



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Public summary of opinion on orphan designation

(E)-2-((2S,4S)-4-(((2R,4S,5S,6S)-4-Amino-5-hydroxy-6-methyltetrahydro-2H-pyran-2-yl)oxy)-2,5,12-trihydroxy-7-methoxy-6,11-dioxo-1,2,3,4,6,11-hexahydrotetracen-2-yl)-10-(carboxymethyl)-1-hydroxy-13-(2-(2-(2-((E)-3-(3-((3-hydroxy-3,3 diphosphonopropyl)(methyl)amino)propoxy)benzylidene)hydrazine-1-carbonothioyl)hydrazineyl)-2-oxoethyl)-8-oxo-5-thioxo-3,4,6,7,10,13-hexaazapentadec-2-en-15-oic acid for the treatment of osteosarcoma

On 16 December 2019, orphan designation EU/3/19/2226 was granted by the European Commission to Atlanterra, France, for (E)-2-((2S,4S)-4-(((2R,4S,5S,6S)-4-amino-5-hydroxy-6-methyltetrahydro-2H-pyran-2-yl)oxy)-2,5,12-trihydroxy-7-methoxy-6,11-dioxo-1,2,3,4,6,11-hexahydrotetracen-2-yl)-10-(carboxymethyl)-1-hydroxy-13-(2-(2-(2-((E)-3-(3-((3-hydroxy-3,3 diphosphonopropyl)(methyl)amino)propoxy) benzylidene)hydrazine-1-carbonothioyl)hydrazineyl)-2-oxoethyl)-8-oxo-5-thioxo-3,4,6,7,10,13-hexaazapentadec-2-en-15-oic acid (also known as 12b80) for the treatment of osteosarcoma.

What is osteosarcoma?

Osteosarcoma is a type of cancer that affects bone-forming cells. It usually affects the growing bone and occurs mainly in teenagers and young adults. Although it can develop in any bone in the body, it most often starts in the bones around the knee joint in the area of bone with the fastest growth. The most common symptom is pain, which may be worse at night. Symptoms also depend on where the cancer has spread to. The most common site of spread for this cancer is the lungs.

Osteosarcoma is a long-term debilitating and life-threatening disease that may require patients to undergo limb amputation and can shorten life.



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

At the time of designation, osteosarcoma affected approximately 2.8 in 10,000 people in the European Union (EU). This was equivalent to a total of around 145,000 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).

What treatments are available?

At the time of designation, the main treatments for osteosarcoma were surgery and chemotherapy (medicines to treat cancer). The goal of surgery was to remove cancerous bone while preserving as much skeletal function as possible. Chemotherapy was normally used to shrink the tumour before surgery and also after surgery to stop any remaining cancer cells from spreading. Chemotherapy medicines authorised in the EU for this condition included doxorubicin, cisplatin, methotrexate and ifosfamide.

The sponsor has provided sufficient information to show that the medicine might be of significant benefit for patients with osteosarcoma because laboratory studies show that the medicine may be more effective at slowing the growth of osteosarcoma than authorised treatments. 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 contains a form of doxorubicin, a cancer medicine that has been used for many years to treat cancers, including osteosarcoma. It works by interfering with the DNA in cells, preventing them from making more copies of DNA and making proteins. This means that cancer cells cannot divide and eventually die. In this medicine, the doxorubicin has been combined with hydroxybisphosphonate, a substance that is taken up by bones. This is expected to concentrate the medicine in bone tissue, increasing the amount of doxorubicin that can act on osteosarcoma cells.

What is the stage of development of this medicine?

At the time of submission of the application for orphan designation, the evaluation of the effects of the medicine in experimental models was ongoing.

At the time of submission of the application for orphan designation, no clinical trials with this medicine in patients with osteosarcoma had been started.

At the time of submission, the medicine was not authorised anywhere in the EU for the treatment of osteosarcoma or designated as an orphan medicinal product elsewhere for this condition.

