



Committee for Orphan Medicinal Products

**Public summary of
positive opinion for orphan designation
of
riloncept
for the treatment of cryopirin-associated periodic syndromes
(Familial Cold Urticaria Syndrome (FCUS), Muckle-Wells Syndrome (MWS),
and Neonatal Onset Multisystem Inflammatory Disease (NOMID),
also known as Chronic Infantile Neurological Cutaneous Articular Syndrome (CINCA))**

On 10 July 2007, orphan designation (EU/3/07/456) was granted by the European Commission to Regeneron UK Limited, United Kingdom, for riloncept for the treatment of cryopirin-associated periodic syndromes (Familial Cold Urticaria Syndrome (FCUS), Muckle-Wells Syndrome (MWS), and Neonatal Onset Multisystem Inflammatory Disease (NOMID), also known as Chronic Infantile Neurological Cutaneous Articular Syndrome (CINCA)).

What is cryopirin-associated periodic syndromes (Familial Cold Urticaria Syndrome (FCUS), Muckle-Wells Syndrome (MWS), and Neonatal Onset Multisystem Inflammatory Disease (NOMID), also known as Chronic Infantile Neurological Cutaneous Articular Syndrome (CINCA))?

Cryopirin is a protein encoded by the CIASI/NAPL3 gene that is involved in the activation of a signalling compound called IL-1 β . This compound is very important for the inflammatory process (the body's response to an infection). In patients affected by cryopirin-associated periodic syndromes, the CIASI/NAPL3 gene is defective, which leads to an excessive activity of the cryopirin protein and subsequently to an excessive signalling by IL-1 β . Symptoms of the resulting systemic (covering the entire body) inflammation include periods of high fever, rash, headaches, fatigue and joint problems. In the long run the condition can cause further complications such as deafness. Cryopirin-associated periodic syndromes are chronically debilitating.

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

At the time of designation, cryopirin-associated periodic syndromes (Familial Cold Urticaria Syndrome (FCUS), Muckle-Wells Syndrome (MWS), and Neonatal Onset Multisystem Inflammatory Disease (NOMID), also known as Chronic Infantile Neurological Cutaneous Articular Syndrome (CINCA)) affected less than 0.05 in 10,000 in 10,000 people in the European Union (EU)*. This is equivalent to a total of fewer than 2,500 people, and is below the threshold for orphan designation, which is 5 people in 10,000. This is based on the information provided by the sponsor and 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 based on data from the European Union (EU 27), Norway, Iceland and Lichtenstein. This represents a population of 498,000,000 (Eurostat 2006).

What treatments are available?

There are no medicinal products authorised for the treatment of the condition in the Community. Severe flares of the disease can sometimes be treated symptomatically with anti-inflammatory products.

How is this medicine expected to work?

Rilonacept is structurally similar to the IL-1 β receptor (the protein that IL-1 β interacts with and through which it signals). Rilonacept binds to IL-1 β and thus inhibits its harmful activity of IL-1 β .

What is the stage of development of this medicine?

The effects of rilonacept were evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials in patients with cryopyrin-associated periodic syndromes were ongoing.

Rilonacept was not authorised anywhere worldwide for the treatment of cryopyrin-associated periodic syndromes nor designated as orphan medicinal product elsewhere for this condition, at the time of submission.

According to Regulation (EC) No 141/2000 of 16 December 1999, the Committee for Orphan Medicinal Products (COMP) adopted on 31 May 2007 a positive opinion recommending the grant of the above-mentioned designation.

Update: Rilonacept (Arcalyst) has been authorised in the EU since 23 October 2009 for the treatment of Cryopyrin-Associated Periodic Syndromes (CAPS) with severe symptoms, including Familial Cold Autoinflammatory Syndrome (FCAS) and Muckle-Wells Syndrome (MWS), in adults and children aged 12 years and older.

For more information on Arcalyst, see:

www.emea.europa.eu/humandocs/Humans/EPAR/arcalyst/arcalyst.htm

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 Community) 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.

