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Public summary of opinion on orphan designation

Itraconazole for the treatment of naevoid basal-cell carcinoma syndrome (Gorlin syndrome)

On 23 August 2017, orphan designation (EU/3/17/1901) was granted by the European Commission to Mayne Pharma UK Limited, United Kingdom, for itraconazole for the treatment of naevoid basal-cell carcinoma syndrome (Gorlin syndrome).

What is naevoid basal-cell carcinoma syndrome?

Naevoid basal-cell carcinoma syndrome (also known as Gorlin syndrome) is a genetic condition where patients have a high risk of developing cancerous and non-cancerous (benign) tumours.

In people with Gorlin syndrome, the most common cancer is basal-cell carcinoma, a slow-growing type of skin cancer, which usually develops on the face, chest and back. Most people also develop non-cancerous tumours of the jaw which cause face swelling and problems with teeth. Skeletal problems in the spine, ribs and skull are also common.

Gorlin syndrome is a long-term debilitating condition because of the multiple tumours which can lead to deformities.

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

At the time of designation, Gorlin syndrome affected approximately 0.3 in 10,000 people in the European Union (EU). This was equivalent to a total of around 15,000 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, imiquimod, sonidegib and vismodegib were authorised in the EU for treating basal-cell carcinoma.

*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 515,700,000 (Eurostat 2017).

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The sponsor has provided sufficient information to show that itraconazole might be of significant benefit for patients with Gorlin syndrome. Early results from an ongoing study showed that it reduced tumour size in patients for whom current treatments did not work. 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?

Itraconazole has been used to treat fungal infections for several years. In Gorlin syndrome, it is expected to work by blocking 'the Hedgehog signalling pathway'. In Gorlin syndrome, the Hedgehog signalling pathway becomes abnormally active and leads to the growth and spread of the cancerous cells. Itraconazole is thought to attach to a protein called 'SMO', which is involved in activating the Hedgehog signalling pathway. By attaching to SMO, itraconazole is expected to block this pathway, thereby slowing down the growth and spread of the cancer cells in Gorlin syndrome.

What is the stage of development of this medicine?

The effects of itraconazole have been evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials with itraconazole in patients with Gorlin syndrome were ongoing.

At the time of submission, itraconazole was not authorised anywhere in the EU for Gorlin syndrome. Orphan designation of itraconazole 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 13 July 2017 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 languages[1], Norwegian and Icelandic

Language	Active ingredient	Indication
English	Itraconazole	Treatment of naevoid basal cell carcinoma syndrome (Gorlin syndrome)
Bulgarian	Итраконазол	Лечение на синдром на Gorlin-невоидна базалноклетъчна карцинома
Croatian	Itrakonazol	Liječenje sindroma nevoidnog karcinoma bazalnih stanica (ili Gorlinovog sindroma)
Czech	Itrakonazol	Léčba nevoidního basaliodního karcinomu (Gorlin syndrome)
Danish	Itraconazol	Behandling af nevoid basalcelle carcinom syndrom (Gorlin syndrom)
Dutch	Itraconazol	Behandeling van naevoid basaalcelcarcinoom syndroom (Gorlin syndroom)
Estonian	Itrakonasool	Nevoidse basaalrakulise kartsinoomi sündroomi (Gorlini sündroom) ravi
Finnish	Itrakonatsoli	Nevoidi tyvisolukarsinoomaoireyhtymän (Gorlinin oireyhtymän) hoito
French	Itraconazole	Traitement de la naevomatose basocellulaire (syndrome de Gorlin)
German	Itraconazol	Behandlung des n*aevoiden* Basalioms (Gorlin-Syndrom)
Greek	Ιτρακοναζόλη	Σύνδρομο σπιλοειδούς βασικοκυτταρικού καρκινώματος (σύνδρομο Gorlin)
Hungarian	Itrakonazol	Basalsejtes naevoid carcinoma szindróma (Gorlin-szindróma) kezelése
Italian	Itraconazolo	Trattamento della sindrome del carcinoma nevoide a cellule basali, (sindrome di Gorlin)
Latvian	Itrakonazols	Bazālo nevus šūnu karcinomas sindroma (Gorlin sindroma) ārstēšanai
Lithuanian	Itrakonazolas	Apgamo pamatinio sluoksnio ląstelių karcinomos sindromo (Gorlin sindromo) gydymas
Maltese	Itrakonazol	Kura tas-sindrome ta' karċinoma taċ-ċelluli bażali nevojdi (sindrome ta' Gorlin)
Polish	Itrakonazol	Leczenie zespół znamionowych nabłoniaków podstawnokomórkowych (Zespół Gorlina)
Portuguese	Itraconazol	Sindroma dos carcinomas basocelulares nevóides (sindrome de Gorlin)
Romanian	Itraconazol	Tratamentul sindromului carcinomului nevilor bazocelulari (sindromul Gorlin)
Slovak	Itrakonazol	Liečba syndrómu névoidného bazaliómu (Gorlinovho syndrómu)
Slovenian	Itrakonazol	Zdravljenje sindroma nevoidnih bazalnoceličnih karcinomov (Gorlinov karcinom),

[1] At the time of designation

Language	Active ingredient	Indication
Spanish	Itraconazol	Síndrome del carcinoma nevoide de células basales (SCNCB) (síndrome de Gorlin)
Swedish	Itrakonazol	behandling av nevoid basalcell karcinom syndrom (Gorlins syndrom)
Norwegian	Itrakonazol	Behandling av nevoid basalcellekarsinom syndrom (Gorlins syndrom)
Icelandic	Ítrakónazól	Meðferð fæðingarbletta grunnfrumukrabbameins heilkennis (Gorlin heilkenni)