In accordance with Regulation (EC) No 141/2000, the COMP adopted a positive opinion on 7 November 2019, recommending the granting of this designation.

*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 518,400,000 (Eurostat 2019).

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:

Contact details of the current sponsor for this orphan designation can be found on [EMA website](#).

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	(E)-2-((2S,4S)-4-(((2R,4S,5S,6S)-4-amino-5-hydroxy-6-methyltetrahydro-2H-pyran-2-yl)oxy)-2,5,12-trihydroxy-7-methoxy-6,11-dioxo-1,2,3,4,6,11-hexahydrotetracen-2-yl)-10-(carboxymethyl)-1-hydroxy-13-(2-(2-(2-((E)-3-(3-((3-hydroxy-3,3-diphosphonopropyl)(methylamino)propoxy)benzylidene)hydrazine-1-carbonothioyl)hydrazineyl)-2-oxoethyl)-8-oxo-5-thioxo-3,4,6,7,10,13-hexaazapentadec-2-en-15-oic acid	Treatment of osteosarcoma
Bulgarian	(E)-2-((2S,4S,4S)-4-((2R,4S,5S,6S)-4-амино-5-хидрокс-6-метилтетрахидро-2H-пиран-2-ил)-окси)-2,5,12-трихидрокс-7-метокси-6,11-диоксо-1,2,3,3,4,6,6,11-хексахидроксahидротетрацен-2-ил)-10-(карбоксиметил)-1-хидрокс-13-(2-(2)3 дифосфонопропил)(метил)амино)пропокси) бензилиден)хидразин-1-карбонотиоил)хидразинил)-2-оксоетил)-8-оксо-5-тиоксо-3,4,6,7,10,13-хексаазапентадек-2-ен-15-оева киселина	Лечение на остеокарком
Croatian	(E)-2-((2S,4S,4S)-4-((2R,4S,5S,6S)-4-amino-5-hidroksi-6-metiltetrahidro-2H-piran-2-il)oksi)-2,5,12-trihidroksi-7-metoksi-6,11-diokso-1,2,3,3,4,6,6,11-heksahidroksahidrotetracen-2-il)-10-(karboksimetil)-1-hidroxi-13-(2-(2)3-difosfonopropil)(metil)amino)propoksi)benziliden)-hidrazin-1-karbonotiol)-hidrazinil)-2-oksoetil)-8-okso-5-tiokso-3,4,6,7,10,13-heksaazapentadek-2-en-15-oik kiselina	Liječenje osteosarkoma
Czech	(E)-2-((2S,4S)-4-(((2R,4S,5S,6S)-4-amino-5-hydroxy-6-methyltetrahydro-2H-pyran-2-yl)oxy)-2,5,12-trihydroxy-7-methoxy-6,11-dioxo-1,2,3,4,6,11-hexahydrotetracen-2-yl)-10-(karboxymethyl)-1-hydroxy-13-(2-(2-(2-((E)-3-(3-((3-hydroxy-3,3-difosfonopropyl)(methylamino)propoxy)benzyliden)hydrazin-1-karbonothioyl)hydrazinyl)-2-oxoethyl)-8-oxo-5-thioxo-3,4,6,7,10,13-hexaazapentadek-2-en-15-ová kyselina	Léčba osteosarkomu
Danish	(E)-2-((2S,4S,4S)-4-(((2R,4S,5S,6S)-4-amino-5-hydroxy-6-methyltetrahydro-2H-pyran-2-yl)oxy)-2,5,12-trihydroxy-7-methoxy-6,11-dioxo-1,2,3,4,6,11-hexahydroxatetracen-2-yl)-10-(carboxymethyl)-1-hydroxy-13-(2-(2-(2-((E)-3-(3-((3-hydroxy-3,3-diphosphonopropyl)(methylamino)propoxy)benzyliden)hydrazin-1-carbonothioyl)hydrazinyl)-2-oxoethyl)-8-oxo-5-thioxo-3,4,6,7,10,13-hexaazapentadec-2-en-15-oic syre	Behandling af osteosarcoma

