'

In relation to Noonan syndrome, NICE received a letter from the British Society for Paediatric Endocrinology and Diabetes in March 2021 noting that some CCGs are refusing to fund somatropin for Noonan syndrome despite the licence on the grounds that it is not included in the NICE guidance. People with Noonan syndrome have physical and health problems.

## Paper sign-off

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# Appendix A – Information from existing guidance

## Original remit

To advise on the clinical and cost effectiveness of the use of human growth hormone in treatment of growth deficiencies and other growth failure in children.

## Current guidance

1.1 Somatropin (recombinant human growth hormone) is recommended as a treatment option for children with growth failure associated with any of the following conditions:

- growth hormone deficiency
- Turner syndrome
- Prader–Willi syndrome
- chronic renal insufficiency
- born small for gestational age with subsequent growth failure at 4 years of age or later
- short stature homeobox-containing gene (SHOX) deficiency.

1.2 Treatment with somatropin should always be initiated and monitored by a paediatrician with specialist expertise in managing growth hormone disorders in children. The choice of product should be made on an individual basis after informed discussion between the responsible clinician and the patient and/or their carer about the advantages and disadvantages of the products available, taking into consideration therapeutic need and the likelihood of adherence to treatment. If, after that discussion, more than one product is suitable, the least costly product should be chosen.

1.3 Treatment with somatropin should be discontinued if any of the following apply:

- growth velocity increases less than 50% from baseline in the first year of treatment

- final height is approached and growth velocity is less than 2 cm total growth in 1 year
- there are insurmountable problems with adherence
- final height is attained.

In Prader–Willi syndrome evaluation of response to therapy should also consider body composition.

Treatment should not be discontinued by default. The decision to stop treatment should be made in consultation with the patient and/or carers either by:

- a paediatrician with specialist expertise in managing growth hormone disorders in children, or
- an adult endocrinologist, if care of the patient has been transferred from paediatric to adult services

## Research recommendations from original guidance

N.B. the current review found no trial publications from NCT00190658 and noted that NCT00625872 was terminated due to insufficient recruitment.

6.1 The following trials are currently ongoing:

- Study NCT00190658 aims to compare the mean first year growth velocity of prepubertal children with SHOX deficiency treated with somatropin with the growth velocity of a control group of untreated prepubertal children with SHOX deficiency. Estimated end date: December 2010.
- Study NCT00625872 focuses on the effect of a 1-year somatropin treatment (35 microgram/kg per day or 67 microgram/kg per day) in short children born small for gestational age on neuromuscular function and cognitive performance. End date not reported.
- There is a controlled cohort study examining health-related quality of life in family members of children prescribed growth hormone treatment for

idiopathic growth hormone deficiency, acquired growth hormone deficiency and Turner syndrome. In September 2009, one of the investigators informed NICE that results were not expected until the end of 2010.

6.2 A standardised quality-of-life assessment measuring quality of life in children and in adults is needed for use in future RCTs and studies designed to measure quality of life.

6.3 Good quality research is needed on the long-term effects of somatropin treatment during childhood on body composition, psychological health, diabetes, cardiovascular disease and bone health, and life expectancy, particularly for people with Prader–Willi syndrome.

6.4 Good quality research is needed on somatropin treatment in short children born small for gestational age using dosages of somatropin matching the licensing criteria.

# Appendix B – Explanation of options

When considering whether to review one of its Technology Appraisals NICE must select one of the options in the table below:

| Options | Consequence | Selected – 'Yes/No' |
|---|---|---|
| A review of the guidance should be planned into the appraisal work programme. The review will be conducted through the specify STA or MTA process. | A review of the appraisal will be planned into the NICE's work programme. | No |
| The decision to review the guidance should be deferred to specify date or trial. | NICE will reconsider whether a review is necessary at the specified date. | No |
| The guidance should be cross referred into an on-going clinical guideline. | The on-going guideline will include the recommendations of the technology appraisal. The technology appraisal will remain extant alongside the guideline. Normally it will also be recommended that the technology appraisal guidance is moved to the static list until such time as the clinical guideline is considered for review.<br><br>This option has the effect of preserving the funding direction associated with a positive recommendation in a NICE technology appraisal. | No |

| Options | Consequence | Selected – 'Yes/No' |
|---|---|---|
| The guidance should be updated in an on-going clinical guideline[1]. | Responsibility for the updating the technology appraisal passes to the NICE Clinical Guidelines programme. Once the guideline is published the technology appraisal will be withdrawn.<br><br>Note that this option does not preserve the funding direction associated with a positive recommendation in a NICE Technology Appraisal. However, if the recommendations are unchanged from the technology appraisal, the technology appraisal can be left in place (effectively the same as incorporation). | No |
| The guidance should not be updated | The guidance will remain in place, in its current form, unless NICE becomes aware of substantive information which would make it reconsider. | Yes |
| The guidance should be withdrawn | The guidance is no longer relevant and an update of the existing recommendations would not add value to the NHS.<br><br>The guidance will be stood down and any funding direction associated with a positive recommendation will not be preserved. | No |

