25 September 2012
EMA/COMP/554957/2012
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 to be used with folic acid for the diagnosis of positive folate receptor status in ovarian cancer

On 10 September 2012, orphan designation (EU/3/12/1043) 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 to be used with 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 called folate 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).

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

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?

The medicine is made up of folic acid attached to another component which contains radioactive technetium (an imaging agent). The medicine can enter the cancer cells by attaching to their folate receptors and once inside the cells it emits radiation which can be seen as an image on a scan. The medicine can therefore be used to identify those patients who have positive folate receptor status in ovarian cancer and are most likely to respond to treatment targeting the folate receptor.

Before this medicine is given, the patient is to receive an injection of folic acid alone, as this has been shown to improve the quality of the image on the scan.

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 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:

Endocyte Europe B.V.
Prins Bernhardplein 200
1097 JB Amsterdam
The Netherlands
Telephone: +31 20 521 4777
Telefax: +31 20 521 4821
E-mail: tjalling.huisman@intertrustgroup.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 to be used with folic acid	Diagnosis of positive 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, който ще бъде използван с фолиева киселина	Диагноза на позитивен статус за фолатни рецептори при рак на яйчника
Czech	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 podávaný s kyselinou listovou	Diagnostika pozitivního statutu 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 til brug sammen med folinsyre	Diagnose af positiv folatreceptorstatus i ovariecancer
Dutch	N-[4-[[(2-amino-3,4-dihydro-4-oxo-6-pteridinyl)methyl]amino]benzoyl]-D-gamma-glutamyl-(2S)-2-amino-bêta-alanyl-L-alpha-aspartyl-L-cysteïne welke dient aangewend tesamen met foliumzuur	Diagnose van positieve folaatreceptor status in ovariële kanker
Estonian	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, mida kasutatakse koos foolhappega	Positiivse folaatretseptori staatuudi diagnoosimine munasarjavähi puhul
Finnish	N-[4-[[(2-amino-3,4-dihydro-4-okso-6-pteridinyyli)metyyli]amino]bentsoyyli]-D-gamma-glutamyyli-(2S)-2-amino-beeta-alanyyli-L-alfa-aspartyyli-L-kysteiini käytettäväksi foolihapon kanssa	Positiivisen 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-beta-alanyl-L-alpha-aspartyl-L-cystéine à utiliser avec l'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-cystein, zu verabreichen mit Folsäure	Diagnose eines positiven Folat-Rezeptor-Status bei Ovarialkarzinomen

[1] At the time of designation

Language	Active ingredient	Indication
Greek	N-[4-[[(2-αμινο-3,4-διυδρο-4-οξο-6-πτεριδινύλο)μεθυλ]αμινο]βενζοϋλ]-D-γ-γλουταμυλο-(2S)-2-αμινο-β-αλανυλ-Λ-άλφα-ασπαρτυλο-L-κυστεΐνη	Διάγνωση της ύπαρξης υποδοχέα φολικού οξέος στον καρκίνο των ωοθηκών
Hungarian	N-[4-[[(2-amino-3,4-dihidro-4-oxo-6-pteridinil)metil]amino]benzoil]-D-gmma-glutamil-(2S)-2-amino-béta-alanil-L-alfa-aszpartil-L-cisztein adása folsavval	Petefészekrák folát-receptor pozitivitásának diagnosztizálása
Italian	N-[4-[[(2-amino-3,4-dihydro-4-oxo-6-ptéridinyl)méthyl]amino]benzoyl]-D-gamma-glutamyl-(2S)-2-amino-beta-alanyl-L-alpha-aspartyl-L-cysteina per uso con acido folico	Diagnosi dello stato positivodel 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 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)metil]amino]benzoil]-D-gama-glutamil-(2S)-2-amino-beta-alanil-L-alfa-aspartil-L-cisteinu	Teigiamų folatų receptorių būklės prie kiaušidžių vėžio diagnozė
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 biex jiġi użat ma' aċidu foliku	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-gamma-glutamylo-(2S)-2-amino-beta-alanylo-L-alfa-aspartylo-L-cysteina do podawania z kwasem foliowym	Diagnostyka raka jajnika z pozytywną ekspresją receptorów dla kwasu foliowego
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 para ser administrado com 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-gamma-glutamil-(2S)-2-amino-beta-alanil-L-alfa-aspartil-L-cisteină pentru a fi utilizată cu acid folic	Diagnosticul statusului pozitiv al 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 na podávanie s kyselinou listovou	Diagnostika pozitívneho 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 za uporabo s folno kislino	Diagnosticiranje statusa folatnih receptorjev pri raku jajčnikov
Spanish	N-[4-[[(2-amino-3,4-dihidro-4-oxo-6-	Diagnóstico del estado positivo

Language	Active ingredient	Indication
	pteridinil)metil]amino]benzoil]-D-gamma-glutamil-(2S)-2-amino-beta-alanil-L-alfa-aspartil-L-cisteina para uso con acido folico	de los receptores de folato en el cáncer de ovario
Swedish	N-[4-[[(2-amino-3,4-dihydro-4-oxo-6-pteridinyl)metyl]amino]benzoyl]-D-gamma-glutamyl-(2S)-2-amino-beta-alanyl-L-alfa-aspartyl-L-cystein att användas med folsyra	Diagnos av folsyrareceptor-positiv 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 til bruk med folsyre	Diagnostisering av folatreseptor-positiv eggstokkreft
Icelandic	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-cystein sem á að gefa ásamt fólín sýru	Greining á fólatviðtaka stöðu eggjastokkakrabbameins