Pattern of use of Human Growth Hormone (Somatropin) in the United Kingdom general practice setting: A Drug Utilization Study in The Health Improvement Network (THIN) database

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Version	1.0

Protocol Synopsis

Title	**Pattern of use of Human Growth Hormone (Somatropin) in the United Kingdom general practice setting: A Drug Utilization Study in The Health Improvement Network (THIN) database**
Study Objectives	The study aims to describe the pattern of use of the Recombinant Human Growth Hormone (somatropin) over two decades in patients selected within the UK primary care setting. Namely, the study will address the following research questions: • For which indication is somatropin prescribed in routine clinical practice • What are the demographic and clinical characteristics of the treated population (i.e. age and sex, co-morbidities/co-medications) • How the clinical profile of somatropin users compare to that of the general population • What is the average duration of therapy • What is the pattern of prescribed dosage
Study population and study period	The study population will include patients newly prescribed any of the study drugs between 1 January 1990 and 30 May 2010.
Study Design	This is a retrospective analysis of recipients of somatropin selected using The Health Improvement Network (THIN) database. The Network collects pseudo-anonymised electronic medical records of patients managed in the UK primary care setting. Comprehensive patient-level data include diagnostic codes, prescriptions and other health-relevant patient information. Within the THIN population, patients prescribed somatropin during the study period will be selected by relevant prescription coding. Inclusion criteria will be applied to define the study population. The index date will be assigned as the date of the first prescription for any study drug. The demographic and clinical profile of study patients will be assessed at start of therapy and at relevant event points thereafter. Clinical characteristics of treated patients will be compared to those of a random sample of untreated patients matched individually on age and sex to treated patients. Dosage patterns will be assessed throughout the treatment duration.
Sample Size	The study will include all patients who are recipients of somatropin selected in THIN throughout the study period. It is estimated that the study population will include approximately 1200 patients.
Summary of Patient Eligibility Criteria	**Inclusion** • A prescription for any of the study drugs • Patient registered as permanent with a minimum of 6 months' registration with the practice at the time of the first prescription of study drugs
Study Measures and Analysis Covariates	Patients' demographic and clinical data available from the THIN database will be used for analyses to describe the study population and to quantify the study outcomes. Study measures will include the following: • Frequency distribution of study population by sex, age groups and indications, including: GH deficiency, Turner syndrome, chronic renal insufficiency, Prader-Willi syndrome, small at birth for gestational age, other indication (i.e. off label use) • Frequency distribution of dosage at start of therapy and of average length

	of treatment • Prevalence of major co-morbidities, such as endocrine, cardiovascular, and respiratory diseases, and neoplasms
Statistical Considerations	Categorical data will be summarized by the number and percentage of patients in each category. Continuous data will be summarized by the number of patients, mean, standard deviation, median, lower and upper quartiles, minimum and maximum values. Where appropriate, two-sided 95% confidence intervals will be presented. Clinical patient characteristics will be presented for the study population overall and by age group, sex, and therapeutic indication. Additionally, the frequency distribution of co-morbidities in somatropin recipients will be compared with that in a control group of patients randomly selected and matched by age, sex and general practice. Prevalence of medical conditions will be estimated at index date as proportion of the study population with a record of pre-defined medical conditions. Other analytic methods, such as survival methods may be used to estimate time to a predefined event across the study population or its subgroups. Any statistical testing will be reported using a 2-sided significance level of 0.05 for each analysis.
Sponsor	The study is entirely funded by the European Medicine Agency (EMA)
Study Team	The study will be conducted by a dedicated team at EMA who will have responsibility for study design, implementation, analyses, and reporting.