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**Translations of the active ingredient and indication in all EU languages
and Norwegian and Icelandic**

Language	Active Ingredient	Indication
English	Rilonacept	Treatment of cryopirin-associated periodic syndromes (Familial Cold Urticaria Syndrome (FCUS), Muckle-Wells Syndrome (MWS), and Neonatal Onset Multisystem Inflammatory Disease (NOMID), also known as Chronic Infantile Neurological Cutaneous Articular Syndrome (CINCA))
Bulgarian	Рилонацепт	Лечение на периодични синдроми, свързани с криопирин (синдром на фамилна студова уртикария (FCAS), синдром на Muckle-Wells (MWS) и мултисистемно възпалително заболяване с начало в неонаталния период (NOMID), известно също като хроничен инфантилен неврологично-кожно-ставен синдром (CINCA))
Czech	Rilonacept	Léčba kryopirin- asociovaného syndromu (Familiárního chladového autozánětlivého syndromu, FCAS) Muckle-Wellsova syndromu (MWS), , multisystémového zánětlivého onemocnění se začátkem v novorozeneckém věku (NOMID) / chronického infantilního neurologického kožního a kloubního syndromu (CINCA)
Danish	Rilonacept	Behandling af kryopyrin-associerede periodiske syndromer (familiært kulde-urticaria syndrom (FCUS), Muckle-Wells syndrom (MWS), og systemisk inflammatorisk sygdom med neonatal debut (NOMID) også kendt som kronisk infantil neurologisk hud- og ledsyndrom (CINCA))
Dutch	Rilonacept	Behandeling van cryopirine geassocieerde periodieke syndromen (familiaal koude-geïnduceerd auto-inflammatoir syndroom [FCAS], Muckle-Wells syndroom [MWS], en neonatale multisystemische inflammatoire aandoening [NOMID], ook omschreven als chronisch infantiel neurologisch cutaan en articulair [CINCA] syndroom).
Estonian	Rilonacept	Krüopiriiniga seotud perioodiliste sündroomide (perekondliku külmast tingitud urtikaaria sündroomi (FCUS), Muckle-Wells sündroomi (MWS), ja neonataalse algusega multisüsteemse põletikulise haiguse (NOMID), tuntud ka kui kroonilise infantiilse neuroloogis-kutaanse-artikulaarse sündroomi (CINCA)) raviks
Finnish	Rilonasepti	Kryopiriiniin liittyvien periodisten oireyhtymien hoito (familiaalinen kylmäurtikaria (FCUS), Muckle-Wellsin oireyhtymä (MWS), imeväisiässä alkava multisysteeminen inflammatorinen tauti (NOMID), joka tunnetaan myös nimellä imeväisiän krooninen neurologinen kutaaninen artikulaarinen oireyhtymä (CINCA))
French	Rilonacept	Traitement des syndromes périodiques associés à la cryopyrine (urticair familial au froid (FCAS), syndrome de Muckle-Wells (MWS), maladie systémique inflammatoire à début néo-natal (NOMID) aussi appelée syndrome chronique infantile neurologique cutané et articulaire (CINCA))

German	Rilonacept	Behandlung von Cryopirin-assoziiertem Syndrom (familiäres autoinflammatorisches Kälte-Syndrom (FACS), Muckle-Wells-Syndrom (MWS) und der multisystemischen entzündlichen Erkrankung mit Beginn im Neugeborenenalter (NOMID), auch bekannt als chronisch infantiles neuro-dermo-artikuläres Syndrom (CINCA))
Greek	Rilonacept	Θεραπεία των περιοδικών συνδρόμων που συσχετίζονται με την κρυοπυρίνη (του οικογενούς συνδρόμου κνησμού μετά από έκθεση στο ψύχος (FCUS), του συνδρόμου Muckle-Wells (MWS), και της πολυσυστηματικής νόσου νεογνικής έναρξης (NOMID) επίσης γνωστή ως χρόνια βρεφικό φλεγμονώδες νευρολογικό δερματικό αρθρικό σύνδρομο (CINCA))
Hungarian	Rilonacept	Cryopirin függő periodikus szindrómák (Familiáris hideg urticaria szindróma), Muckle-Wells szindróma (MWS), újszülöttkori multisisztémás gyulladós betegség, más néven krónikus gyermekkori neuro-dermo-artikuláris szindróma kezelése
Italian	Rilonacept	Trattamento delle sindromi periodiche associate a criopirino-patia (sindrome di Muckle-Wells (MWS), orticaria da freddo (FCAS), malattia infiammatoria multisistemica ad insorgenza neonatale (NOMID)/sindrome cronica infantile neurologica cutanea ed articolare (CINCA))
Latvian	Rilonacepts	Ar kriopirīnu saistītu periodisku sindromu Makla un Velsa sindroma (MWS- <i>Muckle-Wells Syndrome</i>), ģimenes aukstuma nātrene sindroma (FCUS- <i>Familial Cold Urticaria Syndrome</i>) un jaundzimušo multisistēmiskās iekaisuma slimības (NOMID- <i>Neonatal Onset Multisystem Inflammatory Disease</i>) un hroniska zīdaiņu neiroloģiskā ādas un locītavu sindroma (CINCA- <i>Chronic Infantile Neurological Cutaneous Articular Syndrome</i>) ārstēšanai.
Lithuanian	Rilonaceptas	Periodinių sindromų, asocijuotų kriopirino (Šeiminio šalčio urtikarijos sindromo – ŠŠUS/ angl. FCUS - Familial Cold Urticaria Syndrome; Muckle-Wells sindromo (MWS) ir Daugiasisteminės uždegiminės ligos naujagimystės pradžioje – DULNP/angl. NOMID - Neonatal Onset Multisystem Inflammatory Disease, taip pat žinomos kaip Lėtinio kūdikių neurologinio, odos ir sąnarių sindromo – LKNOSS/angl. CINCA -Chronic Infantile Neurological Cutaneous Articular Syndrome) gydymas
Maltese	Rilonacept	Kura tas-sindromi perjodiċi assoċjati mal-cryopyrin (sindrome ta' l-urtikarja tal-kesha (FCAS), sindrome ta' Muckle-Wells (MWS), u l-marda ta' infjammazzjoni multisistemika li tibda mat-twelid (NOMID), magħrufa ukoll bħala sindrome kronika infantili newroloġika, tal-ġilda u artikulari (CINCA))