# Appendix C

[1] Information on the criteria for NICE allowing a technology appraisal in an ongoing clinical guideline can be found in section 6.20 of the guide to the processes of technology appraisal.

## Relevant Institute work

### *Published*

Faltering growth: recognition and management of faltering growth in children (2017) NICE guideline 75

Human growth hormone (somatropin) in adults with growth hormone deficiency (2003) NICE technology appraisal guidance 64
Status: moved to the static list in November 2014.

## Details of changes to the marketing authorisation for the technologies

| Drug | Marketing authorisation considered in TA188 | Marketing authorisation under consideration for this paper |
|---|---|---|
| Genotropin (Pfizer) | • Growth hormone deficiency<br>• Turner syndrome<br>• chronic renal insufficiency (CRI)<br>• Prader–Willi syndrome<br>• Short children born small for gestational age | No change |
| Humatrope (Eli Lilly) | • Growth hormone deficiency<br>• Turner syndrome<br>• CRI<br>• Short children born small for gestational age<br>• SHOX deficiency | No change |
| Norditropin SimpleXx (Novo Nordisk) | • Growth hormone deficiency<br>• Turner syndrome<br>• CRI<br>• Short children born small for gestational age. | • Growth hormone deficiency<br>• Turner syndrome<br>• CRI<br>• Short children born small for gestational age |

| | | |
|---|---|---|
| | | • Growth failure due to Noonan syndrome |
| NutropinAq (Ipsen) | • Growth hormone deficiency<br>• Turner syndrome<br>• CRI | No change |
| Omnitrope (Sandoz) | • Growth hormone deficiency<br>• Turner syndrome<br>• CRI<br>• Prader–Willi syndrome<br>• Short children born small for gestational age | No change |
| Saizen (Merck) | • Growth hormone deficiency<br>• Turner syndrome<br>• CRI<br>• Short children born small for gestational age | No change |
| Zomacton (Ferring) | • Growth hormone deficiency<br>• Turner syndrome | No change |

## Details of changes to the price for the technologies

The cost of treatment with somatropin depends on the dose, which is determined by the weight or body surface area of the child as well as by the indication for growth hormone treatment. Costs may vary in different settings because of negotiated procurement discounts.

| Drug | Price considered in TA188 (from BNF 58) | NHS indicative price (from BNF 6 October 2021) |
|---|---|---|
| Genotropin (Pfizer) | £23.18 per mg | 5.3mg cartridge = £92.15<br>12mg cartridge = £208.65 |
| Humatrope (Eli Lilly) | £18.00 per mg | 6mg cartridge = £108.00<br>12mg cartridge = £216.00<br>24mg cartridge = £432.00 |

| | | |
|---|---|---|
| Norditropin SimpleXx (Novo Nordisk) | £21.39 per mg | 5mg/1.5 ml pre-filled pen = £106.35<br>10mg/1.5 ml pre-filled pen = £212.70<br>15mg/1.5 ml pre-filled pen = £319.05 |
| NutropinAq (Ipsen) | £20.70 per mg | 5mg/ml cartridge<br>1 = £203.00<br>3 = £609.00. |
| Omnitrope (Sandoz) | £18.26 per mg | 5mg/1.5ml cartridge, 5 = £368.74<br>10mg/1.5ml cartridge, 5 = £737.49<br>15ml/1.5ml cartridge, 5 = £1106.22. |
| Saizen (Merck) | £23.18 per mg | 5.825mg/ml cartridge = £139.08<br>8mg/ml x 12mg cartridge = £278.16<br>8mg/ml x 20mg cartridge =£463.60 |
| Zomacton (Ferring) | £19.92 per mg | 4mg powder = £68.28.<br>10mg powder = £170.70 |

