Retrospective registry study evaluating the safety of melatonin use in children and adolescents with attention deficit hyperactivity disorder (ADHD) in Sweden (Safety of melatonin in children with ADHD)

First published: 09/10/2023

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Study Finalised

Administrative details

EU PAS number

EUPAS41367

Study ID

41368

DARWIN EU® study

No

Study countries

☐ Sweden

Study description

AGB-Pharma was provided a post-authorisation commitment by the Medical Products Agency (MPA) to conduct a PASS-study (Category 3) in connection to the approval of Melatonin AGB via a National procedure for the indication: Insomnia in children and adolescents aged 6-17 years with ADHD, where sleep hygiene measures have been insufficient. The background for this commitment was the theoretical concern on the effect of melatonin on sexual maturation in children and adolescents with ADHD. The retrospective aspect of this study was proposed by the MPA, and a feasibility assessment was undertaken by AGB-Pharma, supported by LINK Medical Research. After the feasibility assessment it was found that it is possible to design a retrospective registry study on safety, concerning height development, in children with ADHD. However, it is not feasible to evaluate the safety of long-term treatment with melatonin on sexual maturation, as no data on pubertal timing exists in any central registry in Sweden. The objective of this PASS study is to study the height development in children and adolescents with ADHD, which are prescribed melatonin. The primary objective is to determine whether long-term treatment of melatonin (30≥ days) influences height development in children and adolescence with ADHD. As a secondary reference PC PAL national standard growth chart will be used, which follows growth in relation to age. The exploratory objective of this study is to describe melatonin use in the population of interest, including medicine adherence, duration of treatment and dosing. Also, the study aims to compare the growth of children and adolescents with ADHD and prescribed melatonin with national Swedish growth charts

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Study status

Finalised

Contact details

Study institution contact

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Study contact

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Primary lead investigator

Peik Gustafsson

Primary lead investigator

Study timelines

Date when funding contract was signed

Planned: 01/07/2021

Study start date

Planned: 15/11/2023

Data analysis start date

Planned: 08/01/2024

Date of final study report

Planned: 29/03/2024

Actual: 31/01/2025

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

AGB-Pharma AB

Regulatory

Was the study required by a regulatory body?

Yes

Is the study required by a Risk Management Plan (RMP)?

EU RMP category 3 (required)

Methodological aspects

Study type

Study type list

Study topic:

Human medicinal product

Study type:

Non-interventional study

Scope of the study:

Safety study (incl. comparative)

Main study objective:

The primary objective is to determine whether long-term treatment of melatonin (≥30 days) influences height development in children and adolescence with ADHD. As secondary reference PC PAL standard national Swedish growth chart will be used, which describes the growth in relation to chronological age.

Study drug and medical condition

Name of medicine

MELATONIN

Study drug International non-proprietary name (INN) or common name

MELATONIN

Anatomical Therapeutic Chemical (ATC) code

(N05CH01) melatonin

melatonin

Medical condition to be studied

Attention deficit hyperactivity disorder

Population studied

Short description of the study population

Swedish prescription register showed in 2020 that 56.435 individuals that had been prescribed ADHD medication, the study expect the number to be fewer than this.

Age groups

Children (2 to < 12 years)

Adolescents (12 to < 18 years)

Estimated number of subjects

56435

Study design details

Outcomes

Growth velocity. It is not possible to access data on sexual maturation as it is not available , the growth velocity is the only possible outcome of this study.

Data analysis plan

Data measurements will be unevenly spaced, occur at different ages for different subjects, and there may be missing. Participants with fewer than two height measurements will be further analysed for missing data by comparing the two groups with and without registered measurements. For the primary endpoint, height growth, a linear approach will be used to approximate the growth velocity. Analysis of height growth will be performed with a random coefficients model using PROC MIXED in SAS® where a separate regression line, i.e., intercept and slope, is fitted for each subject. The basic model will include age, subject group, and subject group*age as fixed effects and subject and subject*age as random effects. As a secondary reference the digital tool PC PAL will be used for comparison. Unmeasured confounders will be handled in a complementary analysis with the use of an instrumental variable. Sensitivity analyses of height growth will be performed.

Data management

Data sources

Data source(s)

Sweden National Prescribed Drugs Register / Läkemedelsregistret

Data sources (types)

Disease registry

Drug dispensing/prescription data

Use of a Common Data Model (CDM)

CDM mapping

No

Data quality specifications

Check conformance

Unknown

Check completeness

Unknown

Check stability

Unknown

Check logical consistency

Unknown

Data characterisation

Data characterisation conducted

No