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Committee for Orphan Medicinal Products

## Public summary of opinion on orphan designation

Hydrocortisone (modified release tablet) for the treatment of congenital adrenal hyperplasia

First publication	11 October 2005
Rev.1: transfer of sponsorship	6 March 2007
Rev.2: transfer of sponsorship	27 August 2009
Rev.3: sponsor's change of address	12 November 2009
Rev.4: sponsor's change of address	5 March 2015
<b>Disclaimer</b> Please note that revisions to the Public Summary of Opinion are purely administrative updates. Therefore, the scientific content of the document reflects the outcome of the Committee for Orphan Medicinal Products (COMP) at the time of designation and is not updated after first publication.	

On 27 July 2005, orphan designation (EU/3/05/296) was granted by the European Commission to Professor Richard JM Ross, United Kingdom, for hydrocortisone (modified release tablet) for the treatment of congenital adrenal hyperplasia.

The sponsorship was transferred to Phoqus Pharmaceuticals Limited, United Kingdom, in December 2006 and subsequently to Diurnal Limited, United Kingdom, in February 2009.

### What is congenital adrenal hyperplasia?

Congenital adrenal hyperplasia is an inherited condition that is present from birth and causes a diffuse enlargement of the adrenal glands. The adrenal gland consists of two small glands that are located above the kidneys, in the abdomen. The outer wall (cortex) of the adrenal gland secretes important substances, so-called steroid hormones. Steroid hormones include sex hormones and hormones used to control minerals and sugar in the body. These include cortisol, aldosterone and dehydroepiandrosterone. The formation and activation of these hormones depends on certain specific proteins (enzymes). The lack or malfunctioning of one of these enzymes, due to a genetic defect, will result in the blocking of the production of cortisol and aldosterone from the adrenal gland. This will then lead to an overproduction of male sex hormones.



Congenital adrenal hyperplasia is chronically debilitating. The metabolism of salt and water is disturbed causing dehydration, low blood pressure and loss of weight. The affected individuals may also develop excessive pigmentation in the skin. In boys, the syndrome produces early development of masculine characteristics and, in girls, it may lead to enlargement of the genital tract, lack of menstruation, deep voice and excessive hair (this phenomenon is called "virilisation"). In both sexes, the syndrome may result in short stature.

### **What is the estimated number of patients affected by the condition?**

At the time of designation, congenital adrenal hyperplasia affected not more than 1 in 10,000 people in the European Union (EU). This was equivalent to a total of not more than 47,000 people\*, and is below the ceiling for orphan designation, which is 5 people in 10,000. This is based on the information provided by the sponsor and the knowledge of the Committee for Orphan Medicinal Products (COMP).

### **What treatments are available?**

Several products to treat congenital adrenal hyperplasia have been authorised. In particular, various steroid hormones can be used to replace those which are insufficiently produced by the adrenal gland. Hydrocortisone (modified release tablet) might be of potential significant benefit for the treatment of congenital adrenal hyperplasia because it is designed to mimic more closely the level of cortisol in the body. It may improve patient's acceptance of the treatment and prevent problems of masculinisation (or virilisation), infertility and excess steroid treatment. This assumption will have to be confirmed at the time of marketing authorisation. This will be necessary to maintain the orphan status.

### **How is this medicine expected to work?**

Hydrocortisone (also known as cortisol) is the main steroid hormone secreted by the adrenal gland. Hydrocortisone (modified release tablet) is expected to replace natural the cortisol that is missing due to the congenital adrenal hyperplasia, and this may help to treat the symptoms of the disease.

### **What is the stage of development of this medicine?**

At the time of submission of the application for orphan designation, no clinical trials in patients with congenital adrenal hyperplasia were initiated.

This specific formulation of hydrocortisone (modified release tablet) was not authorised anywhere worldwide for congenital adrenal hyperplasia or designated as orphan medicinal product elsewhere for this condition, at the time of submission.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 15 June 2005 recommending the granting of this designation.

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\*Disclaimer: For the purpose of the designation, the number of patients affected by the condition is estimated and assessed on the basis of data from the European Union (EU 28), Norway, Iceland and Liechtenstein. This represents a population of 512,900,000 (Eurostat 2015).

Opinions on orphan medicinal product designations are based on the following three criteria:

- the seriousness of the condition;
- the existence of alternative methods of diagnosis, prevention or treatment;
- either the rarity of the condition (affecting not more than 5 in 10,000 people in the EU) or insufficient returns on investment.

