5 March 2015
EMA/COMP/1563/2003 Rev.2
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

5-methyl-pyridine-2-sulfonic acid 6-(2-hydroxyethoxy)-5-(2-methoxyphenoxy)-2-(2-1H-tetrazol-5-yl-pyridin-4-yl)-pyrimidin-4-ylamide sodium salt (1:2) for the treatment of aneurysmal subarachnoid haemorrhage

First publication	26 April 2004
Rev.1: transfer of sponsorship	12 December 2005
Rev.2: sponsor's change of address	5 March 2015

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 12 December 2003, orphan designation (EU/3/03/182) was granted by the European Commission to Axovan Europe Ltd., United Kingdom, for 5-methyl-pyridine-2-sulfonic acid 6-(2-hydroxyethoxy)-5-(2-methoxyphenoxy)-2-(2-1H-tetrazol-5-yl-pyridin-4-yl)-pyrimidin-4-ylamide sodium salt (1:2) (clazosentan) for the treatment of aneurysmal subarachnoid haemorrhage.

The sponsorship was transferred to Actelion Registration Limited, United Kingdom, in January 2005.

What is aneurysmal subarachnoid haemorrhage?

A cerebral aneurysm refers to a blood vessel within the brain that weakens over time and undergoes widening. This usually occurs at the junctions of the large arteries at the base of the brain. As the blood vessel weakens, it begins to bulge out like a balloon. The larger the balloon becomes, the greater the risk it may burst, resulting in haemorrhage (bleeding) into the subarachnoid space (membranous space surrounding the brain) and ensuing spasm (uncontrollable tightening) of the brain blood vessels, leading to further oxygen shortage in the brain cells. This cascade of effects can ultimately impair the brain functions.

Aneurysms in the brain are considered to be acquired, in other words they are not present at birth but develop over a lifetime. However, evidence indicates that genetic factors make some people more likely to develop brain aneurysms.

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Aneurysmal subarachnoid haemorrhage is chronically debilitating and life-threatening.

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

At the time of designation, aneurysmal subarachnoid haemorrhage affected approximately 1.25 in 10,000 people in the European Union (EU). This was equivalent to a total of around 48,000 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?

Further to surgical intervention, one medicinal product was authorised for the treatment of aneurysmal subarachnoid haemorrhage in the Community at the time of submission of the application for orphan drug designation.

Clazosentan might be of potential significant benefit for the treatment of aneurysmal subarachnoid haemorrhage. This is because it may prevent the complications that are resulting from insufficient blood supply to the brain. This benefit 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?

Clazosentan opposes the effect of a substance called endothelin. Endothelin, which is naturally produced by some type of cells of the body, can cause narrowing of blood vessels. Clazosentan blocks the effect of endothelin and the blood vessels can become wider. As such it could prevent and relieve spasm of the blood vessels.

What is the stage of development of this medicine?

The effects of clazosentan were evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials in patients with aneurysmal subarachnoid haemorrhage were ongoing.

Clazosentan was not marketed anywhere worldwide for the treatment of aneurysmal subarachnoid haemorrhage 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 6 November 2003 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.
At the time of designation, this represented a population of 382,800,000 (Eurostat 2003).

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 languages[1], Norwegian and Icelandic