Polish	Rilonacept	Leczenie okresowego zespołu zależnego od kriopiryny (rodzina zimna pokrzywka – ang. familial cold autoinflammatory syndrome – FCAS), zespołu Muckle-Wells’a (ang. Muckle-Wells Syndrome - MWS) i noworodkowej zapalnej choroby wieloukładowej (ang. neonatal-onset multisystem inflammatory disease – NOMID) znanej również jako przewlekły niemowlęcy zespół neurologiczno-skróno-stawowy (ang. chronic infantile neurological cutaneous and articular syndrome - CINCA)
Portuguese	Rilonacept	Tratamento dos síndromes periódicos associados à criopirina (Síndrome de urticária ao frio familiar [FCUS], Síndrome de Muckle-Wells [MWS], e Doença inflamatória multissistémica de início neonatal (NOMID), também conhecida por Síndrome neuro-cutâneo-articular crónico do lactente(CINCA)
Romanian	Rilonacept	Tratamentul sindroamelor periodice asociate criopirinei (sindromul familial al urticariei la rece=FCUS, sindromul Muckle-Wells=MWS) și a bolii inflamatorii multisistemice cu debut neonatal, cunoscută și ca sindromul cronic infantil neurologic articular și cutanat (CINCA).
Slovak	Rilonacept	Liečba periodického syndrómu spojeného s kryopirínom (syndróm familiárnej chladovej žihľavky (FCUS), Muckleovho-Wellsovho syndrómu (MWS) a multisystémovej zápalovej choroby s nástupom v novorodeneckom veku (NOMID)/chronického neurologického, kožného a kĺbového syndrómu detí (CINCA)
Slovenian	Rilonacept	Zdravljenje s kriopirinom povezanih sindromov (sindrom familiarne urtikarije na mraz (FCUS), sindrom Muckle-Wells (MWS) in multisistemska vnetna bolezen novorojenčkov (NOMID) znana tudi kot kronični infantilni nevrološki kožni in sklepni sindrom (CINCA)
Spanish	Rilonacept	Tratamiento del los síndromes periódicos asociados a la criopirina (síndrome de Muckle-Wells (MWS), síndrome autoinflamatorio familiar inducido por frío (FCAS), y enfermedad neonatal multissistémica inflamatoria (NOMID), también denominada síndrome articular y cutáneo neurológico infantil crónico (CINCA))
Swedish	Rilonacept	Behandling av cryopirin-förbindade periodiska syndrom (familjärt autoinflammatoriskt köldsyndrom (FCAS), Muckle-Wells syndrom (MWS), och systemisk inflammatorisk sjukdom med neonatal debut (NOMID)/kroniskt neurologiskt, hud och ledsyndrom hos barn (CINCA)),
Norwegian	Rilonacept	Behandling av cryopyrin-assosierte periodiske syndromer (familiært kuldeurticaria-syndrom (FCUS), Muckle-Wells syndrom (MWS), og neonatal multisystem inflammatorisk sykdom (NOMID)/kronisk infantilt nevrologisk hud- og leddsyndrom (CINCA)
Icelandic	Rilónacept	Til meðferðar á crýópýrín-tengdum lotubundnum heilkennum (ættgengur kulda ofsabjúgur (FCUS), Muckle-Wells heilkenni (MWS), og fjölkerfabólgujúkdómi hjá nýburum (NOMID), einnig þekkt sem langvarandi taugarænt húð- og liðaheilkenni hjá ungbörnum (CINCA)