7 May 2013
EMA/COMP/175315/2013
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

(S)-3-(1-(9H-purin-6-ylamino)ethyl)-8-chloro-2-phenylisoquinolin-1(2H)-one for the treatment of chronic lymphocytic leukaemia/small lymphocytic lymphoma

On 26 April 2013, orphan designation (EU/3/13/1125) was granted by the European Commission to Voisin Consulting S.A.R.L, France, for (S)-3-(1-(9H-purin-6-ylamino)ethyl)-8-chloro-2-phenylisoquinolin-1(2H)-one for the treatment of chronic lymphocytic leukaemia/small lymphocytic lymphoma.

What is chronic lymphocytic leukaemia/small lymphocytic lymphoma?

Chronic lymphocytic leukaemia (CLL) is cancer of a type of white blood cell called B-lymphocytes. In this disease, the lymphocytes multiply too quickly and live for too long, so that there are too many of them circulating in the blood. The cancerous lymphocytes look normal, but they are not fully developed and do not work properly. Over a period of time, the abnormal cells replace the normal white cells, red cells and platelets (components that help the blood to clot) in the bone marrow (the spongy tissue inside the large bones in the body).

The disease known as 'small lymphocytic lymphoma' (SLL) is essentially the same disease as CLL. The name SLL is normally used when the cancer cells are located mainly in the lymph nodes.

CLL/SLL is the most common type of leukaemia and mainly affects older people. It is rare in people under the age of 40 years. CLL/SLL is a long-term debilitating and life-threatening disease because some patients develop severe infections.

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

At the time of designation, CLL/SLL affected less than 3.5 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 180,000 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 27), Norway, Iceland and Liechtenstein. This represents a population of 509,000,000 (Eurostat 2013).

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7418 8416
E-mail info@ema.europa.eu **Website** www.ema.europa.eu
An agency of the European Union

What treatments are available?

Treatment for CLL/SLL is complex and depends on a number of factors, including the extent of the disease, whether it has been treated before, and the patient's age, symptoms and general state of health. Patients whose CLL/SLL is not causing any symptoms or is only getting worse very slowly may not need treatment. Treatment for CLL/SLL is only started if symptoms become troublesome. At the time of designation, the main treatment for CLL/SLL was chemotherapy (medicines to treat cancer).

The sponsor has provided sufficient information to show that this medicine might be of significant benefit for patients with CLL/SLL because early studies show that it might improve the outcome of patients whose disease does not respond to or has come back after previous treatment. 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?

This medicine blocks the effects of two enzymes called PI3K-delta and PI3K-gamma. These are members of a family of proteins called phosphoinositide-3-kinase (PI3K) enzymes that play an important role in the growth, migration and survival of white blood cells. These enzymes are active in the abnormal lymphocytes of CLL/SLL patients, stimulating their growth and survival. By blocking the effects of these enzymes, the medicine is expected to reduce the growth and survival of the cancer cells.

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 CLL/SLL were ongoing.

At the time of submission, the medicine was not authorised anywhere in the EU for CLL/SLL 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 13 March 2013 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:

Voisin Consulting
3 rue des Longs Prés
92100 Boulogne-Billancourt
France
Telephone: +33 141 318 300
Telefax: +33 1 46 20 53 38
E-mail: orphan@voisinconsulting.com