Language	Active ingredient	Indication
English	5-methyl-pyridine-2-sulfonic acid {6-(2-hydroxy-ethoxy)-5-(2-methoxy-phenoxy)-2-[2-(1H-tetrazol-5-yl)-pyridin-4-yl]-pyrimidin-4-yl}-amide sodium salt	Treatment of aneurysmal subarachnoid haemorrhage
Czech	5-methyl-pyridine-2-sulfoninová kyselina {6-(2-hydroxy-ethoxy)-5-(2-methoxy-phenoxy)-2-[2-(1H-tetrazol-5-yl)-pyridin-4-yl]-pyrimidin-4-yl}-amid sodné soli	Léčba krvácení subarachnoideálního aneurysmatu .
Danish	5-methylpyridin-2-sulfonsyre {6-(2-hydroxyethoxy)-5-(2-methoxyfenoxy)-2-[2-(1H-tetrazol-5-yl)-pyridin-4-yl]-pyrimidin-4-yl}-amid natriumsalt	Behandling af aneurysmatisk subaraknoidalblødning
Dutch	5-methylpyridine-2-sulfonzuur natriumzout van {6-(2-hydroxyethoxy)-5-(2-methoxyfenoxy)-2-[2-(1H-tetrazol-5-yl)-pyridin-4-yl]-pyrimidin-4-yl}-amide	Behandeling van aneurysmatische subarachnoïdale bloeding
Estonian	5-metüülpüridiin 2-sulfoonhappe {6-(2-hüdroksü-etoksü)-5-(2-metoksü-femoksü)-2-[2-(1H-tetrazol-5-üül)-püridiin-4-üül]-pürimidiin –4-üül}-amiid naatriumi sool	Aneurüsmse subarahnoidaalse hemorraagia ravi
Finnish	5-metyyli-pyridiini-2-sulfonihappo {6-(2-hydroksi-etoksi)-5-(2-metoksi-fenoksi)-2-[2-(1H-tetratsol-5-yyli)-pyridiini-4-yyli]-pyrimidiini-4-yyli}-amidin natriumsuola	Lukinkalvoon liittyvän valtimoverenvuodon hoito
French	Acide 5-méthyl-pyridine-2-sulfonique {6-(2-hydroxy-éthoxy)-5-(2-méthoxy-phénoxy)-2-[2-(1H-tétrazol-5-yl)-pyridine-4-yl]-pyrimidine-4-yl}-amide sel sodique	Traitement de l'hémorragie subarachnoïdienne par rupture d'anévrysme
German	5-Methylpyridin-2-Sulfonsäure {6-(2-Hydroxyethoxy)-5-(2-Methoxyphenoxy)-2-[2-(1H-Tetrazol-5-yl)-Pyridin-4-yl]-Pyrimidin-4-yl}-amid-Natriumsalz	Behandlung von aneurysmalen Subarachnoidalblutungen
Greek	{6-(2-υδροξυ-αιθοξυ)-5-(2-μεθοξυ-φαινοξυ)-2-[2-(1Η-τετραζολο-5-υλο)-πυριδινο-4-υλο]-πυριμιδινο-4-υλο}-αμιδικό άλας νατρίου του 5-μεθυλο-πυριδινο-2-σουλφονικό οξέος	Αντιμετώπιση της ανευρυσματικής υπαραχνοειδούς αιμορραγίας
Hungarian	5-metil-piridin-2-szulfonsav{6-(2-hidroxi-etoxi)-5-(2-metoxi-fenoxi)-2-[2-(1H-tetrazol-5-il)-piridin-4-il]-pirimidin-4-il}-amid nátrium	Aneurizmából eredő subarachnoidális vérzés kezelése

[1] At the time of transfer of sponsorship

Language	Active ingredient	Indication
Italian	Acido 5-metil-piridin-2 sulfonico {6-(2-idrossi-etossi)-5-(2-metossi-fenossi)-2-[2-(1H-tetrazol-5-il)-piridin-4-il]-pirimidin-4-il}-amide sale sodico	Trattamento dell'emorragia da aneurisma subaracnoideo
Latvian	5-metil-piridīn-2-sulfonskābes {6-(2-hidroksi-etoksi)-5-(2-metoksi-fenoksi)-2-[2-(1H-tetrazol-5-il)-piridīn-4-il]-pirimidīn-4-il}-amīda nātrija sāls	Aneirismāla subarahnoidāla asinsizplūduma ārstēšana
Lithuanian	5-metil-piridino-2-sulfono rūgšties {6-(2-hidroksi-etoksi)-5-(2-metoksi-fenoksi)-2 [-(1H-tetrazol-5-il)-piridin-4-il]-pirimidin-4-il}-natrio amido druska	Aneurizminio subarachnoidinio kraujavimo gydymas
Polish	5-metylopyridyno-2-sulfonowego kwasu {6-(2-hydroksyetoksy)-5-(2-metoksyfenoksy)-2-[2-(1H-tetrazol-5-ylo)-pirydyn-4-ylo]-pirymidyn-4-ylo}-amidu sól sodowa	Leczenie krwawienia z tętniaka podpajęczynówkowego
Portuguese	Ácido 5-metil-piridina-2-sulfónico Sal de sódio de {6-(2-hidroxi-etoxi)-5-(2-metoxi-fenoxi)-2-[2-(1H-tetrazol-5-il)-piridina-4-il]-pirimidina-4-il}-amida	Tratamento da hemorragia sub-aracnóideia aneurismática
Slovak	5-metyl-pyridín-2-sulfonová kyselina (6-(2(-hydroxy-etoxy)-5-(2-metoxy-fenoxy)-2-[2-(1H-tetrazol-5-yl)-pyridín-4-yl]-pyrimidín-4-yl)-amid sodná soľ	Liečba aneuryzmálneho subarachnoidálneho krvácania
Slovenian	5-metil-piridin-2-sulfonska kislina {6(2-metoksi-fenoksi)-2-[2-(1H-tetrazol-5-il)-piridin-4-il]-pirimidin-4-il}-amid-natrijeva sol	Zdravljenje anevrizmalne subarahnoidalne krvavitve
Spanish	Ácido 5-metil-piridina-2-sulfónico Sal de sodio de {6-(2-hidroxi-etoxi)-5-(2-metoxi-fenoxi)-2-[2-(1H-tetrazol-5-il)-piridin-4-il]-pirimidin-4-il}-amida	Tratamiento de la hemorragia subaracnoidea por rotura de aneurisma
Swedish	5-metylpyridin-2-sulfonsyra, {6-(2-hydroxietoxi)-5-(2-metoxifenoxi)-2-[2-(1H-tetrazol-5-yl)-pyridin-4-yl]-pyrimidin-4-yl}-amid, natriumsalt	Behandling av aneurysmal subaraknoidalblödning