European Medicines Agency
Pre-authorisation Evaluation of Medicines for Human Use

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Committee for Orphan Medicinal Products

Public summary of positive opinion for orphan designation of mifepristone for the treatment of endogenous hypercortisolism (Cushing's syndrome)

On 27 February 2009, orphan designation (EU/3/09/614) was granted by the European Commission to Exelgyn, France, for mifepristone for the treatment of endogenous hypercortisolism (Cushing's syndrome).

What is endogenous hypercortisolism (Cushing's syndrome)?
Hypercortisolism (Cushing's syndrome) is a set of symptoms caused by an excess of the 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, endogenous hypercortisolism affected around 0.6 in 10,000 people in the European Union (EU)[*]. This is below the threshold for orphan designation, which is 5 in 10,000, and is equivalent to a total of around 30,000 people. 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.
The sponsor has provided sufficient information to show that mifepristone might be of potential significant benefit for the patients because it works in a different way to the other medicines used in endogenous hypercortisolism and because it could be an alternative treatment for the condition. 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

[*]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. This represents a population of 504,800,000 (Eurostat 2009).

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'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, no clinical trials in patients with endogenous hypercortisolism had been started.
At the time of submission, mifepristone was not authorised anywhere in the world for endogenous hypercortisolism. Orphan designation of mifepristone had been granted in the United States of America for the condition.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 7 January 2009 recommending the granting of this designation.

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 Community) 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.

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Translations of the active ingredient and indication in all official EU languages, 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 Кушинг) от ендогенен произход.
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 (síndroma 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
Icelandic	Mifepristón	Meðferð á hyperkortisólisma af innrænum toga (Cushing heilkenni)