6 November 2012
EMA/COMP/853895/2012, Rev. 1
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

N-[4-[[(2-amino-3,4-dihydro-4-oxo-6-pteridinyl)methyl]amino]benzoyl]-D-gamma-glutamyl-(2S)-2-amino-beta-alanyl-L-alpha-aspartyl-L-cysteine and folic acid for the diagnosis of positive folate receptor status in ovarian cancer

Please note that this product was withdrawn from the Community Register of designated orphan medicinal products in September 2012 on request of the sponsor.

On 9 February 2012, orphan designation (EU/3/12/958) was granted by the European Commission to Endocyte Europe B.V., the Netherlands, for N-[4-[[(2-amino-3,4-dihydro-4-oxo-6-pteridinyl)methyl]amino]benzoyl]-D-gamma-glutamyl-(2S)-2-amino-beta-alanyl-L-alpha-aspartyl-L-cysteine and folic acid 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 folate (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 people in 10,000 per year in the

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7523 7040
E-mail info@ema.europa.eu **Website** www.ema.europa.eu
An agency of the European Union

European Union (EU)*. This is equivalent to a total of 65,819 people per year, which was considered to be below the ceiling for orphan designation. This is based on the information provided by the sponsor and the knowledge of the Committee for Orphan Medicinal Products (COMP).

What methods of diagnosis are available?

At the time of designation, there were no satisfactory methods of diagnosing positive folate receptor status of 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?

The medicine is made of two components:

- folic acid, which enables the medicine to attach to the folate receptor of folate receptor-positive ovarian cancer cells;
- a synthetic component containing radioactive technetium (an imaging agent).

Once injected into a vein, the medicine is expected to enter ovarian cancer cells by attaching to the folate receptor. The radioactive technetium is expected to emit radiation which can be detected by an imaging method. The medicine therefore identifies those patients who have folate receptor-positive ovarian cancers and are most likely to respond to treatment targeting the folate receptor.

What is the stage of development of this medicine?

The effects of this medicine have been evaluated in experimental models.

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

At the time of submission, the medicine was not authorised anywhere in the EU for the diagnosis of ovarian cancer 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 October 2011 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.

*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).

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:

Endocyte Europe B.V.
Prins Bernhardplein 200
1097 JB Amsterdam
The Netherlands
Telephone: +31 20 521 4777
Telefax: +31 20 521 4821
E-mail: info@endocyte.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	N-[4-[[(2-amino-3,4-dihydro-4-oxo-6-pteridinyl)methyl]amino]benzoyl]-D-gamma-glutamyl-(2S)-2-amino-beta-alanyl-L-alpha-aspartyl-L-cysteine and folic acid	Diagnosis of folate receptor status in ovarian cancer
Bulgarian	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 и фолиева киселина	Диагноза на статуса на фолатните рецептори при рак на яйчника
Czech	N-[4-[[(2-amino-3,4-dihydro-4-oxo-6-pteridinyl)metyl]amino]benzoyl]-D-gama-glutamyl-(2S)-2-amino-beta-alanyl-L-alfa-aspartyl-L-cystein a kyselina listová	Diagnostika stavu folátového receptoru u karcinomu vaječníků
Danish	N-[4-[[(2-amino-3,4-dihydro-4-oxo-6-pteridinyl)methyl]amino]benzoyl]-D-gamma-glutamyl-(2S)-2-amino-beta-alanyl-L-alpha-aspartyl-L-cystein og folsyre	Diagnose af folatreceptorstatus i ovariecancer
Dutch	N-[4-[[(2-amino-3,4-dihydro-4-oxo-6-pteridinyl)methyl]amino]benzoyl]-D-gamma-glutamyl-(2S)-2-amino-beta-alanyl-L-alpha-aspartyl-L-cysteïne en foliumzuur	Diagnose van folaatreceptor status in ovariële kanker
Estonian	N-[4-[[(2-amino-3,4-dihüdro-4-okso-6-pteridinüül)metüül]amino]bensoüül]-D-gamma-glutamüül-(2S)-2-amino-beeta-alanüül-L-alfa-aspartüül-L-tsüsteiin ja foolhape	Folaatretseptori statuudi diagnoosimine munasarjavähi puhul
Finnish	N-[4-[[(2-amino-3,4-dihydro-4-okso-6-pteridinyyli)metyyli]amino]bentsoyyli]-D-gamma-glutamyyli-(2S)-2-amino-beta-alanyyli-L-alfa-aspartyyli-L-kysteinyyli ja foolihappo	Folaattireseptori-statuksen diagnosointi munasarjasyövässä
French	N-[4-[[(2-amino-3,4-dihydro-4-oxo-6-ptéridinyl)méthyl]amino]benzoyl]-D-gamma-glutamyl-(2S)-2-amino-béta-alanyl-L-alpha-aspartyl-L-cystéine et acide folique	Diagnostic de l'expression du folate recepteur dans le cancer de l'ovaire
German	N-[4-[[(2-amino-3,4-dihydro-4-oxo-6-pteridinyl)methyl]amino]benzoyl]-D-gamma-glutamyl-(2S)-2-amino-beta-alanyl-L-alpha-aspartyl-L-cysteine und Folsäure	Diagnose des Folat-Rezeptor-Status bei Ovarialkarzinomen
Greek	N-[4-[[(2-αμινο-3,4-διυδρο-4-οξο-6-πτεριδινύλο)μεθυλ]αμινο]βενζοϋλ]-D-γ-γλουταμυλ-(2S)-2-αμινο-β-αλανυλ-L-άλφα-ασπαρτυλ-L-κυστεΐνη και φολικό οξύ	Διάγνωση της ύπαρξης υποδοχέα φολικού οξέος στον καρκίνο των ωοθηκών