¹ At the time of designation

Language	Active ingredient	Indication
Dutch	(E)-2-[(2S,4S,4S,4S)-4-[(2R,4S,5S,6S)-4-amino-5-5-hydroxy-6-methyltetrahydro-2H-pyran-2-yl)oxy]-2,5,12-trihydroxy-7-methoxy-7-methoxy-6,11-dioxo-1,2,3,3,3,4,6,6,11-hexahydroxahydrotetracen-2-yl)-10-(carboxymethyl)-1-hydroxy-13-(2-(2)3 difosfonopropyl)-(methyl)amino)propoxy)-benzylideen)-hydrazine-1-carbonothioyl)-hydrazineyl)-2-oxo-ethyl)-8-oxo-5-thoxo-3,4,6,7,10,10,13-hexazapentadec-2-en-15-oic zuur	Behandeling van osteosarcoma
Estonian	(E)-2-((2S,4S)-4-(((2R,4S,5S,6S)-4-amino-5-hüdoksü-6-metüültetrahydro-2H-püraan-2-üül)oksü)-2,5,12-trihüdoksü-7-metoksü-6,11-diokso-1,2,3,4,6,11-heksahüdrotetraseen-2-üül)-10-(karboksümetüül)-1-hüdoksü-13-(2-(2-(2-((E)-3-(3-((3-hüdoksü-3,3 difosfonopropüül)(metüül)amino)propoksü)bensüliideen)hü draziin-1-karbonotioüül)hüdrazineüül)-2-oksoetüül)-8-okso-5-tiokso-3,4,6,7,10,13-heksaasapentadeek-2-een-15-oiihkape	Osteosarkoomi ravi
Finnish	(E)-2-((2S, 4S, 4S)-4-((2R,4S,5S,6S)-4-amino-5-hydroksi-6-metyylitetrahydro-2H-pyran-2-yyli)oksi)-2,5,12-trihydroksi-7-metoksi-6,11-diokso-1,2,3,3,4,6,6,11-hexahydrotetrasen-2-yyli)-10-(karboksिमetyyli)-1-hydroksi-13-(2-(2-(2-((E)-3-(3-((3-hydroksi-3,3 disfosfonopropyli)(metyyli)amino)propoksi)bensylideeni)hydratsiini-1-karbonyyli)hydratsinyyli)-2-oksoetyyli)-8-okso-5-tiokso-3,4,6, 7,10,13-heksaasapentadek-2-eeni-15-happo	Osteosarkoman hoito
French	(E)-2-((2S,4S)-4-(((2R,4S,5S,5S,6S)-4-amino-5-hydroxy-6-méthyltétrahydro-2H-pyran-2-YL)oxy)-2,5,12-trihydroxy-7-méthoxy-6,11-dioxo-1,2,3,4,6,11-hexahydrotetracen-2-YL)-10-(carboxyméthyle)-1-hydroxy-13-(2-(2-(2-((e)-3-(3-((3-hydroxy-3-((3-hydroxy)3-hydroxy3 diphosphonopropyl)méthyl)amino)propoxy)benzylidène)hydrazine-1-carbonothioyl)hydrazineyl)-2-oxoéthyl)-8-oxo-5-thioxo-3,4,6,7,10,13-hexaazapentadec-2-en-15-oic acide	Traitement des ostéosarcomes
German	(E)-2-((2S,4S)-4-(((2R,4S,5S,6S)-4-amino-5-hydroxy-6-methyltetrahydro-2H-pyran-2-YL)oxy)-2,5,12-Trihydroxy-7-methoxy-6,11-dioxo-1,2,3,4,6,11-hexahydrotetracen-2-YL)-10-(carboxymethyl)-1-hydroxy-13-(2-(2-(2-((E)-3-(3-hydroxy-3,3 diphosphonopropyl)(methyl)amino)propoxy)benzyliden)hydrazin-1-carbonothioyl)hydrazin-2-oxoethyl)-8-oxo-5-thioxo-3,4,6,7,10,13-hexaazapentadec-2-en-15-säure	Behandlung von Osteosarkomen