Study Glossary

Abbreviation/Acronym	Definition
CHMP	Committee for Medicinal Products for Human Use
CI	Confidence Interval
CRI	Chronic Renal Insufficiency
CSD	Cegedim Strategic Data
EMA	European Medicines Agency
ENCePP	European Network of Centres for Pharmacoepidemiology and Pharmacovigilance
EU	European Union
GP	General Practitioner
ID	Index date (Date of first THIN record of somatropin prescription)
MREC	Multi-Centre Research Ethic Committee
NICE	National Institute for health and Clinical Excellence
SD	Standard Deviation
SHOX	Short Stature Homeobox-containing gene
THIN	The Health Improvement Network
UK	United Kingdom

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1. BACKGROUND AND STUDY RATIONALE

1.1 Growth Hormone Deficiency

Human growth hormone is produced by the anterior pituitary gland. It is essential for normal growth in children, and to support important metabolic pathways throughout childhood and adult life. In children, growth failure can be due to growth hormone deficiency or to medical conditions, including Turner syndrome, chronic renal insufficiency (CRI), short stature homeobox-containing gene (SHOX) deficiency. Growth failure may also occur in children born small for gestational age.

The prevalence of growth hormone deficiency is estimated to be between 1 in 3500 and 1 in 4000 children. Turner syndrome and Prader–Willi syndrome are both chromosomal disorders characterized by the complete or partial lack of one X chromosome in girls, and abnormality of chromosome 15, respectively. Turner syndrome occurs in between 1 in 1500 and 1 in 2500 live female births, while Prader–Willi syndrome is approximately 10 folds less common (i.e. between 1 in 15,000 and 1 in 25,000 live births).

The most common endocrine cause of short stature is the insufficient production by the pituitary gland and it may occur as an isolated hormonal deficiency or in combination with deficiencies in several pituitary hormones arising from hypopituitarism, central nervous system tumors, cranial irradiation or other physiological causes. Nonetheless, idiopathic growth hormone deficiency accounts for approximately 50% of cases of growth hormone deficiency in children.

A comprehensive review of current knowledge in Growth Hormone deficiency was published recently (Takeda et al., 2010).

1.2 Recombinant Human Growth Hormone - Somatropin

The synthetic form of GH is called somatropin (recombinant human growth hormone, GH). Somatropins include three centrally authorized products in the EU, namely NutropinAq, Omnitrop, and Valtropin. The licensed indications are as follows, with some variation in the wording of each product:

- Growth disturbance in children due to insufficient secretion of growth hormone (growth hormone deficiency).
- Growth failure in girls associated with gonadal dysgenesis (Turner syndrome).
- Growth retardation in prepubertal children associated with chronic renal insufficiency (CRI).
- Improvement of growth and body composition in children with Prader–Willi syndrome. The diagnosis of Prader–Willi syndrome should be confirmed by appropriate genetic testing.
- Growth disturbance (current height standard deviation score [SDS] < -2.5 and parental adjusted height SDS < -1) in short children born small for gestational age, with a birth weight and/or length below −2 SD, who failed to show catch-up growth (height velocity SDS less than 0 during the past year) by 4 years of age or later.
- Growth failure associated with *SHOX* deficiency, as confirmed by DNA analysis.

The summary of product characteristics for somatropin states that the dosage and the administration of somatropin should be tailored to the treated medical condition and the needs of each individual child. For instance, 23–39 microgram/kg daily or 0.7–1.0 mg/m² daily is the posology for growth hormone deficiency; 45–50 microgram/kg daily or 1.4 mg/m² daily for Turner syndrome and CRI; 35 microgram/kg daily or 1.0 mg/m² daily for growth disturbance in children born small for gestational age; 35 microgram/kg daily or 1.0 mg/m² daily (with a maximum of 2.7 mg daily) for Prader–Willi syndrome; and 45–50 microgram/kg daily for *SHOX* deficiency. Somatropin is self-administered or given to the child by an adult, at home, usually as a subcutaneous injection, 6–7 times a week.

