



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Folic acid to be used with N-[4-[[[(2-amino-3,4-dihydro-4-oxo-6-pteridiny)l)methyl]amino]benzoyl]-D-gamma-glutamyl-(2S)-2-amino-beta-alanyl-L-alpha-aspartyl-L-cysteine for the diagnosis of positive folate receptor status in ovarian cancer

On 10 September 2012, orphan designation (EU/3/12/1044) was granted by the European Commission to Endocyte Europe B.V., the Netherlands, for folic acid to be used with N-[4-[[[(2-amino-3,4-dihydro-4-oxo-6-pteridiny)l)methyl]amino]benzoyl]-D-gamma-glutamyl-(2S)-2-amino-beta-alanyl-L-alpha-aspartyl-L-cysteine for the diagnosis of positive folate receptor status in ovarian cancer.

What is ovarian cancer?

Ovarian cancer is cancer of the ovaries (two organs in the female reproductive system that produce eggs). Most ovarian cancers occur in women over the age of 50 years. Due to the absence of symptoms in the early stages of the disease, the majority of patients are diagnosed when the cancer has spread to other parts of the body.

Most ovarian cancers are 'folate receptor positive'. This means that the surface of the cancer cell contains high amounts of a receptor which folic acid (a vitamin required for cell division) attaches to. This receptor can be targeted for treatment.

Ovarian cancer is a life-threatening disease that is associated with poor long-term survival.

What is the estimated number of patients eligible for diagnosis of positive folate receptor status in ovarian cancer?

At the time of designation, the number of patients eligible for diagnosis of positive folate receptor status in ovarian cancer was estimated to be not more than 1.3 in 10,000 people in the European Union (EU)*. This is equivalent to a total of not more than 66,000 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 506,300,000 (Eurostat 2011).



What methods of diagnosis are available?

At the time of designation, there were no satisfactory methods of diagnosing positive folate receptor status in ovarian cancer in the EU. Existing methods were limited to detecting the presence of ovarian cancer cells. They included vaginal examination to check for any visible abnormalities of the womb or ovaries. In addition, blood tests and ultrasound were used to help identify masses in the abdomen. If a mass was discovered, the patient underwent surgery to determine the nature of the mass.

How is this medicine expected to work?

Folic acid injections are used to improve the image on scans for diagnosing positive folate receptor status in ovarian cancer. It is given before the injection of another medicine that is radioactive and also contains folic acid. The radioactive medicine can enter the cancer cells by attaching to their folate receptors and once inside it emits radiation which can be seen as an image on a scan.

The folic acid injections are given before the radioactive medicine as this has been shown to improve the quality of the image on the scan. This is because the folic acid attaches to many receptors in non-cancer cells, thereby ensuring that more of the radioactive medicine attaches to the receptors on the cancer cells.

What is the stage of development of this medicine?

The effects of folic acid have been evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials with folic acid in patients with ovarian cancer were ongoing.

