



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

12 November 2013
EMA/COMP/793876/2011 Rev.2
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Mifepristone for the treatment of hypercortisolism (Cushing's syndrome) of endogenous origin

First publication	22 November 2011
Rev.1: transfer of sponsorship	5 March 2013
Rev.2: transfer of sponsorship	12 November 2013
Disclaimer 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 October 2011, orphan designation (EU/3/11/925) was granted by the European Commission to Voisin Consulting S.A.R.L., France, for mifepristone for the treatment of hypercortisolism (Cushing's syndrome) of endogenous origin.

The sponsorship was transferred to Dr Ulrich Granzer, Germany, in December 2012 and subsequently to FGK Representative Service GmbH, Germany, in October 2013.

What is hypercortisolism (Cushing's syndrome) of endogenous origin?

Hypercortisolism (Cushing's syndrome) is a set of symptoms caused by an excess of the glucocorticoid hormone cortisol in the blood. The symptoms include weight gain (particularly in the face and neck), easy bruising, excessive growth of coarse hair on the face, weakening of the muscles and bones, and high blood pressure. 'Endogenous' means that the excess cortisol is caused by the body producing too much of the hormone and not by the patient taking medicines that can cause the condition. Endogenous hypercortisolism is usually caused by a tumour of the glands that are involved in the production of cortisol.

Endogenous hypercortisolism is a severe disease that is long lasting and may be life threatening because of its complications, including diabetes, high blood pressure and mental problems.



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

At the time of designation, hypercortisolism (Cushing's syndrome) of endogenous origin affected approximately 0.6 in 10,000 people in the European Union (EU). This was equivalent to a total of around 30,000 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?

At the time of designation, the main treatments for endogenous hypercortisolism involved treating the tumour responsible for causing the high cortisol levels, such as by surgery or radiotherapy (treatment with radiation) and using medicines to block the production of cortisol. Metyrapone was authorised in some EU countries for the management of patients with Cushing's syndrome.

The sponsor has provided sufficient information to show that mifepristone might be of significant benefit for patients with hypercortisolism (Cushing's syndrome) of endogenous origin because it works in a different way to existing medicines for endogenous hypercortisolism and may offer an alternative for patients who do not respond to currently authorised treatments. This assumption will need to be confirmed at the time of marketing authorisation, in order to maintain the orphan status.

How is this medicine expected to work?

Mifepristone has several medical uses. In endogenous hypercortisolism, mifepristone is expected to act as a 'glucocorticoid receptor antagonist'. This means that it blocks the receptors that 'glucocorticoids' such as cortisol normally attach to. By blocking these receptors, mifepristone prevents cortisol from working and reduces the symptoms of high cortisol levels.

What is the stage of development of this medicine?

The effects of mifepristone have been evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials with mifepristone in patients with hypercortisolism (Cushing's syndrome) of endogenous origin had started.

At the time of submission, mifepristone was not authorised anywhere in the world for the treatment of hypercortisolism (Cushing's syndrome) of endogenous origin. Orphan designation of mifepristone had been granted in the EU for hypercortisolism (Cushing's syndrome) of endogenous origin and for Cushing's syndrome secondary to ectopic ACTH secretion. In the United States, orphan designation of mifepristone had been granted for the clinical manifestations of endogenous Cushing's syndrome and for Cushing's syndrome secondary to ectopic ACTH secretion.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 16 September 2011 recommending the granting of this designation.

*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 27), Norway, Iceland and Liechtenstein. At the time of designation, this represented a population of 507,700,000 (Eurostat 2011).

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:

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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 languages¹, Norwegian and Icelandic

Language	Active ingredient	Indication
English	Mifepristone	Treatment of hypercortisolism (Cushing's syndrome) of endogenous origin
Bulgarian	Mifepristone (Мифепристон)	Лечение хиперкортицизъм (Синдром на Къшинг) от ендогенен произход.
Croatian	Mifepristone	Liječenje hiperkortizolizma (Cushingov sindrom) endogenog podrijetla
Czech	Mifepristone	Terapie endogenního hyperkortizolismu (Cushingova syndromu)
Danish	Mifepriston	Behandling af endogen hypercortisolisme (Cushings syndrom)
Dutch	Mifepristone	Behandeling van hypercortisolisme (Cushing syndroom) van endogene oorsprong
Estonian	Mifepristoon	Endogeense hüperkortisolismi (Cushingi sündroom) ravi.
Finnish	Mifepristone	Sisäsyntyisen hyperkortisolismin (Cushing-oireyhtymän) hoito
French	Mifépristone	Traitement de l'hypercortisolisme endogène (syndrome de Cushing)
German	Mifepristone	Behandlung des endogenen Hyperkortisolismus (Cushing-Syndrom)
Greek	Mifepristone	Θεραπεία του ενδογενούς υπερκορτισολισμού (σύνδρομο του Cushing)
Hungarian	Mifepriston	Endogén eredetű hiperkortizolizmus (Cushing-szindróma) kezelése
Italian	Mifepristone	Trattamento dell'ipercortisolismo (sindrome di Cushing) di origine endogena
Latvian	Mifepristone	Endogēnas izcelsmes hiperkortizolisma (Kušinga sindroma) ārstēšana
Lithuanian	Mifepristonas	Endogeninės kilmės hiperkortizolizmo (Kušingo sindromo) gydymas
Maltese	Mifepristone	Kura ta' l-iperkortisoliżmu ta' nisel endoġenu (sindromu ta' Cushing)
Polish	Mifepriston	Leczenie hiperkortyzolizmu endogennego (zespołu Cushinga)
Portuguese	Mifepristone	Tratamento do hipercortisolismo endógeno (síndrome de Cushing)
Romanian	Mifepristonă	Tratamentul hipercorticismului endogen (sindromul Cushing)
Slovak	Mifepriston	Liečba hyperkortizolizmu (Cushingov syndróm) endogénneho pôvodu
Slovenian	Mifepriston	Zdravljenje endogenega hiperkortizolizma (Cushingov sindrom)
Spanish	Mifepristona	Tratamiento del hipercortisolismo endógeno (síndrome de Cushing)
Swedish	Mifepristone	Behandling av hyperkortisolism (Cushings syndrom) av endogent ursprung
Norwegian	Mifepriston	Behandling av hyperkortisolisme (Cushings syndrom) av endogen opprinnelse

¹ At the time of designation

Language	Active ingredient	Indication
Icelandic	Mifepristón	Meðferð á hyperkortisólisma af innrænum toga (Cushing heilkenni)