1.3 Study Rationale

Further to information received from the French medicines agency on a long-term epidemiological study in patients treated during childhood for idiopathic lack of growth hormone and idiopathic or gestational short stature with somatropin-containing medicines, the European Medicines Agency's Committee for Medicinal Products for Human Use (CHMP) has

started a review of the safety of somatropin-containing medicines authorised centrally or by national procedures in the EU (www.ema.europa.eu).

The Safety and Appropriateness of Growth hormone treatments in Europe (SAGhE) study is a large observational study funded by the European Commission and conducted by a European consortium of paediatric endocrinologists, epidemiologists and biostatisticians, involving eight EU countries, including France (http://saghe.aphp.fr/site/spip.php). The study is still ongoing and further results are expected in the future.

At its meeting of December 2010, the CHMP confirmed that there is no immediate safety concern with respect to the use of somatropins. However, prescribers were reminded to strictly follow the indications and the approved doses. The maximum recommended dose of 50µg/kg weight/day for somatropin-containing medicines should not be exceeded (www.ema.europa.eu). The CHMP review is ongoing and in this context, it would be informative to assess how somatropin has been used over the past two decades in routine clinical practice. To this purpose, the Pharmacovigilance and Risk Management Sector at EMA proposes to conduct a drug utilization study in the United Kingdom (UK), one of the largest European countries in which comprehensive prescription and clinical records are ready available in an electronic database.

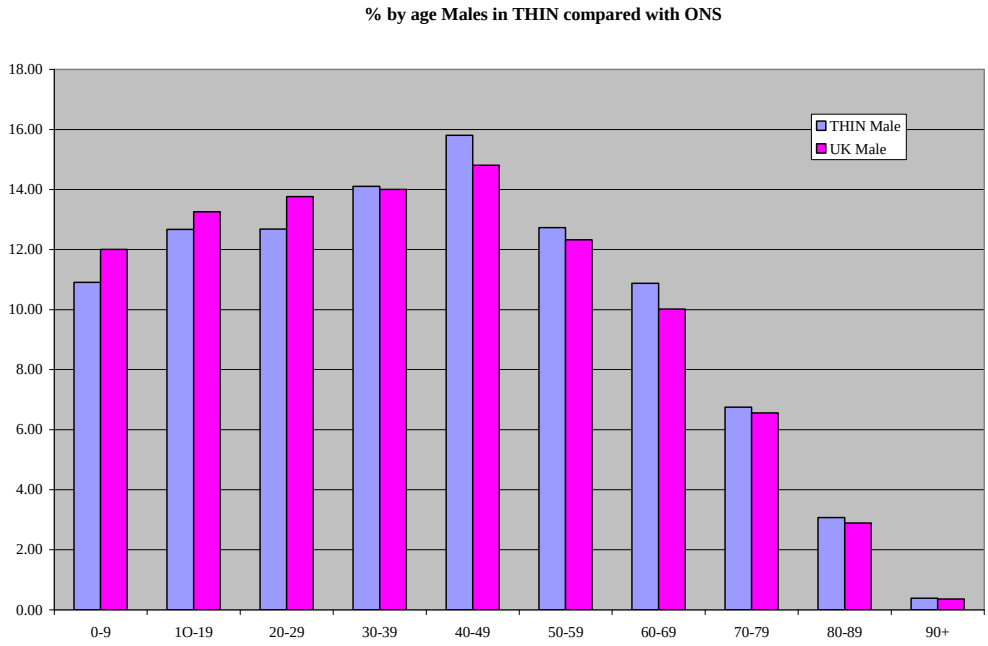
Therefore, this study will provide information on how somatropin is used in one EU Member State including on whether maximum recommended doses are being respected, and on authorised indications are being followed. Furthermore, comparison with match patients not receiving somatropin will give an indication of the comparability of morbidity between the populations therefore giving some insight into the likelihood of confounding by indication in the longitudinal studies.

