



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

(2R,3R,4S,5R)-2-(6-amino-9H-purin-9-yl)-5-((((1r,3S)-3-(2-(5-(*tert*-butyl)-1H-benzo[d]imidazol-2-yl)ethyl)cyclobutyl)(isopropyl) amino)methyl)tetrahydrofuran-3,4-diol for the treatment of acute lymphoblastic leukaemia

On 16 January 2014, orphan designation (EU/3/13/1231) was granted by the European Commission to Voisin Consulting S.A.R.L., France, for (2R,3R,4S,5R)-2-(6-amino-9H-purin-9-yl)-5-((((1r,3S)-3-(2-(5-(*tert*-butyl)-1H-benzo[d]imidazol-2-yl)ethyl)cyclobutyl)(isopropyl) amino)methyl)tetrahydrofuran-3,4-diol for the treatment of acute lymphoblastic leukaemia.

What is acute lymphoblastic leukaemia?

Acute lymphoblastic leukaemia (ALL) is a cancer of the white blood cells called lymphocytes. In ALL, the lymphocytes multiply too quickly and live for too long so there are too many of them circulating in the blood. These abnormal lymphocytes are not fully developed and do not work properly. Over a period of time, they replace the normal white blood cells, red blood cells and platelets in the bloodstream and the bone marrow (the spongy tissue inside the large bones in the body, where blood cells are produced).

ALL is a long-term debilitating and life-threatening disease because the abnormal immature cells take the place of the normal blood cells, reducing the patient's ability to fight infections and causing organ damage.

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

At the time of designation, ALL 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 512,200,000 (Eurostat 2013).



What treatments are available?

Treatment for ALL 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. At the time of designation, the main treatment for ALL was chemotherapy (medicines to treat cancer) followed by or combined with radiotherapy (treatment with radiation). Haematopoietic (blood) stem-cell transplantation was also used. This is a complex procedure where the patient receives stem cells from a matched donor to help restore the bone marrow.

The sponsor has provided sufficient information to show that the medicine might be of significant benefit for some patients with ALL because early clinical studies show beneficial effects in patients whose leukaemia came back after previous treatments. 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?

This medicine is expected to block the activity of an enzyme called DOT1L histone methyltransferase, which is involved in 'turning on' genes within cells. In ALL, DOT1L is thought to work abnormally by 'turning on' certain genes that increase the division and growth of leukaemia cells. By blocking DOT1L, this medicine is expected to prevent abnormal activity of such genes, thus leading to a reduction in the growth of the cancer.

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 ALL were ongoing.

At the time of submission, the medicine was not authorised anywhere in the EU for ALL. Orphan designation of the medicine had been granted in the United States of America for treatment of ALL and acute myeloid leukaemia.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 12 December 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:

