

5 February 2015
EMA/COMP/658320/2009 Rev.2
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

N-[6-(*cis*-2,6-dimethylmorpholin-4-yl)pyridine-3-yl]-2-methyl-4'-(trifluoromethoxy)[1,1'-biphenyl]-3-carboxamide for the treatment of naevoid basal cell carcinoma syndrome (Gorlin syndrome)

First publication	8 December 2009
Rev.1: withdrawal from the Community Register	18 February 2013
Rev.2: sponsor's change of address	5 February 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.	

Please note that this product was withdrawn from the Community Register of designated Orphan Medicinal Products in January 2013 on request of the Sponsor.

On 25 November 2009, orphan designation (EU/3/09/697) was granted by the European Commission to Novartis Europharm Limited, United Kingdom, for N-[6-(*cis*-2,6-dimethylmorpholin-4-yl)pyridine-3-yl]-2-methyl-4'-(trifluoromethoxy)[1,1'-biphenyl]-3-carboxamide for the treatment of naevoid basal cell carcinoma syndrome (Gorlin syndrome).

What is naevoid basal cell carcinoma syndrome (Gorlin syndrome)?

Naevoid basal cell carcinoma syndrome (also known as Gorlin syndrome) is a hereditary genetic disease that affects mostly the skin and the connective tissue (the tissue that supports the skin and internal organs). Gorlin syndrome is caused by an abnormality in a chromosome, chromosome 9. As a result, cells start to grow uncontrollably and form tumours.

Patients with Gorlin syndrome have a predisposition for basal cell carcinomas (a slow-growing type of skin cancer), which often develop early in life. Other symptoms are skin problems, including cysts on the jaw, and bone abnormalities.

Gorlin syndrome is a long-term debilitating disease because of the development of a large number of basal cell carcinomas leading to different types of deformities.

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

At the time of designation, Gorlin syndrome affected less than 0.2 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 10,000 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 time of designation, basal cell carcinoma in Gorlin syndrome was mainly treated with surgery. Other treatments included topical chemotherapy (medicines to treat cancer given locally, on the skin) and photodynamic therapy. This is a method of treatment that uses light to activate a 'photosensitising' agent, which becomes toxic when exposed to light. In addition, patients with Gorlin syndrome were given genetic counselling and general support.

The sponsor has provided sufficient information to show that N-[6-(*cis*-2,6-dimethylmorpholin-4-yl)pyridine-3-yl]-2-methyl-4'-(trifluoromethoxy)[1,1'-biphenyl]-3-carboxamide might be of significant benefit for patients with Gorlin syndrome because it has a new mode of action and early studies in experimental models indicate that it might improve the overall outcome of patients with Gorlin syndrome. In addition, it may contribute to patients' quality of life by reducing the need for surgery. The medicine will be available as a cream. These assumptions 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?

In patients with Gorlin syndrome, the abnormality in chromosome 9 causes a protein called PTCH1 to lose control over another protein, called SMO. As a consequence, SMO becomes too active in the body. SMO is one of the proteins that control cell growth and division. N-[6-(*cis*-2,6-dimethylmorpholin-4-yl)pyridine-3-yl]-2-methyl-4'-(trifluoromethoxy)[1,1'-biphenyl]-3-carboxamide is expected to work by blocking SMO. This is expected to control cell growth and division and prevent the formation of basal cell carcinomas in patients with this disease.

What is the stage of development of this medicine?

The effects of N-[6-(*cis*-2,6-dimethylmorpholin-4-yl)pyridine-3-yl]-2-methyl-4'-(trifluoromethoxy)[1,1'-biphenyl]-3-carboxamide have been evaluated in experimental models.

At the time of orphan designation, clinical trials with the designated product in patients with Gorlin syndrome were ongoing.

At the time of submission for orphan designation, this medicine was not authorised anywhere in the EU for Gorlin syndrome or designated as orphan medicinal product elsewhere for this condition.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 7 October 2009 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 504,800,000 (Eurostat 2009).