1.4 THIN Database

The Health Improvement Network Ltd collects pseudo-anonymised patient data in a non-interventional way from the daily record keeping of general practices which use Vision practice management software and have agreed to contribute to the scheme. Currently THIN database contains primary care medical records collected in approximately 479 general practices nationwide in the UK from more than 9 million patients, of which over 3.3 million are actively registered. The patient population of THIN data is representative of the UK patient population, with respect to sex and age distribution and for the prevalence of major diseases (see Figures 1 and 2 below; also Bourke et al, 2004).

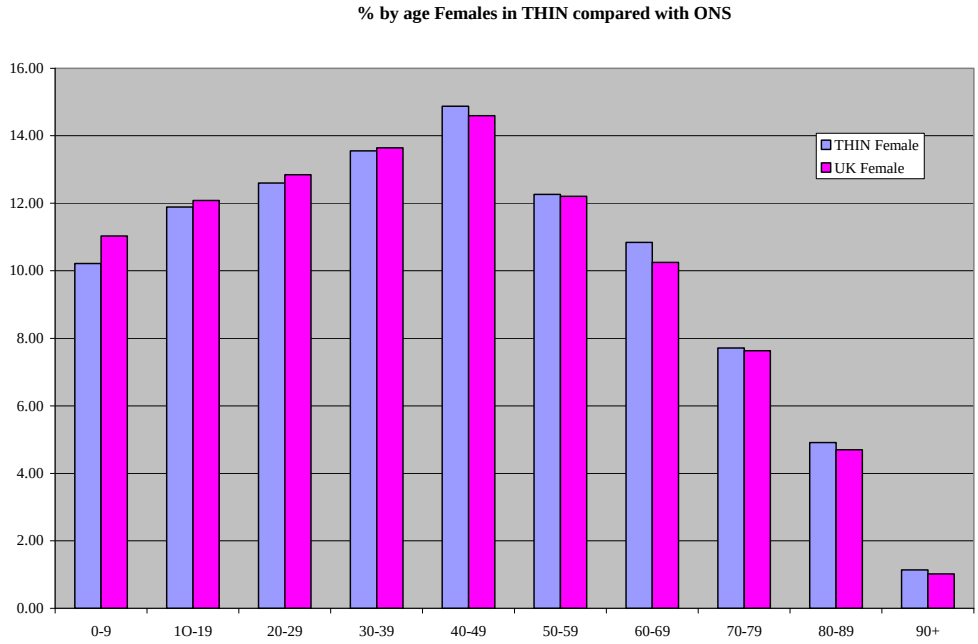
Patient level medical records in THIN include demographic and comprehensive clinical information, such as diagnoses and symptoms, diagnostic tests, referrals and hospitalisation, and other health-relevant data. Mostly relevant to this study are the comprehensive prescription records available in THIN. The gatekeeper role that the General Practitioner (GP) plays within the National Healthcare Service (NHS) in the UK insures that all prescriptions funded by the NHS are released by the GP, even if therapy is initiated in a specialist setting. THIN data have been used extensively in medical research since 2003 in the UK, Europe and the United States and represent an appropriate setting for the drug utilization study described in this protocol.

Figure 1a THIN population by age – in males



ONS: Office for National Statistics, England and Wales, UK

Figure 1b THIN population by age – in females



ONS: Office for National Statistics, England and Wales, UK

Somatropin use in the United Kingdom

The National Institute for Clinical Excellence (NICE) provides guidance for optimizing clinical practice in the NHS in England and Wales and it is anticipated that the clinical records used in this analysis should reflect to some extent NICE guidance. The first NICE guidelines on treatment with recombinant human growth hormone dated May 2002 and recommended use of somatropin for the treatment of growth failure in children with growth hormone deficiency, Turner syndrome, Prader–Willi syndrome and chronic renal insufficiency. With the guidance update of May 2010, NICE extended the recommended use of somatropin to treat children born small for gestational age with subsequent growth failure at 4 years of age or later and short stature homeobox-containing gene (SHOX) deficiency.