Designated orphan medicinal products are products that are still under investigation and are considered for orphan designation on the basis of potential activity. An orphan designation is not a marketing authorisation. As a consequence, demonstration of quality, safety and efficacy is necessary before a product can be granted a marketing authorisation.

### **For more information**

Sponsor's contact details:

Diurnal Limited  
Cardiff Medicentre  
Heath Park  
Cardiff CF14 4UJ  
United Kingdom  
Tel. +44 (0)871 716 8848  
<http://www.diurnal.co.uk/contact>

For contact details of patients' organisations whose activities are targeted at rare diseases see:

- [Orphanet](#), a database containing information on rare diseases, which includes a directory of patients' organisations registered in Europe;
- [European Organisation for Rare Diseases \(EURORDIS\)](#), a non-governmental alliance of patient organisations and individuals active in the field of rare diseases.

## Translations of the active ingredient and indication in all official EU languages<sup>1</sup>, Norwegian and Icelandic

Language	Active ingredient	Indication
English	Hydrocortisone (modified release tablet)	Treatment of congenital adrenal hyperplasia
Bulgarian	Хидрокортизон (таблетка с изменено освобождаване)	Лечение на вродена надбъбречна хиперплазия
Czech	Hydrocortizon ( upravené uvolňovací tablety)	Léčba vrozené hyperplazie nadledvin
Danish	Hydrocortison (tablet med modificeret udløsning)	Behandling af medfødt binyrebarkhyperplasi
Dutch	Hydrocortisone (tablet met gereguleerde afgifte)	Behandeling van congenitale bijnierhyperplasia
Estonian	Hüdrokortisoon (modifitseeritud vabanemisega tablett)	Kaasasündinud neerupealise hüperplaasia ravi
Finnish	Hydrokortisoni (depottabletti)	Lisämunuaisen synnyynnäisen liikakasvun hoito
French	Hydrocortisone (comprimé à libération modifiée)	Traitement de l'hyperplasie surrénale congénitale
German	Hydrocortison (Tabletten mit veraendertem Wirkstoffreisetzung)	Behandlung der Kongenitalenb Adrenalen Hyperplasie
Greek	Υδροκορτιζόνη (δισκίο τροποποιημένης απελευθέρωσης)	Θεραπεία της σύμφυτης επινεφριδίου υπερπλασίας
Hungarian	Hidrokorizon (módosított hatóanyagleadású tableta)	Congenitalis adrenalis hyperplasia kezelése
Italian	Idrocortisone (compressa a rilascio modificato)	Trattamento dell'iperplasia surrenale congenita
Latvian	Hidrokorizons (mainīgas darbības tabletes)	Iedzimta virsnieru hiperplāzija
Lithuanian	Hidrokorizonas (modifikuota atpalaiduota tabletė)	Įgimtos antinksčių hiperplazijos gydymas
Maltese	Hydrocortisone (pillola li terfi l-medicina b'mod modifikat)	Kura ta' l-iperplasia adrenalni kongenitali
Polish	Hydrokortyzon (tabletki o zmodyfikowanym uwalnianiu)	Leczenie wrodzonego przerostu nadnerczy
Portuguese	Hydrocortisone (comprimido de libertação modificada)	Tratamento da hiperplasia adrenal congenita
Romanian	Hidrokorizon (comprimat cu eliberare modificată)	Tratamentul hiperplaziei congenitale corticosuprarenale
Slovak	hydrokorizón (tableta s riadeným uvoľňovaním)	Liečba kongenitálnej nadobličkovej hyperplázie
Slovenian	Hidrokorizon (tablete s prirejenim sproščanjem)	Kongenitalna adrenalna hiperplazija

<sup>1</sup> At the time of transfer of sponsorship

Language	Active ingredient	Indication
Spanish	Hidrocortisona (comprimido de liberación modificada)	Tratamiento de la hiperplasia suprarrenal congénita
Swedish	Hydrocortison (tablett med modifierad frisättning)	Behandling av adrenogenitalt syndrom
Norwegian	Hydrokortison (tablett med modifisert frisetting)	Behandling av kongenitt binyrebarkhyperplasi
Icelandic	Hýdrókortisón (tafla með aðlagaðri losun)	Meðfædd nýrnahefðu hyperplasia

Withdrawn