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EMA/COMP/696157/2015
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-(ethoxymethyl)-[1,1'-biphenyl]-2-sulfonamide for the treatment of focal segmental glomerulosclerosis

On 11 November 2015, orphan designation (EU/3/15/1574) was granted by the European Commission to Retrophin Europe Limited, Ireland, for 4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-(ethoxymethyl)-[1,1'-biphenyl]-2-sulfonamide for the treatment of focal segmental glomerulosclerosis.

What is focal segmental glomerulosclerosis?

Focal segmental glomerulosclerosis is a disease where the glomeruli (small filtering units in the kidneys which filter waste products from the blood and start urine production) are damaged and become scarred. This stops them from working properly, so that substances needed by the body, such as proteins, pass into the urine. Focal segmental glomerulosclerosis can affect both adults and children. Symptoms include swelling, low blood protein levels and high blood pressure. It is called 'focal segmental' because only parts of some glomeruli are affected.

The cause of focal segmental glomerulosclerosis is usually unknown but there are some factors such as certain diseases and drugs that may trigger it.

Focal segmental glomerulosclerosis is a long-term debilitating and life-threatening disease because it may lead to kidney failure.

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

At the time of designation, focal segmental glomerulosclerosis affected approximately 3.5 in 10,000 people in the European Union (EU). This was equivalent to a total of around 180,000 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).

*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).

What treatments are available?

At the time of designation, ciclosporin was authorised in some EU countries specifically for the treatment of focal segmental glomerulosclerosis, while other medicines were authorised to treat the symptoms.

The sponsor has provided sufficient information to show that the medicine might be of significant benefit for patients with focal segmental glomerulosclerosis because studies in experimental models suggest that it works in a different way to existing treatments and can improve the functioning of the kidneys. 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?

The medicine acts in two complementary ways on the kidney, as an angiotensin receptor blocker (ARB) and an endothelin receptor antagonist. ARBs block receptors for a hormone called angiotensin II. Blocking the action of this hormone allows blood vessels to widen, reducing blood pressure, and helps to reduce the amount of water re-absorbed by the kidneys, improving urine production. Endothelin receptor antagonists block the action of a substance called endothelin, which is thought to be involved in the progression of focal segmental glomerulosclerosis and the increased loss of protein in the urine. Combining both actions is expected to improve symptoms of the condition and reduce damage and scarring to the glomeruli.

What is the stage of development of this medicine?

The effects of the medicine have been evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials with this medicine in patients with focal segmental glomerulosclerosis were ongoing.

At the time of submission, the medicine was not authorised anywhere in the EU for focal segmental glomerulosclerosis. Orphan designation of the medicine had been granted in the United States for this condition.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 8 October 2015 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 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:

Contact details of the current sponsor for this orphan designation can be found on EMA website, on the medicine's [rare disease designations page](#).

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	4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-(ethoxymethyl)-[1,1'-biphenyl]-2-sulfonamide	Treatment of focal segmental glomerulosclerosis
Bulgarian	4'-[(2-бутил-4-оксо-1,3-диазаспиро[4.4]нон-1-ен-3-ил)метил]-N-(4,5-диметил-3-изоксазолил)-2'-(етоксиметил)-[1,1'-бифенил]-2-сулфонамид	Лечение на огнищно-сегментна гломерулна склероза
Croatian	4'-[(2-butyl-4-okso-1,3-diazaspiro[4.4]non-1-en-3-il)metil]-N-(4,5-dimetil-3-izoksazolil)-2'-(etoksimetil)-[1,1'-bifenil]-2-sulfonamid	Liječenje fokalne segmentalne glomeruloskleroze
Czech	4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-(ethoxymethyl)-[1,1'-bifenyl]-2-sulfonamid	Léčba fokálně segmentální glomerulosklerózy
Danish	4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-(ethoxymethyl)-[1,1'-bifenyl]-2-sulfonamid	Behandling af fokal segmental glomerulosklerose
Dutch	4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-(ethoxymethyl)-[1,1'-bifenyl]-2-sulfonamide	Behandeling van focale segmentale glomerulosclerose
Estonian	4'-[(2-butüül-4-okso-1,3-diasaspiro[4.4]noon-1-een-3-üül)metüül]-N-(4,5-dimetüül-3-isoksasolüül)-2'-(etoksümetüül)-[1,1'-bifenüül]-2-sulfoonamiid	Fokaal-segmentaarse glomeruloskleroosi ravi
Finnish	4'-[(2-butyli-4-okso-1,3-diatsaspiro[4.4]non-1-en-3-yyli)metyyli]-N-(4,5-dimetyyli-3-isoksatsolyyli)-2'-(etoksिमetyyli)-[1,1'-bifenyli]-2-sulfonamidi	Fokaalisen segmentaalisen glomeruloskleroosin hoito
French	4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)méthyl]-N-(4,5-diméthyl-3-isoxazolyl)-2'-(éthoxyméthyl)-[1,1'-biphényl]-2-sulfonamide	Traitement de la glomérulonéphrite focale segmentaire
German	4'-[(2-Butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-(ethoxymethyl)-[1,1'-biphenyl]-2-sulfonamid	Behandlung der fokal segmentalen Glomerulosklerose
Greek	4'-[(2-βουτυλο-4-οξο-1,3-διαζασπειρο[4.4]μη-1-εν-3-υλο)μεθυλο]-N-(4,5-διμέθυλο-3-ισοξαζολυλο)-2'-(αιθοξυμεθυλο)-[1,1'-διφαινυλο]-2-σουλφοναμίδη	Θεραπεία εστιακής τμηματικής σπειραματοσκλήρυνσης
Hungarian	4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-én-3-il)metil]-N-(4,5-dimetil-3-izoxazolil)-2'-(etoximetil)-[1,1'-bifenil]-2-szulfonamid	Focalis szegmentális glomerulosclerosis kezelése
Italian	4'-[(2-butyl-4-osso-1,3-diazaspiro[4.4]non-1-en-3-il)metil]-N-(4,5-dimetil-3-isossazolil)-2'-(etossimetil)-[1,1'-bifenil]-2-sulfonamide	Trattamento della glomerulosclerosi focale segmentaria