2. STUDY OBJECTIVES

The study aims to assess the pattern of use of somatropin in routine clinical practice since 1990 to date in a European country, namely the UK. Specifically the study has the following objectives:

- To describe prescription patterns of somatropin over time throughout the study period, including:
    - Indication
    - Dosage
    - Length of therapy
- To describe the demographic and clinical profile of somatropin recipients (i.e. age and sex, co-morbidities/co-medications)
- To compare the clinical profile of somatropin recipients with that of the general population

3. STUDY DESIGN

To meet the objectives of this drug utilization study we will conduct a retrospective analysis of patient's medical records selected in THIN. The study population will include recipients of somatropin who meet the eligibility criteria. Longitudinal records in the database will be screened to select the study population and to quantify the study measures.

3.1 Study Period

The study period represents the time during which eligible patients can enter the study. The study period will start 1 January 1990 and end 30 May 2010. Such a study period will ensure that data quality standard in THIN are met and that somatropins were available in the UK.

3.2 Selection of patients

The electronic medical records collected in THIN will be used as source population. The date of entry of the first prescription code for any study drug will be the index date. Appendix A includes the complete listing of study drugs.

3.3 Eligibility Criteria

1. Patient has a prescription for any of the study drug
2. Patient is registered as permanent at the general practice for a minimum of 6 months before index date

4. STUDY MEASURES

Operational definitions of study measures are provided below. Algorithms developed to define the study variables will be detailed in the specification of data extraction and analysis procedures.

4.1 Prescription pattern

Prescription, medical and demographic data will be used to describe the pattern of use of somatropin, namely its indication, dosage and duration of therapy.

4.1.1 Indications

Indication for somatropin therapy will be defined by screening Read codes for symptoms/diagnosis and referral to specialist care within 6 months before and after the index date. The expected indication would include the following medical conditions:

- GH deficiency
- Turner syndrome,
- Chronic Renal Insufficiency,
- Prader-Willi syndrome,
- Small at birth for gestational age,
- Other indication (i.e. off label use)

Should the time window of 12 months around the index date not include an indication code the search will be extended to the entire medical record of the patient. The time window to define indication will be finalized based on the observed time distribution of the records around index date. Should any indication code be unavailable in the patient's file, the indication will be accounted in the analysis as missing data.

4.1.2 Dosage

Therapy records in THIN contain details of prescriptions issued to patients. A new record is generated with each prescription issued including prescriptions initiated in the specialist setting (i.e. the GP issues a prescription under specialist advice). Information recorded includes formulation and strength of the medicine prescribed, the dose and quantity prescribed. Additionally, information recorded as a free text is linked to the packsize field in the therapy records, which can be used to derive length of prescription. Dosage will be

grouped in order to provide the frequency distribution of different strengths of therapy and grouping will be finalized based on the observed data. Growth hormone dosage is often dependent on body weight. Information on both weight and height is intermittently recorded in the THIN dataset but will be used when available to clarify the dosing strategy

4.1.3 Length of Therapy

Since length of therapy is not a ready available variable in THIN, therapy duration will be estimated as the difference between last and first prescription date. Prescription records will be screening to identify gaps in therapy.

4.2 Demographic and clinical profile

Demographic and medical records will be used to define the profile of somatropin recipients (i.e. age, sex, and co-morbidities)

4.2.1 Demographic

Age of the study population will be derived from the year of birth, assuming the 30 June of the birth year, since day and month of birth are not available for adult patients. For patients under 16 years of age, the month of birth will also be available in the database and will be used for the age estimate. Age at index date will be estimated from date of birth and date of the first prescription for a study drug. The patients' gender data will be extracted form the demographic files.