[1] At the time of designation

Language	Active ingredient	Indication
Hungarian	N-[4-[[(2-amino-3,4-dihidro-4-oxo-6-pteridinil)methil]amino]benzoil]-D-gamma-glutamil-(2S)-2-amino-beta-alanil-L-alpha-aspartil-L-cisztein és folsav	Petefészekrák folát-receptor állapotának diagnosztikája
Italian	N-[4-[[(2-amino-3,4-deidro-4-oxo-6-pteridinil)metil]amino]benzoil]-D-gamma-glutamil-(2S)-2-amino-beta-alanil-L-alfa-aspartil-L-cisteina e acido folico	Diagnosi dell'espressione 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-glutamil-(2S)-2-amino-beta-alanil-L-alfla-aspartil-L-cisteīns un folijskābe	Folātreceptoru pozitīva olnīcu vēža diagnostikai
Lithuanian	N-[4-[[(2-amino-3,4-dihidro-4-okso-6-pteridinil)metil]amino]benzoil]-D-gama-gliutamil-(2S)-2-amino-beta-alanil-L-alfa-aspartil-L-cisteinas ir folio rūgštis	Kiaušidžių vėžio pagal folatų receptoriaus statusą diagnozės nustatymas
Maltese	N-[4-[[(2-amino-3,4-dihydro-4-oxo-6-pteridinyl)methyl]amino]benzoyl]-D-gamma-glutamyl-(2S)-2-amino-beta-alanyl-L-alpha-aspartyl-L-cysteine u folic acid	Dijanjosi tal-istatus tar-riċettur tal-folate fil-kanċer tal-ovarji
Polish	N-[4-[[(2-amino-3,4-dihydro-4-okso-6-pterydynylo)metylo]amino]benzoilo]-D-γ-glutamylo-(2S)-2-amino-β-alanylo-L-α-aspartylo-L-cysteina i kwas foliowy	Diagnostyka stanu receptorów kwasu foliowego w raku jajnika
Portuguese	N-[4-[[(2-amino-3,4-di-hidro-4-oxo-6-pteridinil)metilo]amino]benzoilo]-D-gama-glutamil-(2S)-2-amino-beta-alanil-L-alfa-aspartil-L-cisteína e ácido fólico	Determinação dos receptores de folato no cancro do ovário
Romanian	N-[4-[[(2-amino-3,4-dihidro-4-oxo-6-pteridinil)metil]amino]benzoil]-D-gama-glutamil-(2S)-2-amino-beta-alanil-L-alfa-aspartil-L-cisteină şi acid folic	Diagnosticul expresiei receptorului pentru folat în cancerul ovarian
Slovak	N-[4-[[(2-amino-3,4-dihydro-4-oxo-6-pteridinyl)metyl]amino]benzoyl]-D-gama-glutamyl-(2S)-2-amino-beta-alanyl-L-alfa-aspartyl-L-cysteín a kyselina listová	Diagnóza statusu folátového receptora pri rakovine vaječníkov
Slovenian	N-[4-[[(2-amino-3,4-dihidro-4-okso-6-pteridinil)metil]amino]benzoil]-D-gama-glutamil-(2S)-2-amino-beta-alanil-L-alfa-aspartil-L-cistein in folna kislina	Diagnosticiranje raka jajčnikov glede statusa folatnih receptorjev
Spanish	N-[4-[[(2-amino-3,4-dihidro-4-oxo-6-pteridinil)metil]amino]benzoíl]-D-gamma-glutamil-(2S)-2-amino-beta-alanil-L-alfa-aspartil-L-cisteína y ácido fólico	Diagnóstico del estado de los receptores de folato en el cáncer de ovario

Language	Active ingredient	Indication
Swedish	N-[4-[[(2-amino-3,4-dihydro-4-oxo-6-pteridinyl)metyl]amino]bensoyl]-D-gamma-glutamyl-(2S)-2-amino-beta-alanyl-L-alfa-aspartyl-L-cystein och folsyra	Diagnos av folatreceptorstatus i ovarialcancer
Norwegian	N-[4-[[(2-amino-3,4-dihydro-4-okso-6-pteridinyl)metyl]amino]benzoyl]-D-gamma-glutamyl-(2S)-2-amino-beta-alanyl-L-alfa-aspartyl-L-cystein og folinsyre	Diagnostisering av folatreseptor-positiv eggstokkreft
Icelandic	N-[4-[[(2-amínó-3,4-díhýdró-4-oxó-6-pteridínýl)metýl]amínó]bensóýl]-D-gamma-glútamýl-(2S)-2-amínó-beta-alanýl-L-alfa-aspartýl-L-systein og fólínsýra	Greining á fólatviðtaka stöðu eggjastokkakrabbameins