¹ At the time of designation

Language	Active ingredient	Indication
Latvian	4'-[(2-butyl-4-okso-1,3-diazaspiro[4.4]non-1-ēn-3-il)metil]-N-(4,5-dimetil-3-izoksazolil)-2'-(etoksimetil)-[1,1'-bifenil]-2-sulfonamīds	Fokālas segmentāras glomeruloskleroze ārstēšana
Lithuanian	4'-[(2-butyl-4-okso-1,3-diazaspiro[4.4]non-1-en-3-il)metil]-N-(4,5-dimetil-3-izoksazolil)-2'-(etoksimetil)-[1,1'-bifenil]-2-sulfonamidas	Židininės segmentinės glomerulosklerozės gydymas
Maltese	4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)methyl]-N-(4,5-dimethyl-3-isoxazolyl)-2'-(ethoxymethyl)-[1,1'-biphenyl]-2-sulfonamide	Kura tal-glomeruloskleroži segmentali fokali
Polish	4'-[(2-butylo-4-okso-1,3-diazaspiro[4.4]non-1-en-3-ylo)metylo]-N-(4,5-dimetylo-3-izoksazolilo)-2'-(etoksymetylo)-[1,1'-bifenylo]-2-sulfonamid	Leczenie ogniskowego segmentalnego szklwienia kłębuszków nerkowych
Portuguese	4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-il)metil]-N-(4,5-dimetil-3-isoxazolil)-2'-(etoximetil)-[1,1'-bifenil]-2-sulfonamida	Tratamento da glomeruloesclerose focal e segmentar
Romanian	4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-il)metil]-N-(4,5-dimetil-3-izoxazolil)-2'-(etoximetil)-[1,1'-bifenil]-2-sulfonamidă	Tratamentul glomerulosclerozei focale și segmentare
Slovak	4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]nón-1-én-3-yl)metyl]-N-(4,5-dimetyl-3-izoxazolyl)-2'-(etoxymetyl)-[1,1'-bifeny]-2-sulfónamid	Liečba fokálnej segmentálnej glomerulosklerózy
Slovenian	4'-[(2-butyl-4-okso-1,3-diazaspiro[4.4]non-1-en-3-il)metil]-N-(4,5-dimetil-3-izoksazolil)-2'-(etoksimetil)-[1,1'-bifenil]-2-sulfonamid	Zdravljenje fokalne segmentne glomeruloskleroze
Spanish	4'-[(2-butyl-4-oxo-1,3-diazaespiro[4.4]non-1-en-3-il)metil]-N-(4,5-dimetil-3-isoxazolil)-2'-(etoximetil)-[1,1'-bifenil]-2-sulfonamida	Tratamiento de la glomeruloesclerosis focal y segmentaria
Swedish	4'-[(2-butyl-4-oxo-1,3-diazaspiro[4.4]non-1-en-3-yl)metyl]-N-(4,5-dimetyl-3-isoxazolyl)-2'-(etoximetyl)-[1,1'-bifeny]-2-sulfonamid	Behandling av fokal segmentell glomeruloskleros
Norwegian	4'-[(2-Butyl-4-okso-1,3-diazaspiro[4.4]non-1-en-3-yl)metyl]-N-(4,5-dimetyl-3-isoksazolyl)-2'-(etoksymetyl)-[1,1'-bifeny]-2-sulfonamid	Behandling av fokal segmental glomeruloskleroze
Icelandic	4'-[(2-bútýl-4-oxó-1,3-díasaspíró[4.4]nón-1-en-3-ýl)metýl]-N-(4,5-dímetýl-3-ísoxasólýl)-2'-(etoxýmetýl)-[1,1'-bífenýl]-2-súlfónamíð	Meðferð við staðbundnu hlutanýrnaðnahersli