4.2.2 Clinical profile - Selected morbidities

In order to characterize the clinical profile of patients treated with somatropin, the study will quantify the prevalence of selected diseases, including, but not limited to:

- Cardiovascular and cerebrovascular diseases
- Metabolic diseases
- Neoplasms
- Respiratory diseases
- Mental health

- Gastrointestinal diseases
- Genitourinary diseases

Electronic medical records of each patient will be screened in the 12 months before and after the index date in order to identify the co-morbidities of interest. Using relevant coding the study will also quantify hospitalization and referral to specialist care as proxies of health status. THIN Data files containing diagnoses/symptoms, hospitalisation, and other health data will be used for the operational definition of these conditions.

History of disease will be based on relevant selected coding in the medical record within the one year before the index date (recent history). Concomitant morbidities will be defined based on relevant coding in the 12 months following index date.

4.3 Somatropin recipients versus general population

To compare the clinical profile of somatropin recipients with that of the general population, a random sample of 'control' patients will be selected within the database. Up to 10 'control' patient will be matched to each patient of the study population on sex, year of birth (± 2 years), and practice. The matching will also ensure that each control patient is active (i.e. registered at the practice) at the index date of the respective matched patient, with a minimum of 12 months records before and after the index date of the respective case.

The clinical characteristics of the control group will be assessed as described above for the somatropin recipients.

5. STATISTICAL ANALYSES

5.1 General Approach / Considerations

All analyses will be conducted using SAS Enterprise Guide version 4.1. All analyses will be presented for all patients and separately by indication subgroup, in particular for the group of children with idiopathic GH deficiency.

Categorical data will be summarised by the number and percentage of patients in each category. Continuous data will be summarised by the number of patients, mean, standard deviation, median, minimum and maximum values. Where appropriate, two-sided 95% confidence intervals will be presented. Any statistical testing will be reported using a 2-sided

significance level of 0.05 for each analysis or, when equivalence is asserted, using confidence intervals.

Any difference in clinical characteristics of somatropin versus control patients will be examined with chi square tests. Summaries will also be provided for age sub-groups of patients, as appropriate.

5.2 Sample Size Considerations

The study is descriptive in nature and is not design to test statistically any predefined hypothesis. The study population will include all eligible patients selected in THIN throughout 1 January 1990 - 30 May 2010 who meet the inclusion criteria. Preliminary estimates indicate that the study population will include in excess of 1200 patients. A number of patents up to 10 fold larger will be randomly selected as a representative sample of the general population (matched on age, sex and general practice).

5.3 Study Objectives and Measures: Planned Methods of Analysis

1. *To describe the demographic characteristic of the study population*

   Mean age at first prescription and age distribution of treated population at start of therapy will be presented. Age grouping will be finalized based on the observation of data and is anticipated to include the following strata: 0-4, 5-9, 10-14, 15-19, 20-29, >30.

   Frequency distribution will be presented as number and percentage of patients in each age group. Age distribution of the study population will be stratified by sex and by indication.

2. *To describe the frequency distribution of indications for somatropin use*

   Frequency distribution of indication will be presented as number and percentage of patients with any of the indications.

   Additional information related to indication may be derived from age-adjusted growth and so, when available for children, the relationship of height to age and sex will be examined.

3. *To describe the frequency distribution of dosage of somatropin and length of therapy in the study population*

Therapy dosage will be computed in *mg/day* and grouped as appropriate. Frequency distribution will be expressed as number and percentage of patients in each stratum.

When weight measurement are recorded within 3 months of a prescription the dosage will also be expressed as mg/(kg.day).

Dosage and length of therapy will be presented as mean value in the total population and stratified by indication.

4. To describe the medical history and comorbidities in somatropin recipients

The prevalence of selected conditions describing the medical history and the comorbidities will be estimated as the number of patients with a record of the disease divided by the total number of patients treated with somatropin and expressed as percentage.

5. To compare prevalence of selected medical conditions (medical history and co-morbidities) in somatropin users and general population

Patient clinical characteristics will be described in the somatropin and control patients as reported above. Any difference between the study population and the control will be examined with chi square tests for the categorical variables. Additional analysis sub-groups may be defined based on the observed distribution of the study variables.