## Registered and unpublished trials

### Updates to the May 2013 proposal paper

| Trial name and registration number | Details |
|---|---|
| Long-Term Growth and Skeletal Effects of Early Growth Hormone Treatment in Turner Syndrome<br>Phase 4<br>NCT00266656 | Status: recruiting<br>Purpose: to determine whether girls who received 2 years of GH treatment before 6 years of age achieve taller adult height than girls who were untreated during this time.<br>Methods: Open Label Parallel Assignment<br>Enrolment: 69<br>Completion: September 2015<br>Results available from the registry |
| Long-term Safety Follow-up After Growth Hormone Treatment (rhGH) of Short Children Born Small for Gestational Age (SGA), Sandoz<br>NCT01491854 | Status: terminated<br>Purpose: part of the Marketing Authorisation Holder's post-marketing pharmacovigilance plan to investigate the long-term safety, in particular the diabetogenic potential and immunogenicity.<br>Enrolment: 130<br>Completion: October 2018<br>Results available from the registry |
| A Phase IV, Open Label, Multicenter, Case-controlled Study of Growth in Patients Using the Nutropin AQ Nuspin<br>NCT01243892<br>Phase 4 | Status: terminated due to slow enrolment<br>Enrolment: 18<br>Completion: August 2011<br>Results available from the registry |

| Trial name and registration number | Details |
|---|---|
| Long-term Phase IV Multicentre Study on the Safety and Efficacy of Omnitrope (rhGH) in Short Children Born Small for Gestational Age (SGA)<br>NCT00537914<br>Phase 4 | Status: ongoing, not recruiting<br>Enrolment: 278<br>Completion: January 2022 |
| A Multi-center, Randomized, Positive-control, Phase 2&3 Combined Study of Y-shape Pegylated Somatropin in Prepubertal Children With Growth Hormone Deficiency<br>NCT04513171<br>Phase 2/3 | Status: recruiting<br>Enrolment: 400<br>Completion: December 2022 |
| A phase 3 multicenter, open label, multi cohort study to evaluate the efficacy and safety of somatropin in Japanese participants with Prader-Willi syndrome<br>NCT04697381<br>Phase 3 | Status: recruiting<br>Enrolment: 30<br>Completion: June 2024 |

**Norditropin for treating Noonan Syndrome**

| Trial name and registration number | Details |
|---|---|
| A 52-week, Multi-centre, Randomised, Double-blind, Parallel-group, no Treatment Controlled (Open-label) Trial Investigating the Efficacy and Safety of Two Doses of NN-220 in Short Stature With Noonan Syndrome<br>NCT01927861<br>Phase 3 | Status: completed<br>Enrolment: 51<br>Completion: July 2018<br>Results available from the registry |
| Norditropin Treatment in Subjects With Noonan Syndrome. Effects on Linear Growth and Final Height<br>NCT01529840<br>Phase 3 | Status: completed<br>Enrolment: 24<br>Methods: Open Label Parallel Assignment<br>Completion: September 2005 |
| Post Marketing Surveillance on Long-term Use With Norditropin (Short Stature Due to Noonan Syndrome)<br>NCT03435627 | Status: active, not recruiting<br>Enrolment: 60<br>Methods: prospective cohort<br>Completion: November 2021 |

**Somatrogon (Pfizer)**

| Trial name and registration number | Details |
|---|---|
| A Phase 3, Open-Label, Randomized, Multicenter, 12-month, Efficacy and Safety Study of Weekly MOD-4023 Compared to Daily Genotropin Therapy in Japanese Pre-pubertal Children With Growth Hormone Deficiency<br><br>NCT03874013<br><br>Phase 3 | Status: completed<br><br>Enrolment: 44<br><br>Completion: March 2020<br><br>Results available from the registry |
| A Phase 3, Open-label, Randomized, Multicenter, 12 Months, Efficacy and Safety Study of Weekly MOD-4023 Compared to Daily Genotropin - Therapy in Pre-pubertal Children With Growth Hormone Deficiency<br><br>NCT02968004<br><br>Phase 3 | Status: active, not recruiting<br><br>Enrolment: 224<br><br>Completion: December 202<br><br>Results available from the registry |
| Safety and Dose Finding Study of Different MOD-4023 Dose Levels Compared to Daily R-human Growth Hormone (hGH) Therapy in Pre-pubertal Growth Hormone Deficient Childrenv<br><br>NCT02500316<br><br>Phase 2 | Status: active, not recruiting<br><br>Enrolment: 48<br><br>Completion: December 2021 |

| Trial name and registration number | Details |
|---|---|
| Safety and Dose Finding Study of Different MOD-4023 Dose Levels Compared to Daily r-hGH Therapy in Pre-pubertal Growth Hormone Deficient Children<br>NCT01592500<br>Phase 2 | Status: completed<br>Enrolment: 56<br>Completion: January 2020<br>Results available from the registry |
| A phase 3, randomized, multicenter, open-label, crossover study assessing subject perception of treatment burden with use of weekly growth hormone (somatrogon) versus daily growth hormone (genotropin) injections in children with growth hormone deficiency<br>NCT03831880 | Status: completed<br>Enrolment: 87<br>Completion: August 2020<br>Results available from the registry |

