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Public summary of opinion on orphan designation

Pyrazolo[1,5-a]pyrimidine, 3-[4-chloro-2-(4-morpholinyl)-5-thiazolyl]-7-(1-ethylpropyl)-2,5-dimethyl-pyrazolo[1,3-a]pyrimidine for the treatment of congenital adrenal hyperplasia

On 17 January 2018, orphan designation (EU/3/17/1968) was granted by the European Commission to RegIntel Limited, Ireland, for pyrazolo[1,5-a]pyrimidine, 3-[4-chloro-2-(4-morpholinyl)-5-thiazolyl]-7-(1-ethylpropyl)-2,5-dimethyl-pyrazolo[1,3-a]pyrimidine (also known as SPR001) for the treatment of congenital adrenal hyperplasia.

What is congenital adrenal hyperplasia?

Congenital adrenal hyperplasia is a group of inherited conditions where patients are unable to produce normal amounts of the steroid hormones cortisol and aldosterone. These hormones play an important role in responding to stress and regulating salt and water in the body. The hormones are produced by the adrenal glands, two small glands that are located above the kidneys. In patients with the condition, the adrenal glands produce male sex hormones instead of cortisol and aldosterone. Congenital adrenal hyperplasia can be caused by many different changes (mutations) in the genes controlling the production of cortisol and aldosterone.

Congenital adrenal hyperplasia is long-term debilitating and life-threatening condition due to a failure of the response to stress (adrenal insufficiency), altered amounts of salt and water in the body, low blood pressure, and early puberty in boys or development of masculine characteristics in girls, which can lead to growth stopping early and short stature.

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

At the time of designation, congenital adrenal hyperplasia affected less than 1 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 51,000 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 515,700,000 (Eurostat 2017).



What treatments are available?

At time of designation, several products to treat congenital adrenal hyperplasia were authorised in the EU. In particular, various steroid hormones were used to replace those which are insufficiently produced by the adrenal gland and to control the production of excess male sex hormones.

The sponsor has provided sufficient information to show that the medicine might be of significant benefit for patients with congenital adrenal hyperplasia. This is because early studies in patients showed reduced levels of male sex hormones and other substances associated with the condition, when the medicine was used in combination with the usual 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?

The production of steroid hormones by the adrenal glands is normally stimulated by another hormone called adrenocorticotrophic hormone (ACTH). In patients with congenital adrenal hyperplasia, the low levels of cortisol and aldosterone cause the body to make more ACTH, in an attempt to increase their production. However, because the adrenal glands are incapable of making these hormones, ACTH only stimulates the production of male sex hormones.

This medicine is expected to block the chemical switch that leads to the release of ACTH, thus lowering the amount of ACTH released. This action is expected to reduce the production of male sex hormones, and thereby relieve the symptoms of the condition and make it more responsive to other treatments.

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 the medicine in patients with congenital adrenal hyperplasia were ongoing.

At the time of submission, the medicine was not authorised anywhere in the EU for congenital adrenal hyperplasia or designated as an 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 December 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 languages¹, Norwegian and Icelandic

Language	Active ingredient	Indication
English	Pyrazolo[1,5-a]pyrimidine, 3-[4-chloro-2-(4-morpholinyl)-5-thiazolyl]-7-(1-ethylpropyl)-2,5-dimethyl-pyrazolo[1,3-a]pyrimidine	Treatment of congenital adrenal hyperplasia
Bulgarian	Пиразоло[1,5-а]пиримидин, 3-[4-хлоро-2-(4-морфолинил)-5-тиазолил]-7-(1-етилпропил)-2,5-диметил-пиразоло[1,3-а]пиримидин	Лечение на вродена надбъбречна хиперплазия
Croatian	Pirazolo[1,5-a]pirimidin, 3-[4-kloro-2-(4-morfolinil)-5-tiazolil]-7-(1-etilpropil)-2,5-dimetil-pirazolo[1,3-a]pirimidin	Liječenje kongenitalne adrenalne hiperplazije
Czech	Pyrazolo[1,5-a]pyrimidine, 3-[4-chloro-2-(4-morpholinyl)-5-thiazolyl]-7-(1-ethylpropyl)-2,5-dimethyl-pyrazolo[1,3-a]pyrimidin	Léčba vrozené hyperplazie nadledvin
Danish	Pyrazolo[1,5-a]pyrimidin, 3-[4-chloro-2-(4-morpholinyl)-5-thiazolyl]-7-(1-ethylpropyl)-2,5-dimethyl-pyrazolo[1,3-a]pyrimidin	Behandling af medfødt binyrebarkhyperplasi
Dutch	Pyrazolo[1,5-a]pyrimidine, 3-[4-chloro-2-(4-morpholinyl)-5-thiazolyl]-7-(1-ethylpropyl)-2,5-dimethyl-pyrazolo[1,3-a]pyrimidine	Behandeling van congenitale bijnierhyperplasia
Estonian	Pürazolo[1,5-a]pürimidiin, 3-[4-kloro-2-(4-morfolinüül)-5-tiazolüül]-7-(1-etüülpropüül)-2,5-dimetüül-pürazolo[1,3-a]pürimidiin	Kaasasündinud neerupealise hüperplaasia ravi
Finnish	Pyratsolo[1,5-a]pyrimidiini, 3-[4-kloro-2-(4-morfolinyyli)-5-tiatsolyyli]-7-(1-etyylipropyyli)-2,5-dimetyyli-pyratsolo[1,3-a]pyrimidini	Lisämunuaisen synnyynnäisen liikakasvun hoito
French	Pyrazolo[1,5-a]pyrimidine, 3-[4-chloro-2-(4-morpholinyl)-5-thiazolyl]-7-(1-ethylpropyl)-2,5-dimethyl-pyrazolo[1,3-a]pyrimidine	Traitement de l'hyperplasie surrénale congénitale
German	Pyrazolo[1,5-a]pyrimidin, 3-[4-chloro-2-(4-morpholinyl)-5-thiazolyl]-7-(1-ethylpropyl)-2,5-dimethyl-pyrazolo[1,3-a]pyrimidin	Behandlung der Kongenitalen Adrenalen Hyperplasie
Greek	Πυραζόλο[1,5-α]πυριμιδίνη, 3-[4-χλωρο-2-(4-μορφολινο)-5-θειαζολυλ]-7-(1-αιθυλπροπυλ)-2,5-διμεθυλ-πυραζολο[1,3-α]πυριμιδίνη	Θεραπεία της συγγενούς επινεφριδιακής υπερπλασίας
Hungarian	Pirazolo[1,5-a]piyrimidin, 3-[4-kloro-2-(4-morfolinil)-5-tiazolil]-7-(1-etilpropil)-2,5-dimetil-pirazolo[1,3-a]pirimidin	Congenitalis adrenalis hyperplasia kezelése
Italian	Pirazol[1,5-a]pirimidina, 3-[4-cloro-2-(4-morfolinil)-5-tiazolil]-7-(1-etilpropil)-2,5-dimetil-pirazol[1,3-a]pirimidina	Trattamento dell'iperplasia surrenale congenita
Latvian	Pirazol[1,5-a]pirimidīna, 3-[4-hloro-2-(4-morfolinil)-5-tiazolil]-7-(1-etilpropil)-2,5-dimetil-pirazol[1,3-a]pirimidīns	Iedzimtas virsnieru hiperplāzijas ārstēšana