5.4 Missing Data

Missing data are common in observational research based on large electronic databases such as THIN. This study will use secondary data that were collected for the management of patients in primary care rather than for research purposes. At the stage of data downloading in THIN, data quality procedures include checks for acceptable completeness and consistency of data. A common approach in such a setting is not to adopt any of the probabilistic methods to impute missing data (e.g. missing at random assumptions; multivariate imputation by chained equations method of multiple multivariate imputation). The following assumptions will be made wherever dates of events are incomplete:

- Where day is missing, default to 15/mm/yyyy
- Day and month missing default to 01/07/yyyy

Events for which year is missing will not be included in the analyses. The frequency of such missing data will be reported.

6. STUDY LIMITATIONS

The main strengths of the planned study design are: i) the selection of a study population in many respects representative of the UK general population; and ii) access to data collected in routine clinical practice, which will allow the generation of evidence about prescription of somatropin in the 'real world' setting. Additionally the database analysis minimizes the risk of information and selection bias because longitudinal data will be analyzed retrospectively. Medical records in THIN are collected prospectively and routinely for the purpose of patent's management, a process which does not require specific follow up of patients, nor introduce biased data recording.

However, the study has some limitations, including the fact that this analysis describes prescription patterns only in one European country. Inference to the medical practice in other EU Member States might not stand.

Furthermore, in database analyses such as this one, numerous assumptions are made including the fact that therapy is assumed on the basis of prescription records and that diagnoses are established by mean of medical coding. This approach may pose some challenges, particularly in the evaluation of somatropin dosage. Additionally, the granularity of clinical diagnoses that might be required for defining therapeutic indication would be missed in the electronic coding, especially since it is likely that specialist diagnoses are transferred and coded into the primary care setting.

7. PROTECTION OF HUMAN SUBJECTS

7.1 Ethical approval

Medical research conducted with THIN data and including additional data collection requires approval by a Multi-Centre Research Ethics Committees (MREC).

A copy of the protocol will be submitted to the MREC for written approval. EMA staff will be responsible for the MREC submission.

7.2 Patient Confidentiality

This is an observational study conducted while maintaining in full the anonymity of participating GPs and patients. Study procedures do not interfere in any way with routine clinical practice of study sites and/or management of study patients.

8. GOOD PRACTICE

This is a retrospective analysis of electronic medical records collected routinely for the purpose of patent's management in the UK primary care. The study is designed and conducted according to the ethical and scientific principles adopted in observational research, including the "Guidelines for Good Pharmacoepidemiology Practices (GPP)" (http://www.pharmacoepi.org/resources/guidelines_08027.cfm) and Good Epidemiology Practice (GEP): IEA Guidelines for Proper conduct in Epidemiological Research (http://www.ieatemp.com/pdfs/GEPNov07.pdf)

Reporting of study results will follow GPP recommendations. Publication material will be developed in line with the recommendations of the STROBE initiative for the publication of observational research http://www.strobe-statement.org.

The study will be conducted according to the criteria of the European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP)

(See http://www.encepp.eu/encepp_studies/index.html).

9. STUDY TEAM

The EMA has a licence with CSD EPIC to facilitate access to THIN data for the purposes of medical research. CSD EPIC is an expert in the supply, management and application of UK anonymised primary care patient data to support medical research within the healthcare industry. The study will be sponsored and conducted by staff at EMA. Specifically, Annalisa Rubino and Jim Slattery will have overall scientific responsibility, including study design, analysis and reporting. Xavier Kurz will input with clinical epidemiology expertise. Yolanda Alvarez and Gianmario Candore will support the data extraction and analysis effort.

10. QUALITY ASSURANCE AND QUALITY CONTROL PROCEDURES

THIN data files relevant to this study will be downloaded and maintained on a dedicated server at EMA with access limited to named project team members.