## Additional information

British Society for Paediatric Endocrinology and Diabetes (2015) Shared Care Guidelines: Paediatric use of Recombinant human Growth Hormone (r-hGH, Somatropin)

British Society for Paediatric Endocrinology and Diabetes (2017) Clinical Standards for GH Treatment in Childhood & Adolescence

British Society for Paediatric Endocrinology and Diabetes (2019) Clinical Guideline. Monitoring growth in children with chronic kidney disease

European Commission (2020) The Impact of Biosimilar Competition in Europe

European Society for Paediatric Nephrology (2019) Clinical practice recommendations for growth hormone treatment in children with chronic kidney disease

International Turner Syndrome Consensus Group (2017) Clinical practice guidelines for the care of girls and women with Turner syndrome: proceedings from the 2016 Cincinnati International Turner Syndrome Meeting

NHS England (2013) 2013/14 NHS standard contract paediatric medicine: endocrinology & diabetes

NHS England (2018) Manual for prescribed specialised services 2018/19 Chapter 109. Specialist endocrinology and diabetes services for children

## References

1. Online Mendelian Inheritance in Man (OMIM) (2020) Noonan syndrome Accessed November 2021

2. Medicines.ie (2021) Norditropin SimpleXx 5 mg/1.5 ml, solution for injection in cartridge Accessed December 2021

3. MHRA (2021) Norditropin SimpleXx 5 mg/1.5 ml, solution for injection in cartridge Accessed December 2021

4. EMC (2021) Norditropin SimpleXx 5 mg/1.5 ml, summary of product characteristics. Accessed November 2021

5. Lee PA, et al (2012) Effect of 4 years of growth hormone therapy in children with Noonan syndrome in the American Norditropin Studies: Web-Enabled Research (ANSWER) Program registry. *International Journal of Pediatric Endocrinology* 15.

6. Lee, PA et al (2015) Noonan syndrome and Turner syndrome patients respond similarly to 4 years' growth-hormone therapy: longitudinal analysis of growth-hormone-naïve patients enrolled in the NordiNet® International Outcome Study and the ANSWER Program. *International Journal of Pediatric Endocrinology* 17.

7. NHS England (2021) NHS England drugs list v16.1, 2021-2022. Accessed November 2021.
8. Specialist Pharmacy Service (2021) Somatrogon. Accessed November 2021.
9. Drugs (2021) Somatrogon, Pfizer and OPKO Announce Extension of U.S. FDA Review of Biologics License Application of Somatrogon for Pediatric Growth Hormone Deficiency. Accessed November 2021.
10. Zelinska N, et al (2017) Long-acting C-terminal peptide–modified hGH (MOD-4023): results of a safety and dose-finding study in GHD children. *The Journal of Clinical Endocrinology & Metabolism* 102(5), 1578–1587.
11. Deal C et al (2021) Somatrogon growth hormone in the treatment of pediatric growth hormone deficiency: result of the pivotal pediatric phase 3 clinical trial. *Revista Argentina de Endocrinologia y Metabolismo* 58 (suppl1), 247.
12. Choe J, et al (2020) Long-term safety and efficacy of a once-weekly somatrogon (hGH-CTP): A 5-year phase 2 extension study in children with growth hormone deficiency. *Hormone Research in Paediatrics* 93 (suppl1), 68.
13. Loftus J et al (2020) PDB4 Evaluation of Quality of Life in PRE-Pubertal Children Using the Quality of Life in Short Stature Youth (QOLISSY) Questionnaire, Following 12 Months of Growth Hormone Treatment with Either a Weekly Somatrogon or a Daily Genotropin Injection Schedule. *Value in Health* 23 (supplement2), 506.
14. Ma L, et al (2021) Effect of weekly long-acting growth hormone replacement therapy compared to daily growth hormone on children with short stature: a meta-analysis. Frontiers in Endocrinology, 29 November 2021.
15. Specialist Pharmacy Service (2021) Sompacitan. Accessed November 2021.
16. Miller BS, et al (2020) Long-acting growth hormone preparations – current status and future consideration. *J Clin Endocrinol Metab* 2020, 105(6), e2121-e2133.