Language	Active ingredient	Indication
Greek	(E)-2-((2S,4S)-4-(((2R,4S,5S,6S)-4-αμινο-5-υδροξυ-6-μεθυλοτετραϋδρο-2H-πυραν-2-υλ)οξυ)-2,5,12-τριυδροξυ-7-μεθοξυ-6,11-διοξο-1,2,3,4,6,11-εξαϋδροτετρακεν-2-yl)-10-(καρβοξυλομεθυλ)-1-υδροξυ-13-(2-(2-(2-((E)-3-(3-((3-υδροξυ-3,3 διφωσφονοπροπυλ)(μεθυλ)αμινο)προποξυ)βενζυλιδενο)υδρ αζινο-1-καρβονοθειοϋλ)υδραζινυλ)-2-οξοαιθυλ)-8-οξο-5- θειοξο-3,4,6,7,10,13-εξααζαπενταδεκ-2-εν-15-οϊκό οξϋ	Θεραπεία του οστεοσαρκώματος
Hungarian	(E)-2-((2S,4S,4S)-4-((2R,4S,5S,6S)-4-amino-5-hidroxi-6-metil-tetrahidro-2H-pirán-2-il)-oxi)-2,5,12-trihidroxi-7-metoxi-6,11-dioxo-1,2,3,3,4,4,6,6,11-hexahidroxahydrotetracen-2-il)-10-(karboxi-metil)-1-hidroxy-13-(2-(2 3-dosfonopropyl)(mety)-mino)-ppoxi)-bidilidene)hidrazin-1-karbonothiyl)-hidrazinil)-2-oxo-hyl)-8-oxo-5-thioxo-3,4,6,7,10,13-hexaazapentadec-2-hu-15-oic-sav	Osteosarcoma kezelése
Italian	(E)-2-((2S,4S,4S,4S)-4-((2R,4S,5S,6S)-4-amino-5-idrossi-5-6-metiltetraidro-2H-piran-2-yl)oxy)-2,5,12-triidrossi-7-metossi-6,11-diosso-1,2,3,3,3,4,4,6,6,6,11-esaidroxahydrotetracen-2-yl)-10-(carbrossimetil)-1-idrossi-13-(2-(2)3 difosfonopropil)(metil)ammino)ammino)propoxy)benziliden e)idrazina-1-carboniotil)idrazineyl)-2-ossoetil)-8-osso5-5- tiosso-3,4,6,7,10,10,13-esazapentadec-2-en-15-oic acid	Trattamento dell'osteosarcoma
Latvian	(E)-2-((2S,4S)-4-(((2R,4S,5S,6S)-4-amino-5-hidroksi-6-metiltetrahidro-2H-pirān-2-il)oksi)-2,5,12-trihidroksi-7-metoksi-6,11-diokso-1,2,3,4,6,11-heksahidrotetracēn-2-il)-10- (karboksimetil)-1-hidroksi-13-(2-(2-(2-((E)-3-(3-((3-hidroksi-3,3 difosfonopropil)(metil)amino)propoksi)benzilidēna)hidrazīna -1-karbonotiilil)hidrazīnil)-2-oksoetil)-8-okso-5-tiokso- 3,4,6, 7,10,13-heksaazapentadek-2-ēn-15-ānskābe	Osteosarkomas ārstēšana
Lithuanian	(E)-2-((2S, 4S)-4-(((2R, 4S, 5S, 6S) -4-amino-5-hidroksi-6-metiltetrahidro-2H-piran-2-il)oksi)-2,5,12-trihidroksi-7-metoksi-6,11-diokso-1,2,3,4,6, 11-heksahidrotetracen-2-il)-10-(karboksimetil)-1- hidroksi-13-(2-(2-(2-((E)-3-(3-((3-hidroksi-3,3 difosfonopropil)(metil)amino)propoksi)benzilideno)hidrazino -1-karbonotioil)hidrazineil)-2-oksoetil)-8-okso-5-tiokso- 3,4,6,7,10,13-heksaazapentadek-2-en-15-oinė rūgštis	Osteosarkomos gydymas