Experienced programmers and the study statistician will perform all data management and analysis using SAS for Windows statistical software. To ensure the integrity and quality of the study results, we will follow our programming validation lifecycle process for all analyses, including quality checking programs, logs, and output for accuracy.

11. ADMINISTRATIVE AND LEGAL OBLIGATIONS

11.1 Protocol Amendments

Protocol amendments will be made if necessary. The MREC must be informed of all substantial amendments to the protocol and give approval.

11.2 Study Documentation and Archive

Source documents for this study are the THIN data extracts and analyses files.

The EMA analysts are responsible for maintaining a comprehensive and centralised filing system of all study-related (essential) documentation, suitable for inspection at any time by representatives from applicable regulatory authorities. Elements should include:

- Study files containing the protocol with all amendments
- Correspondence to and from the MREC

Raw dataset and analysis files, as well as all documentations related to this project will be archived at EMA for a minimum period of 5 years following production of a study report.

11.3 Publication Policy

Authorship of any publications resulting from this study will be determined according to the EMA publication policy, which reflects in substance the Uniform Requirement for Manuscripts Submitted to Biomedical Journals (International Committee of Medical Journal Editors, 2004). Specifically:

- Authorship credit should be based on (1) substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; (2) drafting the article or

revising it critically for important intellectual content; (3) final approval of the version to be published. Authors should meet conditions 1, 2, and 3.

- When a large, multicentre group has conducted the work, the group should identify the individuals who accept direct responsibility for the manuscript. These individuals should fully meet the criteria for authorship defined above.

- Acquisition of funding, collection of data, or general supervision of the research group, alone, does not justify authorship.

- All persons designated as authors should qualify for authorship, and all those who qualify should be listed.

- Each author should have participated sufficiently in the work to take public responsibility for appropriate portions of the content.

The study is registered in the ENCePP studies database (http://www.encepp.eu/encepp_studies/index.html).

12. REFERENCES

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NICE: Somatropin Quick Reference Guide, 2010 (Last accessed at: http://guidance.nice.org.uk/CG36/QuickRefGuide/pdf/English)

Takeda A, Cooper K, Bird A, Baxter L, Frampton GK, Gospodarevskaya E, Welch K, Bryant J. Recombinant human growth hormone for the treatment of growth disorders in children: a systematic review and economic evaluation. Health Technol Assess. 2010 Sep;14(42):1-209.

Appendix A:

Therapeutic products selected for the definition of the study population

SOMATROPIN (rbe) pwdr/inj.soln 12mg
SOMATROPIN (rbe) pwdr/inj.soln 0.8mg
SOMATROPIN (rbe) pwdr/inj.soln 12mg
SOMATROPIN (rbe) pwdr/inj.soln 5.3mg
SOMATROPIN (rbe) pwdr/inj.soln 12mg
SOMATROPIN (rbe) pwdr/inj.soln 12mg
SOMATROPIN (rbe) pwdr/inj.soln 12mg
SOMATROPIN (rbe) pwdr/inj.soln 0.8mg
SOMATROPIN (rbe) refill cartridge 12mg
SOMATROPIN (rbe) pwdr/inj.soln 12mg
SOMATROPIN (rbe) pwdr/inj.soln 12mg
GENOTROPIN 16 I/U INJ
SOMATROPIN (rbe) pwdr/inj.soln 12mg
SOMATROPIN (rbe) refill cartridge 5.3mg
GENOTROPIN 16 I/U INJ
SOMATROPIN (rbe) pwdr/inj.soln 0.6mg
SOMATROPIN (rbe) pwdr/inj.soln 4mg
SOMATROPIN (rbe) refill cartridge 5.3mg
SOMATROPIN (rbe) pwdr/inj.soln 0.6mg
SOMATROPIN (rbe) pwdr/inj.soln 12mg
SOMATROPIN (rbe) pwdr/inj.soln 12mg
SOMATROPIN (rbe) pwdr/inj.soln 12mg