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	N-[6-(cis-2,6-dimethylmorpholin-4-yl)pyridine-3-yl]-2-methyl-4'-(trifluoromethoxy)[1,1'-biphenyl]-3-carboxamide	Treatment of naevoid basal cell carcinoma syndrome (Gorlin syndrome)
Bulgarian	N-[6-(цис-2,6-диметилморфолин-4-ил)пиридин-3-ил]-2-метил-4'-(трифлуорометокси)[1,1'-бифенил]-3-карбоксамид	Лечение на синдром на Gorlin - невоидна базалноклетъчна карцинома
Czech	N-[6-(cis-2,6-Dimethylmorpholin-4-yl)pyridin-3-yl]-2-methyl-4'-(trifluoromethoxy)[1,1'-bifenyl]-3-karboxamid	Léčba nevoidního basalioidního karcinomu (Gorlin syndrome)
Danish	N-[6-(cis-2,6-Dimethylmorpholin-4-yl)pyridin-3-yl]-2-methyl-4'-(trifluoromethoxy)[1,1'-biphenyl]-3-carboxamid	Behandling af nevoid basalcelle carcinom syndrom (Gorlin syndrom)
Dutch	N-[6-(cis-2,6-Dimethylmorpholin-4-yl)pyridine-3-yl]-2-methyl-4'-(trifluoromethoxy)[1,1'-bifenyl]-3-carboxamide	Behandeling van naevoid basaalcelcarcinoom syndroom (Gorlin syndroom)
Estonian	N-[6-(tsis-2,6-dimetüülmorfoliin-4-üül)püridiin-3-üül]-2-metüül-4'-(trifluorometoksü)[1,1'-bifenüül]-3-karboksamiid	Nevoidse basaarakulise kartsinoomi sündroomi (Gorlini sündroom) ravi
Finnish	N-[6-(cis-2,6-dimetyylimorfolin-4-yyli)pyridin-3-yyli]-2-metyyli-4'-(trifluorometoksi)[1,1'-bifenyli]-3-karboksamidi	Nevoidi tyvisolukarsinoomaoireyhtymän (Gorlinin oireyhtymän) hoito
French	N-[6-(cis-2,6-diméthylmorpholine-4-yl)pyridine-3-yl]-2-méthyl-4'-(trifluorométhoxy)[1,1'-biphényl]-3-carboxamide	Traitement de la naevomatose basocellulaire (syndrome de Gorlin)
German	N-[6-(cis-2,6-Dimethylmorpholin-4-yl)pyridin-3-yl]-2-methyl-4'-(trifluoromethoxy)[1,1'-biphenyl]-3-carboxamid	Behandlung des naevoiden Basalioms (Gorlin-Syndrom)
Greek	N-[6-(cis-2,6-διμεθυλμορφολιν-4-υλ) πυριδιν-3-υλ]-2-μεθυλ-4'-(τριφθορομεθοξυ)[1,1'-διφενυλ]-3-καρβοξαμίδη	Σύνδρομο σπιλοειδούς βασικοκυτταρικού καρκινώματος (σύνδρομο Gorlin)
Hungarian	N-[6-(cis-2,6-dimetilmorfolin-4-il)piridin-3-il]-2-metil-4'-(trifluorometoxi)[1,1'-bifenil]-3-carboxamid	Basalsejtes naevoid carcinoma szindróma (Gorlin-szindróma) kezelése
Italian	N-[6-(cis-2,6-dimetilmorfolin-4-il)piridin-3-il]-2-metil-4'-(trifluorometossi)[1,1'-bifenil]-3-carbossamide	Trattamento della sindrome del carcinoma nevoide a cellule basali, (sindrome di Gorlin)
Latvian	N-[6-(cis-2,6-dimetilmorfolīn-4-il)piridīn-3-il]-2-metil-4'-(trifluorometoksi)[1,1'-bifenil]-3-karboksamīds	Bazālo nevus šūnu karcinomas sindroma (Gorlin sindroma) ārstēšanai
Lithuanian	N-[6-(cis-2,6-dimetilmorfolin-4-yl)piridino-3-yl]-2-metil-4'-(trifluorometoksi)[1,1'-bifenil]-3-karboksamidas	Apgamo pamatinio sluoksnio ląstelių karcinomos sindromo (Gorlin sindromo) gydymas

¹ At the time of designation

Language	Active ingredient	Indication
Maltese	N-[6-(cis-2,6-dimethylmorpholin-4-yl)pyridine-3-yl]-2-methyl-4'-(trifluoromethoxy)[1,1'-biphenyl]-3-carboxamide	Kura tas-sindrome ta' karċinoma taċ-ċelluli bażali nevojdi (sindrome ta' Gorlin)
Polish	N-[6-(cis-2,6-dimetylo-morfolin-4-yl)pirydyno-3-yl]-2-metylo-4'-(trifluorometoksy)[1,1'-biphenyl]-3-carboksamid	Leczenie zespołu nabłoniaków znamionowych (Zespół Gorlina)
Portuguese	N-[6-(cis-2,6-Dimetilmorfolina-4-il)piridina-3-il]-2-metil-4'-(trifluorometoxi)[1,1'-bifenil]-3-carboxamida	Síndrome dos carcinomas basocelulares nevídeos (síndrome de Gorlin)
Romanian	N-[6-(cis-2,6-dimetilmorfolină-4-il)piridină-3-il]-2-metil-4'-(trifluorometoxi)[1,1'-bifenil]-3-carboxamidă	Tratamentul sindromului carcinomului nevilor bazocelulari (sindromul Gorlin)
Slovak	N-[6-(cis-2,6-dimetylmorfolín-4-yl)pyridín-3-yl]-2-metyl-4'-(trifluorometoxy)[1,1'-bifenyl]-3-karboxamid	Liečba syndrómu névoidného bazaliómu (Gorlinovho syndrómu)
Slovenian	N-[6-(cis-2,6-dimetilmorfolin-4-il)piridin-3-il]-2-metil-4'-(trifluorometoksi)[1,1'-bifenil]-3-karboksamid	Zdravljenje sindroma nevoidnih bazalnoceličnih karcinomov (Gorlinov karcinom),
Spanish	N-[6-(cis-2,6-dimetilmorfolin-4-il)piridina-3-il]-2-metil-4'-(trifluorometoxi)[1,1'-bifenil]-3-carboxamida	Síndrome del carcinoma nevoide de células basales (SCNCB) (síndrome de Gorlin)
Swedish	N-[6-(cis-2,6-Dimetylmorfolin-4-yl)pyridin-3-yl]-2-metyl-4'-(trifluorometoxy)[1,1'-bifenyl]-3-karboxamid	behandling av nevoid basalcell karcinom syndrom (Gorlins syndrom)
Norwegian	N-[6-(cis-2,6-dimetylmorfolin-4-yl)pyridin-3-yl]-2-metyl-4'-(trifluormetoksy)[1,1'-bifenyl]-3-karboksamid	Behandling av nevoid basalcellekarsinom syndrom (Gorlins syndrom)
Icelandic	N-[6-(cis-2,6-Dímethýlmorphólín-4-ýl)pýridín-3-ýl]-2-methýl-4'-(tríflúorómethoxý)[1,1'-bíphenýl]-3-carboxamíð	Meðferð fæðingarbletta grunnfrumukrabbameins heilkennis (Gorlin heilkenni)