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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	(2 <i>R</i> ,3 <i>R</i> ,4 <i>S</i> ,5 <i>R</i>)-2-(6-amino-9 <i>H</i> -purin-9-yl)-5-(((1 <i>r</i> ,3 <i>S</i>)-3-(2-(5-(<i>tert</i> -butyl)-1 <i>H</i> -benzo[<i>d</i>]imidazol-2-yl)ethyl)cyclobutyl)(isopropyl amino)methyl)tetrahydrofuran-3,4-diol	Treatment of acute lymphoblastic leukaemia
Bulgarian	(2 <i>R</i> ,3 <i>R</i> ,4 <i>S</i> ,5 <i>R</i>)-2-(6-амино-9 <i>H</i> -пурин-9-ил)-5-(((1 <i>r</i> ,3 <i>S</i>)-3-(2-(5-(<i>терт</i> -бутил)-1 <i>H</i> -бензо[<i>d</i>]имидазол-2-ил)етил)циклобутил)(изопропил)амино)метил)тетраhydroфуран-3,4-диол	Лечение на остра лимфобластна левкемия
Czech	(2 <i>R</i> ,3 <i>R</i> ,4 <i>S</i> ,5 <i>R</i>)-2-(6-amino-9 <i>H</i> -purin-9-yl)-5-(((1 <i>r</i> ,3 <i>S</i>)-3-(2-(5-(<i>tert</i> -butyl)-1 <i>H</i> -benzo[<i>d</i>]imidazol-2-yl)ethyl)cyklobutyl)(isopropyl amino)methyl)tetrahydrofuran-3,4-diol	Léčba akutní lymfoblastické leukémie
Croatian	(2 <i>R</i> ,3 <i>R</i> ,4 <i>S</i> ,5 <i>R</i>)-2-(6-amino-9 <i>H</i> -purin-9-il)-5-(((1 <i>r</i> ,3 <i>S</i>)-3-(2-(5-(<i>tert</i> -butil)-1 <i>H</i> -benzo[<i>d</i>]imidazol-2-il)etil)ciklobutil)(izopropil amino)metil)tetrahidrofuran-3,4-diol	Liječenje akutne limfoblastične leukemije
Danish	(2 <i>R</i> ,3 <i>R</i> ,4 <i>S</i> ,5 <i>R</i>)-2-(6-amino-9 <i>H</i> -purin-9-yl)-5-(((1 <i>r</i> ,3 <i>S</i>)-3-(2-(5-(<i>tert</i> -butyl)-1 <i>H</i> -benzo[<i>d</i>]imidazol-2-yl) ætyl) cyclobutyl) (isopropyl) amino) metyl) tetrahydrofuran-3,4-diol	Behandling af akut lymfoblastær leukæmi
Dutch	(2 <i>R</i> ,3 <i>R</i> ,4 <i>S</i> ,5 <i>R</i>)-2-(6-amino-9 <i>H</i> -purine-9-yl)-5-(((1 <i>r</i> ,3 <i>S</i>)-3-(2-(5-(<i>tert</i> -butyl)-1 <i>H</i> -benzo[<i>d</i>]imidazool-2-yl)ethyl)cyclobutyl)(isopropyl amino)methyl)tetrahydrofuraan-3,4-diol	Behandeling van acute lymfoblastaire leukemie
Estonian	(2 <i>R</i> ,3 <i>R</i> ,4 <i>S</i> ,5 <i>R</i>)-2-(6-amino-9 <i>H</i> -puriin-9-yl)-5-(((1 <i>r</i> ,3 <i>S</i>)-3-(2-(5-(<i>tert</i> -butüül)-1 <i>H</i> -bensoo[<i>d</i>]imidasool-2-üül)etüül)cüklobutüül)(isopropüül) amino)metüül)tetrahüdrofuraan-3,4-diool	Ägeda lümfoblastilise leukeemia ravi
Finnish	(2 <i>R</i> ,3 <i>R</i> ,4 <i>S</i> ,5 <i>R</i>)-2-(6-amino-9 <i>H</i> -puriini-9-yl)-5-(((1 <i>r</i> ,3 <i>S</i>)-3-(2-(5-(tertiaalinenbutyyli)-1 <i>H</i> -bentso[<i>d</i>]imidatsoli-2-yl)etyyli)syklobutyyli)(isopropyli)amino)metyyli)tetrahydrofuraani-3,4-glykoli	Akuutin lymfoblastileukemian hoito