Language	Active ingredient	Indication
Maltese	(E)-2-((2S,4S)-4-(((2R,4S,5S,6S)-4-ammino-5-idrossi-6-metiltetraidro-2H-piran-2-il)ossi)-2,5,12-triidrossi-7-metossi-6,11-diosso-1,2,3,4,6,11-hežaidrotetračen-2-yl)-10-(karbossimetil)-1-idrossi-13-(2-(2-(2-((E)-3-(3-((3-idrossi-3,3-difosfonopropil)(metil)ammino)propossi)benžiliden)idražina-1-karbonotijojl)idražinejl)-2-ossoetil)-8-osso-5-tiosso-3,4,6,7,10,13-ežaažapentadek-2-en-15-ačidu ojku	Kura ta' l-osteosarkoma
Polish	(E)-2-((2S,4S,4S,4S)-4-(((2R,4S,5S,6S)-4-amino-5-hydroksy-6-metyltetrahydro-2H-pyran-2-yl)oksy)-2,5,12-trihydroksy-7-metoksy-6,11-dioksy-1,2,3,3,4,6,6,kwas 11-heksahydroksahydrotetracen-2-ylo)-10-(karboksymetylo)-1-hydroksy-13-(2-(2)3-difosfonopropylo)(metylo)amino)propoksy)benzylideno)hydrazyno-1-karbozylo)hydrazyno)-2-oksoetylo)-8-okso-5-tiokso-3,4,6,7,10,13-heksaazapentadek-2-en-15-oiksu	Leczenie mięsaka kościopochodnego
Portuguese	Ácido (E)-2-((2S,4S,4S)-4-(((2R,4S,5S,6S)-4-amino-5-hidroxi-6-metiltetrahidro-2H-piran-2-il)oxi)-2,5,12-tri-hidroxi-7-metoxi-6,11-dioxo-1,2,3,3,3,4,6,6,6,11-hexa-hidroxidroxihidrotetracen-2-il)-10-(carboximetil)-1-hidroxi-13-(2-(2)3-difosfonopropil)(metil)amino)propoxi)benzilideno)hidrazina-1-carbonotiol)hidrazineil)-2-oxoetil)-8-oxo-5-tioxo-3,4,6,7,10,13-hexa-azapentadec-2-en-15-óico	Tratamento do osteosarcoma
Romanian	Acid (E)-2-((2S,4S)-4-(((2R,4S,5S,6S)-4-amino-5-hidroxi-6-metiltetrahidro-2H-piran-2-il)oxi)-2,5,12-trihidroxi-7-metoxi-6,11-dioxo-1,2,3,4,6,11-hexahidrotetracen-2-il)-10-(carboximetil)-1-hidroxi-13-(2-(2-(2-((E)-3-(3-((3-hidroxi-3,3-difosfonopropil)(metil)amino)propoxi)benziliden)hidrazin-1-carbonotioil)hidrazineil)-2-oxoetil)-8-oxo-5-tioxo-3,4,6,7,10,13-hexaazapentadec-2-en-15-oic	Tratamentul osteosarcomului
Slovak	(E)-2-((2S,4S, 4S)-4-(((2R,4S,5S,6S)-4-amino-5-hydroxy-6-metyltetrahydro-2H-pyrán-2-yl) oxy)-2,5,12-trihydroxy-7-metoxy-6,11-dioxo-1,2,3,3,4,6,6,11-hexahydroxahydrotetracen-2-yl)-10-(karboxymetyl) -1 hydroxy-13-(2-(2) 3-difosfonopropyl)(metyl) amino)propoxy)benzyliden)hydrazín-1-karbonotioyl) hydrazínyl)-2-oxytyl)-8-oxo-5-tioxo-3,4,6, 7,10,13-hexaazapentadec-2-en-15-ová kyselina	Liečba osteosarkómu