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	(S)-3-(1-(9H-purin-6-ylamino)ethyl)-8-chloro-2-phenylisoquinolin-1(2H)-one	Treatment of chronic lymphocytic leukaemia/small lymphocytic lymphoma
Bulgarian	(S)-3-(1-(9H-пурин-6-иламино)етил)-8-хлоро-2-фенилизохинолин-1(2H)-едно	Лечение на хронична лимфоцитна левкемия/малък лимфоцитен лимфом
Czech	(S)-3-(1-(9H-purin-6-ylamino)ethyl)-8-chloro-2-fenylisochinolin-1(2H)-jedna	Léčba chronické lymfatické leukémie/lymfom z malých lymfocytů
Danish	(S)-3-(1-(9H-purin-6-ylamino)ethyl)-8-chlor-2-phenylisoquinolin-1(2H)-on	Behandling af kronisk lymfocytær leukæmi/småcellet lymfocytært lymfom
Dutch	(S)-3-(1-(9H-purine-6-ylamino)ethyl)-8-chloor-2-fenylisochinoline-1(2H)-one	Behandeling van chronische lymfocytaire leukemie/kleincellig lymfocytair lymfoom
Estonian	(S)-3-(1-(9H-puriin-6-üülamino)etüül)-8-kloro-2-fenüülisokinoliin-1(2H)-oon	Kroonilise lümfoidleukeemia/väike-lümfotsüütlümfoomi ravi
Finnish	(S)-3-(1-(9H-puriini-6-ylamino)etyyli)-8-kloori-2-fenyyli isokinoliini-1(2H)-oni	Kroonisen lymfosyyttileukemian ja pienisoluisen lymfosyyttisen lymfooman hoito
French	(S)-3-(1-(9H-purine-6-ylamino)éthyle)-8-chloro-2-phényl-isoquinoline-1(2H)-one	Traitement de la leucémie lymphoïde chronique/lymphome lymphocytaire à petites cellules
German	(S)-3-(1-(9H-Purin-6-ylamino)Ethyl)-8-Chlor-2-Phenylisochinolin-1(2H)-on	Behandlung der chronisch-lymphatischen Leukämie/kleinzellig lymphozytisches Lymphom
Greek	(S)-3-(1-(9H-πουρινο-6-υλαμινο)αιθυλο)-8-χλωρο-2-φαινυλοϊσοκινολιν-1(2H)-όνη	Θεραπεία της χρόνιας λεμφοκυτταρικής λευχαιμίας/λεμφώματος από μικρά λεμφοκύτταρα
Hungarian	(S)-3-(1-(9H-purin-6-ilamino)etil)-8-klór-2-fenil-izokinolin-1(2H)-egy	krónikus lymphocytás leukaemia/kissejtes lymphoma kezelése
Italian	(S)-3-(1-(9H-purin-6-ylammino)etil)-8-cloro-2-fenilisochinolino-1(2H)-one	Trattamento della leucemia linfatica cronica/linfoma linfocitico a piccole cellule
Latvian	(S)-3-(1-(9H-purīn-6-ilamino)etil)-8-hloro-2-fenilizokvinolīn-1(2H)-ons	Hroniskas limfocītiskās leikēmijas/mazās limfocītiskās limfomas ārstēšana
Lithuanian	(S)-3-(1-(9H-purino-6-ilamino)etilo)-8-chloro-2-fenilosokvinolinas-1(2H)-onas	Lėtinės limfocitinės leukemijos gydymas/smulkių limfocitų limfoma
Maltese	(S)-3-(1-(9H-purin-6-ylamino)ethyl)-8-chloro-2-phenylisoquinolin-1(2H)-one	Kura tal-lewkimja limfoċitika kronika/limfoma limfoċitika żgħira

[1] At the time of designation

Language	Active ingredient	Indication
Polish	(S)-3-(1-(9H-puryno-6-ylamino)etylo)-8-chloro-2-fenyloizochinolin-1(2H)-on	Leczenie przewlekłej białaczki limfatycznej/chłoniaka z małych limfocytów
Portuguese	(S)-3-(1-(9H-purina-6-ilamino)etil)-8-cloro-2-fenilisoquinolina-1(2H)-ona	Tratamento da leucémia linfocítica crónica/linfoma linfocítico de células B pequenas
Romanian	(S)-3-(1-(9H-purin-6-ilamino)etil)-8-clor-2-fenilizochinolin-1(2H)-onă	Tratamentul leucemiei limfoide cronice/limfomului limfocitic cu celule mici
Slovak	(S)-3-(1-(9H-purín-6-ylamino)etyl)-8-chloro-2-fenylizochinolín-1(2H)-ón	Liečba chronickej lymfocytovej leukémie/lymfómu z malých lymfocytov
Slovenian	(S)-3-(1-(9H-purin-6-ilamino)etil)-8-kloro-2-fenilizokinolin-1(2H)-on	Zdravljenje kronične limfatske levkemije (majhnocelični limfom)
Spanish	(S)-3-(1-(9H-purin-6-ilamino)etil)-8-cloro-2-fenilisoquinolin-1(2H)-ona	Tratamiento de la leucemia linfocítica crónica linfoma linfocítico pequeño
Swedish	(S)-3-(1-(9H-purin-6-ylamin)etyl)-8-klor-2-fenylisokinolin-1(2H)-on	Behandling av kronisk lymfatisk leukemic/småcelligt lymfocytärt lymfom
Norwegian	(S)-3-(1-(9H-purin-6-ylamin)etyl)-8-klor-2-fenylisokinolin-1(2H)-on	Behandling av kronisk lymfatisk leukemi/småcellet lymfocytært lymfom
Icelandic	(S)-3-(1-(9H-púrín-6-ýlamín)etýl)-8-klór-2-fenýlísókínólín-1(2H)-ón	Meðferð á langvinnu eitilfrumuhvítblæði/smáfrumu lýmfósýtískt eitilfrumukrabbamein