¹ At the time of designation

Language	Active ingredient	Indication
Lithuanian	Pirazolo[1,5-a]pirimidino,3-[4-chloro-2-(4-morfolinil)-5-tiazolil]-7-(1-etilpropil)-2,5-dimetil-pirazolo[1,3-a]pirimidinas	Įgimtos antinksčių hiperplazijos gydymas
Maltese	Pirazolo[1,5-a]pirimidina, 3-[4-kloro-2-(4-morfolinil)-5-tiazolil]-7-(1-etilpropil)-2,5-dimetil-pirazolo[1,3-a]pirimidina	Kura ta' l-iperplasia adrenali kongenitali
Polish	Pirazolo[1,5-a]pirimidina, 3-[4-chloro-2-(4-morfolinyl)-5-tiazolyl]-7-(1-etylpropyl)-2,5-dimetyl-pirazolo[1,3-a]pirimidina	Leczenie wrodzonego przerostu nadnerczy
Portuguese	Pirazolo[1,5-a]pirimidina, 3-[4-cloro-2-(4-morfolinil)-5-tiazolil]-7-(1-etilpropil)-2,5-dimetil-pirazolo[1,3-a]pirimidina, pirazolo[1,5-a]pirimidina	Tratamento da hiperplasia adrenal congenita
Romanian	Pirazolo[1,5-a]pirimidin, 3-[4-cloro-2-(4-morfolinil)-5-tiazolil]-7-(1-etilpropil)-2,5-dimetil-pirazolo[1,3-a]pirimidină	Tratamentul hiperplaziei congenitale corticosuprenale
Slovak	Pyrazolo[1,5-a]pyrimidín, 3-[4-chloro-2-(4-morfolinyl)-5-tiazolyl]-7-(1-etylpropyl)-2,5-dimetyl-pyrazolo[1,3-a]pyrimidín	Liečba kongenitálnej nadobličkovej hyperplázie
Slovenian	Pirazol[1,5-a]pirimidin, 3-[4-kloro-2-(4-morfolinil)-5-tiazolil]-7-(1-etilpropil)-2,5-dimetil-pirazolo[1,3-a]pirimidin	Kongenitalna adrenalna hiperplazija
Spanish	Pirazolo[1,5-a]pirimidina, 3-[4-chloro-2-(4-morfolinil)-5-tiazolil]-7-(1-etilpropil)-2,5-dimetil-pirazolo[1,3-a]pirimidina	Tratamiento de la hiperplasia suprarrenal congénita
Swedish	Pyrazolo[1,5-a]pyrimidin, 3-[4-chloro-2-(4-morpholinyli)-5-thiazolyli]-7-(1-etylpropyl)-2,5-dimetyl-pyrazolo[1,3-a]pyrimidin	Behandling av adrenogenitalt syndrom
Norwegian	Pyrazolo[1,5-a]pyrimidin, 3-[4-kloro-2-(4-morfolinyl)-5-tiazolyl]-7-(1-etylpropyl)-2,5-dimetyl-pyrazolo[1,3-a]pyrimidin	Behandling av kongenitt binyrebarkhyperplasi
Icelandic	Pýrazóló[1,5-] pýrimídín, 3-[4-klóró-2(4-morfólíyl) 7-(etýlprópyl)-2,5-dímetyl-pýrazóló [1,3 -a] pýrimídín	Meðfædd nýrnahefðu hyperplasia