At the time of submission, folic acid was not authorised anywhere in the EU for the diagnosis of positive folate receptor status in ovarian cancer or designated as an orphan medicinal product elsewhere for diagnosing this condition.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 23 July 2012 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	Folic acid to be used with N-[4-[[[(2-amino-3,4-dihydro-4-oxo-6-pteridiny]methyl)amino]benzoyl]-D-gamma-glutamyl-(2S)-2-amino-beta-alanyl-L-alpha-aspartyl-L-cysteine	Diagnosis of positive folate receptor status in ovarian cancer
Bulgarian	Фолиева киселина, която ще бъде използвана с N-[4-[[[(2-амино-3,4-дихидро-4-оксо-6-птеридинил)метил]амино]бензоил]-D-гама-глутамил-(2S)-2-амино-бета-аланил-L-алфа-аспартил-L-цистеин	Диагноза на позитивен статус за фолатни рецептори при рак на яйчника
Czech	Kyselina listová podávaná s N-[4-[[[(2-amino-3,4-dihydro-4-oxo-6-pteridiny]methyl)amino]benzoyl]-D-gamma-glutamyl-(2S)-2-amino-beta-alanyl-L-alpha-aspartyl-L-cysteinem	Diagnostika pozitivního statutu folátového receptoru u karcinomu vaječníků
Danish	Folinsyre til brug sammen med N-[4-[[[(2-amino-3,4-dihydro-4-oxo-6-pteridiny]methyl)amino]benzoyl]-D-gamma-glutamyl-(2S)-2-amino-beta-alanyl-L-alpha-aspartyl-L-cystein	Diagnose af positiv folatreceptorstatus i ovariecancer
Dutch	Foliumzuur welke dient aangewend tesamen met N-[4-[[[(2-amino-3,4-dihydro-4-oxo-6-pteridiny]methyl)amino]benzoyl]-D-gamma-glutamyl-(2S)-2-amino-bêta-alanyl-L-alpha-aspartyl-L-cysteïne	Diagnose van positieve folaatreceptor status in ovariële kanker
Estonian	Foolhape, mida kasutatakse koos N-[4-[[[(2-amino-3,4-dihüdro-4-okso-6-pteridinüül)metüül]amino]benzoüül]-D-gamma-glutamüül-(2S)-2-amino-beta-alanüül-L-alfa-aspartüül-L-tsüsteiin	Positiivse folaatreseptori statuudi diagnoosimine munasarjavähi puhul
Finnish	Foolihappo käytettäväksi N-[4-[[[(2-amino-3,4-dihydro-4-okso-6-pteridinyyli)metyyli]amino]bentsoyli]-D-gamma-glutamyyli-(2S)-2-amino-beeta-alanyyli-L-alfa-aspartyyli-L-kysteiinin kanssa	Positiivisen folaattireseptori-statuksen diagnosointi munasarjasyövässä
French	Acide folique à utiliser avec N-[4-[[[(2-amino-3,4-dihydro-4-oxo-6-ptéridiny]méthyl)amino]benzoyl]-D-gamma-glutamyl-(2S)-2-amino-beta-alanyl-L-alpha-aspartyl-L-cystéine	Diagnostic de l'expression du folate recepteur dans le cancer de l'ovaire
German	Folsäure, zu verabreichen mit N-[4-[[[(2-amino-3,4-dihydro-4-oxo-6-pteridiny]methyl)amino]benzoyl]-D-gamma-glutamyl-(2S)-2-amino-beta-alanyl-L-alpha-aspartyl-L-cystein	Diagnose eines positiven Folat-Rezeptor-Status bei Ovarialkarzinomen
Greek	Φολικό οξύ για χρήση μαζί με N-[4-[[[(2-αμινο-3,4-διυδρο-4-οξο-6-πτεριδινύλο)μεθυλ]αμινο]βενζοΐλ]-D-γ-γλουταμυλο-(2S)-2-αμινο-β-αλανυλ-L-άλφα-ασπαρτυλο-L-κυστεΐνη	Διάγνωση της ύπαρξης υποδοχέα φολικού οξέος στον καρκίνο των ωοθηκών