Language	Active ingredient	Indication
Slovenian	(E)-2-((2S,4S,4S)-4-((2R,4S,5S,6S)-4-amino-5-hidroksi-6-metiltetrahidro-2H-piran-2-IL) oksi)-2,5,12-trihidroksi-7-metoksi-6,11-diokso-1,2,3,3,4,6,6,11-heksahidroksahidrotetracen-2-il)-10-(karboksmetil)-1-hidroksi-13-(2-(2)3-difosfonopropil)(metil)amino)propoksi benziliden)hidrazin-1-karbonotiol)hidrazin)-2-okso-8-okso-5-tiokso-3,4,6,7,10,13-heksazapentadek-2-en-15-oičnakislina	Zdravljenje osteosarkoma
Spanish	Acido de (E)-2-((2S,4S,4S)-4-((2R,4S,5S,6S)-4-amino-5-hidroxi-6-metiltetrahidro-2H-piran-2-IL)oxi)-2,5,12-trihidroxi-7-metoxi-6,11-dioxo-1,2,3,3,4,6,6,11-hexahidroxahidrotetracen-2-IL)-10-(carboximetil)-1-hydroxi-13-(2-(2)3-difosfonopropil)(metil)amino)propoxi)benzilidene)hidrazina-1-carbonotioil)hidrazineil)-2-oxoetil)-8-oxo-5-tioxo-3,4,6,7,10,13-hexaazapentadec-2-en-15-oic	Tratamiento del osteosarcoma
Swedish	(E)-2-((2S,4S,4S)-4-((2R,4S,5S,6S)-4-amino-5-hydroxi-6-metyltetrahydro-2H-pyran-2-yl) oxi)-2,5,12-trihydroxi-7-metoxi-6,11-dioxo-1,2,3,3,4,6,6,11-hexahidroxahidrotetracen-2-yl) -10-(karboxymetyl)-1-hydroxyl-13-(2-(2-(2-((E)-3-(3-((3-hydroxy-3,3-difosfonopropyl)(metyl)amino)propoxy)benzyliden)hydrazin e-1-karbonothioyl)hydrazinyl)-2-oxoetyl)-8-oxo-5-thioxo-3,4,6,7,10,13-hexaazapentadec-2-en-15-oicsyra	Behandling av osteosarkom
Norwegian	(E)-2-((2S,4S)-4-(((2R,4S,5S,6S)-4-amino-5-hydroksy-6-metyltetrahydro-2H-pyran-2-yl)oksy)-2,5,12-trihydroksy-7-metoksy-6,11-diokso-1,2,3,4,6,11-heksahidrotetracen-2-yl)-10-(karboksymetyl)-1-hydroksy-13-(2-(2-(2-((E)-3-(3-((3-hydroksy-3,3-difosfonopropyl)(metyl)amino)propoksy)benzyliden)hydrazin-1-karbonotioyl)hydrazinyl)-2-oksoetyl)-8-okso-5-tiokso-3,4,6,7,10,13-heksaazapentadek-2-en-15-syre	Behandling av osteosarkom
Icelandic	(E)-2-((2S,4S,4S)-4-((2R,4S,5S,6S)-4-amino-5-hydroxy-6-methyltetrahydro-2H-pyran-2-yl) oxy)-2,5,12-tríhýdroxý-7-metoxý-6,11-díoxó-1,2,3,3,4,6,6,11-hexahýdroxýdrótetrasen-2-ýl)-10-(karboxýmetýl)-1-hydroxy-13-(2-(2) 3-diphosphonopropyl) (methyl) amino) propoxy) benzylidene) hydrazine-1-carbonothioyl) hydrazineyl) -2-oxoethyl)-8-oxo-5-thioxo-3,4,6, 7,10,13-hexaazapentadec-2-en-15-oic acid	Meðferð við beinsarkmeini