# A Phase III study of efficacy, safety and tolerability of Chronocort® compared with standard glucocorticoid replacement therapy in the treatment of congenital adrenal hyperplasia.

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The purpose of this research study is to compare the safety and effectiveness of Chronocort® with current glucocorticoid treatment regimens in the treatment of CAH over a 6 month period.

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| **Ethical review** | Approved WMO |
| **Status** | Recruitment stopped |
| **Health condition type** | Adrenal gland disorders |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON46149

**Source**
ToetsingOnline

**Brief title**
Diur005

### Condition

- Adrenal gland disorders

**Synonym**
Congenital Adrenal Hyperplasia

**Research involving**
Human

## Sponsors and support

**Primary sponsor:** MediServ
**Source(s) of monetary or material Support:** Diurnal Ltd

## Intervention

**Keyword:** CAH, endocrinology, glucocortocoide

## Outcome measures

### Primary outcome

To demonstrate the superior efficacy of Chronocort® compared with standard

glucocorticoid replacement therapy in the treatment of CAH based on 17-OHP.

### Secondary outcome

In adult subjects with CAH:

* To assess the safety and tolerability of Chronocort® treatment in adult

subjects with CAH over a

6-month period.

* To assess the efficacy of Chronocort® with regard to the effect on A4 over

the 6-month treatment period.

* To assess the impact of Chronocort® on body composition (using dual energy

X-ray absorbtimetry

[DEXA]) * fat mass, lean mass and total bone density * at selected sites.

# Study description

### Background summary

The glucocorticoid medications currently used to treat CAH are like cortisol, but they cannot simulate natural cortisol in terms of how it is produced in the body. This is because cortisol is normally released in different amounts

throughout the day with a pulse, or burst, during the early morning hours and very low amounts in the body in the evening.

Chronocort® has been designed so that the amounts of cortisol in the body more closely mimic the human body*s normal release pattern of cortisol.
It is expected that the better metabolic control results in less adverse effects, such as obesitas, and consequently to a better quality of life.

**Study objective**

The purpose of this research study is to compare the safety and effectiveness of Chronocort® with current glucocorticoid treatment regimens in the treatment of CAH over a 6 month period.

**Study design**

randomized, open-label study with parallel groups

**Intervention**

Chronocort treatment versus standard regimen

**Study burden and risks**

Chronocort is a new formulation of a medicine, hydrocortisone, that has been used as a treatment for CAH and similar conditions for several years There is a lot of published information regarding the safety of this hydrocortisone. The dose of hydrocortisone being administered as Chronocort® in this study is within the expected dose level to replace cortisone in the body for patients with CAH. Commons side effects from Hydrocortisone can include (occurring in around 30% of patients):
*Increased appetite
*Irritability
*Difficulty sleeping (insomnia)
*Swelling in ankles and feet (fluid retention)
*Nausea (take with food)
*Heartburn
*Muscle weakness
*Impaired wound healing
*Increased blood sugar levels

Further to this, adverse effects may occur if too much or too little medication is used. In these cases patients may experience symptoms of too little cortisol replacement (e.g., fatigue) or too much cortisol replacement (e.g., weight gain). Patient will undergo four 24 hour endocrine profiles to assess if they are being treated with the correct amount of glucocorticoid to treat their CAH

adequately
The study involves a DEXA scan which will expose patient to radiation. The study involves the inconvenience of needing to attend four overnight stays at the hospital in order to have a 24 hour endocrine profile performed. Patients will be advised in advance of the schedule for these visits* which will also form part of the informed consent process

# Contacts

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MediServ

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# Trial sites

## Listed location countries

Netherlands

# Eligibility criteria

**Age**
Adults (18-64 years)
Elderly (65 years and older)

## Inclusion criteria

1. Known CAH due to 21-hydroxylase deficiency (classic CAH) diagnosed in childhood with documented (at any time) elevated 17-hydroxyprogesterone (17-OHP) and/or androstenedione (A4) and currently treated with hydrocortisone, prednisone, prednisolone or dexamethasone (or a combination of the aforementioned glucocorticoids) on a stable

glucocorticoid therapy for a minimum of 6 months.
2. Male or female subjects aged 18 and above.
3. Provision of signed written informed consent.
4. Non-pregnant, non-lactating females who are post menopausal, naturally or surgically sterile, or of childbearing potential with a negative urinary pregnancy test and using a medically acceptable method of contraception. (Note: female subjects with oligomenorrhoea or amenorrhoea aged 55 or under should be considered potnetially fertile and therefore it is expected that they, besides undergoing pregnancy testing, should use an acceptable method of contraception.
5. Plasma renin activity (PRA) less than 1.5 times the upper limit of normal (ULN) at screening or within 3 months prior to screening, except in subjects who have been diagnosed with hypertension where the renin is not being used to monitor fludrocortisone replacement.

### Exclusion criteria

1. Co-morbid condition requiring daily administration of a medication (or consumption of any material) that interferes with the metabolism of glucocorticoids.
2. Clinical or biochemical evidence of hepatic or renal disease. Creatinine over twice the ULN or elevated liver function tests (ALT or AST >2 times the ULN).
3. Subjects on regular daily inhaled, topical, nasal or oral steroids for any indication other than CAH.
4. Subjects with any other significant medical or psychiatric conditions that in the opinion of the investigator would preclude participation in the trial.
5. History of malignancy (other than basal cell carcinoma successfully treated >6 months prior to entry into the study).
6. Participation in another clinical trial of an investigational or licensed drug or device within the 3 months prior to inclusion in this study.
7. Subjects with a history of bilateral adrenalectomy.
8. Subjects having previously been exposed to Chronocort®.
9. Subjects working routinely in night shifts and therefore do not sleep during the usual night time.
10. Subjects unable to comply with the requirements of the protocol.

## Study design

### Design

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| Study phase: | 3 |
| Study type: | Interventional |
| Intervention model: | Parallel |
| Allocation: | Randomized controlled trial |

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|---|---|
| Masking: | Open (masking not used) |
| Control: | Active |
| Primary purpose: | Treatment |

### Recruitment

NL

| | |
|---|---|
| Recruitment status: | Recruitment stopped |
| Start date (anticipated): | 05-07-2016 |
| Enrollment: | 18 |
| Type: | Actual |

### Medical products/devices used

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|---|---|
| Product type: | Medicine |
| Brand name: | Chronocort |
| Generic name: | hydrocortisone |

## Ethics review

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| Approved WMO Date: | 17-11-2015 |
| Application type: | First submission |
| Review commission: | CMO regio Arnhem-Nijmegen (Nijmegen) |
| Approved WMO Date: | 28-04-2016 |
| Application type: | First submission |
| Review commission: | CMO regio Arnhem-Nijmegen (Nijmegen) |
| Approved WMO Date: | 04-08-2017 |
| Application type: | Amendment |
| Review commission: | CMO regio Arnhem-Nijmegen (Nijmegen) |
| Approved WMO Date: | 19-09-2017 |
| Application type: | Amendment |
| Review commission: | CMO regio Arnhem-Nijmegen (Nijmegen) |

# Study registrations

## Followed up by the following (possibly more current) registration

No registrations found.

## Other (possibly less up-to-date) registrations in this register

No registrations found.

## In other registers

| Register | ID |
|---|---|
| EudraCT | EUCTR2015-000711-40-NL |
| CCMO | NL54707.091.15 |