¹ At the time of designation

Language	Active ingredient	Indication
Hungarian	Folsav és N-[4-[[[(2-amino-3,4-dihidro-4-oxo-6-pteridinil)metil]amino]benzoil]-D-gamma-glutamyl-(2S)-2-amino-béta-alanil-L-alfa-aszpartil-L-cisztein	Petefészekrák folát-receptor pozitívitásának diagnosztizálása
Italian	Acido folico per uso con N-[4-[[[(2-amino-3,4-dihydro-4-oxo-6-ptéridinil)méthyl]amino]benzoyl]-D-gamma-glutamyl-(2S)-2-amino-beta-alanyl-L-alpha-aspartyl-L-cysteina	Diagnosi dello stato positivo del recettore dei folati nel cancro dell'ovaio
Latvian	N-[4-[[[(2-amino-3,4-dihidro-4-okso-6-pteridinil)metil]amino]benzoil]-D-gamma-glutamyl-(2S)-2-amino-beta-alanil-L-alfa-aspartil-L-cisteīns ievadīts kopā ar folijskābi	Folātreceptoru pozitīva olnīcu vēža diagnostikai
Lithuanian	Folio rūgštis turi būti vartojama su N-[4-[[[(2-amino-3,4-dihidro-4-okso-6-pteridinil)methyl]amino]benzoil]-D-gama-glutamyl-(2S)-2-amino-beta-alanil-L-alfa-aspartil-L-cisteinu	Teigiamų folatų receptorių būklės prie kiaušidžių vėžio diagnozė
Maltese	Aċidu foliku biex jiġi użat ma' N-[4-[[[(2-amino-3,4-dihydro-4-oxo-6-pteridinil)methyl]amino]benzoyl]-D-gamma-glutamyl-(2S)-2-amino-beta-alanyl-L-alpha-aspartyl-L-cysteine	Dijanjosi tal-istatus tar-riċettur tal-folate fil-kanċer tal-ovarji
Polish	Kwas foliowy do podawania z N-[4-[[[(2-amino-3,4-dihydro-4-okso-6-ptyrydynilo)metylo]amino]benzoilo]-D-gamma-glutamyl-(2S)-2-amino-beta-alanylo-L-alfa-aspartylo-L-cysteina	Diagnostyka raka jajnika z pozytywną ekspresją receptorów dla kwasu foliowego
Portuguese	Ácido fólico para ser administrado com N-[4-[[[(2-amino-3,4-di-hidro-4-oxo-6-pteridinil)metilo]amino]benzoilo]-D-gama-glutamyl-(2S)-2-amino-beta-alanil-L-alfa-aspartil-L-cisteína	Determinação dos receptores de folato no cancro do ovário
Romanian	Acid folic pentru a fi utilizat cu N-[4-[[[(2-amino-3,4-dihidro-4-oxo-6-pteridinil)metil]amino]benzoil]-D-gamma-glutamyl-(2S)-2-amino-beta-alanil-L-alfa-aspartil-L-cisteină	Diagnosticul statusului pozitiv al receptorului pentru folat în cancerul ovarian
Slovak	Kyselina listová na podávanie s N-[4-[[[(2-amino-3,4-dihydro-4-oxo-6-pteridinil)metyl]amino]benzoyl]-D-gama-glutamyl-(2S)-2-amino-beta-alanyl-L-alfa-aspartyl-L-cysteínom	Diagnostika pozitívneho statusu folátového receptora pri rakovine vaječníkov
Slovenian	Folna kislina za uporabo z N-[4-[[[(2-amino-3,4-dihidro-4-okso-6-pteridinil)metil]amino]benzoil]-D-gama-glutamyl-(2S)-2-amino-beta-alanil-L-alfa-aspartil-L-cisteinom	Diagnosticiranje statusa folatnih receptorjev pri raku jajčnikov
Spanish	Acido folico para uso con N-[4-[[[(2-amino-3,4-dihidro-4-oxo-6-pteridinil)metil]amino]benzoil]-D-gamma-glutamyl-(2S)-2-amino-beta-alanil-L-alfa-aspartil-L-cysteina	Diagnóstico del estado positivo de los receptores de folato en el cáncer de ovario
Swedish	Folsyra att användas med N-[4-[[[(2-amino-3,4-dihydro-4-oxo-6-pteridinil)metyl]amino]benzoyl]-D-gamma-glutamyl-(2S)-2-amino-beta-alanyl-L-alfa-aspartyl-L-cystein	Diagnos av folsyrareceptor-positiv ovarialcancer
Norwegian	Folsyre til bruk med N-[4-[[[(2-amino-3,4-dihydro-4-okso-6-pteridinil)metyl]amino]benzoyl]-D-gamma-glutamyl-	Diagnostisering av folatreseptor-positiv

Language	Active ingredient	Indication
	(2S)-2-amino-beta-alanyl-L-alfa-aspartyl-L-cystein	eggstokkreft
Icelandic	Fólin sýra sem á að gefa með N-[4-[[[(2-amínó-3,4-díhýdró-4-oxó-6-pteridínýl)methýl]amínó]benzóýl]-D-gamma-glútamýl-(2S)-2-amínó-beta-alanýl-L-alpha-aspartýl-L-cýstein	Greining á fólátviðtaka stöðu eggjastokkakrabbameins