¹ At the time of designation

Language	Active ingredient	Indication
French	(2 <i>R</i> ,3 <i>R</i> ,4 <i>S</i> ,5 <i>R</i>)-2-(6-amino-9 <i>H</i> -purin-9-yl)-5-(((1 <i>r</i> ,3 <i>S</i>)-3-(2-(5-(<i>tert</i> -butyl)-1 <i>H</i> -benzo[<i>d</i>]imidazol-2-yl)ethyl)cyclobutyl)(isopropyl)amino)methyl)tétrahydrofuran-3,4-diol	Traitement de la leucémie lymphoblastique aiguë
German	(2 <i>R</i> ,3 <i>R</i> ,4 <i>S</i> ,5 <i>R</i>)-2-(6-Amino-9 <i>H</i> -Purin-9-yl)-5-(((1 <i>r</i> ,3 <i>S</i>)-3-(2-(5-(<i>Tert</i> -Butyl)-1 <i>H</i> -Benzo[<i>d</i>]Imidazol-2-yl)Ethyl)Cyclobutyl)(Isopropyl)Amino)Methyl)Tetrahydrofuran-3,4-diol	Behandlung der akuten lymphatischen Leukämie
Greek	(2 <i>R</i> ,3 <i>R</i> ,4 <i>S</i> ,5 <i>R</i>)-2-(6-αμινό-9 <i>H</i> -πουρίνο-9-υλο)-5-(((1 <i>r</i> ,3 <i>S</i>)-3-(2-(5-(<i>τετρα</i> βουτυλο)-1 <i>H</i> -βενζο[<i>d</i>]ιμιδαζολο-2-υλο)αιθυλο)κυκλοβουτυλο)(ισοπροπυλο)αμινο)μεθυλο)τετραϋδροφουρανική-3,4-διόλη	Θεραπεία της οξείας λεμφοβλαστικής λευχαιμίας
Hungarian	(2 <i>R</i> ,3 <i>R</i> ,4 <i>S</i> ,5 <i>R</i>)-2-(6-amino-9 <i>H</i> -purin-9-il)-5-(((1 <i>r</i> ,3 <i>S</i>)-3-(2-(5-(<i>terc</i> -butil)-1 <i>H</i> -benzo[<i>d</i>]imidazol-2-il)etil)ciklobutil)(izopropil)amino)metil)tetrahidrofurán-3,4-diol	Akut lymphoblastos leukaemia kezelése
Italian	(2 <i>R</i> ,3 <i>R</i> ,4 <i>S</i> ,5 <i>R</i>)-2-(6-ammino-9 <i>H</i> -purin-9-il)-5-(((1 <i>r</i> ,3 <i>S</i>)-3-(2-(5-(<i>terz</i> -butil)-1 <i>H</i> -benzo[<i>d</i>]imidazolo-2-il)etil)ciclobutil)(isopropil)amino)metil)tetraidrofurano-3,4-diolo	Trattamento della leucemia linfoblastica acuta
Latvian	(2 <i>R</i> ,3 <i>R</i> ,4 <i>S</i> ,5 <i>R</i>)-2-(6-amino-9 <i>H</i> -purīn-9-il)-5-(((1 <i>r</i> ,3 <i>S</i>)-3-(2-(5-(<i>terc</i> -butil)-1 <i>H</i> -benzo[<i>d</i>]imidazol-2-il)etil)ciklobutil)(izopropil)amino)metil)tetrahidrofurān-3,4-diols	Akūtas limfoblastiskas leikozes ārstēšana
Lithuanian	(2 <i>R</i> ,3 <i>R</i> ,4 <i>S</i> ,5 <i>R</i>)-2-(6-amino-9 <i>H</i> -purin-9-il)-5-(((1 <i>r</i> ,3 <i>S</i>)-3-(2-(5-(<i>tert</i> -butil)-1 <i>H</i> -benzo[<i>d</i>]imidazol-2-il)etil)ciklobutil)(izopropil)amino)metil)tetrahidrofuran-3,4-diolis	Ūmios limfoblastinės leukemijos gydymas
Maltese	(2 <i>R</i> ,3 <i>R</i> ,4 <i>S</i> ,5 <i>R</i>)-2-(6-amino-9 <i>H</i> -purin-9-yl)-5-(((1 <i>r</i> ,3 <i>S</i>)-3-(2-(5-(<i>tert</i> -butyl)-1 <i>H</i> -benzo[<i>d</i>]imidazol-2-yl)ethyl)cyclobutyl)(isopropyl)amino)methyl)tetrahydrofuran-3,4-diol	Kura tal-lewkimja limfoblastika akuta
Polish	(2 <i>R</i> ,3 <i>R</i> ,4 <i>S</i> ,5 <i>R</i>)-2-(6-amino-9 <i>H</i> -puryn-9-ylo)-5-(((1 <i>r</i> ,3 <i>S</i>)-3-(2-(5-(<i>tert</i> -butylo)-1 <i>H</i> -benzo[<i>d</i>]imidazol-2-ylo)etylo)cyklobutylo)(izopropylo)amino)metylo)tetrahydrofurano-3,4-diol	Leczenie ostrej białaczki limfoblastycznej
Portuguese	(2 <i>R</i> ,3 <i>R</i> ,4 <i>S</i> ,5 <i>R</i>)-2-(6-amino-9 <i>H</i> -purina-9-il)-5-(((1 <i>r</i> ,3 <i>S</i>)-3-(2-(5-(<i>tert</i> -butil)-1 <i>H</i> -benzo[<i>d</i>]imidazol-2-yl)etil)ciclobutil)(isopropil)amino)metil)tetrahidrofurano-3,4-diol	Tratamento da leucémia linfoblástica aguda

Language	Active ingredient	Indication
Romanian	(2 <i>R</i> ,3 <i>R</i> ,4 <i>S</i> ,5 <i>R</i>)-2-(6-amino-9 <i>H</i> -purin-9-il)-5-(((1 <i>r</i> ,3 <i>S</i>)-3-(2-(5-(<i>tert</i> -butil)-1 <i>H</i> -benzo[<i>d</i>]imidazol-2-il)etil)ciclobutil)(izopropil)amino)metil)tetrahidrofuran-3,4-diol	Tratamentul leucemiei limfoblastice acute
Slovak	(2 <i>R</i> ,3 <i>R</i> ,4 <i>S</i> ,5 <i>R</i>)-2-(6-amino-9 <i>H</i> -purín-9-yl)-5-(((1 <i>r</i> ,3 <i>S</i>)-3-(2-(5-(<i>tert</i> -butyl)-1 <i>H</i> -benzo[<i>d</i>]imidazol-2-yl)etyl)cyklobutyl)(izopropyl)amino)metyl)tetrahydrofuran-3,4-diol	Liečba akútnej lymfoblastickej leukémie
Slovenian	(2 <i>R</i> ,3 <i>R</i> ,4 <i>S</i> ,5 <i>R</i>)-2-(6-amino-9 <i>H</i> -purin-9-il)-5-(((1 <i>r</i> ,3 <i>S</i>)-3-(2-(5-(<i>tert</i> -butil)-1 <i>H</i> -benzo[<i>d</i>]imidazol-2-il)etil)ciklobutil)(izopropil)amino)metil)tetrahidrofuran-3,4-diol	Zdravljenje akutne limfoblastne levkemije
Spanish	(2 <i>R</i> ,3 <i>R</i> ,4 <i>S</i> ,5 <i>R</i>)-2-(6-amino-9 <i>H</i> -purin-9-il)-5-(((1 <i>r</i> ,3 <i>S</i>)-3-(2-(5-(<i>ter</i> butil)-1 <i>H</i> -benzo[<i>d</i>]imidazol-2-il)etil)ciclobutil)(isopropil)amino)metil)tetrahidrofurano-3,4-diol	Tratamiento de la leucemia linfoblástica aguda
Swedish	(2 <i>R</i> ,3 <i>R</i> ,4 <i>S</i> ,5 <i>R</i>)-2-(6-amino-9 <i>H</i> -purin-9-yl)-5-(((1 <i>r</i> ,3 <i>S</i>)-3-(2-(5-(<i>tert</i> -butyl)-1 <i>H</i> -benzo[<i>d</i>]imidazol-2-yl)etyl)cyklobutyl)(isopropyl)amino)metyl)tetrahydrofuran-3,4-diol	Behandling av akut lymfatisk leukemi
Norwegian	(2 <i>R</i> ,3 <i>R</i> ,4 <i>S</i> ,5 <i>R</i>)-2-(6-amino-9 <i>H</i> -purin-9-yl)-5-(((1 <i>r</i> ,3 <i>S</i>)-3-(2-(5-(<i>tert</i> -butyl)-1 <i>H</i> -benzo[<i>d</i>]imidazol-2-yl)etyl)sykllobutyl)(isopropyl)amino)metyl)tetrahydrofuran-3,4-diol	Behandling av akutt lymfoblastisk leukemi
Icelandic	(2 <i>R</i> ,3 <i>R</i> ,4 <i>S</i> ,5 <i>R</i>)-2-(6-amínó-9 <i>H</i> -púrín-9-ýl)-5-(((1 <i>r</i> ,3 <i>S</i>)-3-(2-(5-(<i>tert</i> -bútýl)-1 <i>H</i> -bensó[<i>d</i>]ímídasól-2-ýl)etýl)sýklóbútýl)(ísóprópýl)amínó)metyl) tetrahýdrófúran-3,4-díól	Meðferð við bráðu eitilfrumuhvítblæði