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EMA/COMP/452094/2014
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Macromolecular conjugate of heparin sodium on a polymer backbone for the prevention of ischaemia/reperfusion injury associated with solid organ transplantation

On 22 August 2014, orphan designation (EU/3/14/1332) was granted by the European Commission to Corline Systems AB, Sweden, for macromolecular conjugate of heparin sodium on a polymer backbone for the prevention of ischaemia/reperfusion injury associated with solid organ transplantation.

What is ischaemia/reperfusion injury associated with solid organ transplantation?

Ischaemia and reperfusion injury are problems that can occur to transplant organs as a result of being preserved during the time between donation and transplant. In the course of a transplant, the organ to be transplanted (the 'graft') needs to survive outside the body with no blood supply for a short while. This decrease in blood supply, if prolonged, can cause damage to the organ because of the lack of oxygen and nutrients, a condition called ischaemia. When the graft is attached to the recipient's blood circulation, the restoration of blood supply to the organ (reperfusion) can cause inflammation and damage to the organ, known as reperfusion injury. These processes increase the risk of the graft not working or being rejected by the recipient.

Because ischaemia/reperfusion injury in solid organ transplantation impairs the functioning of the graft, it is a life-threatening condition for the recipient of the graft.

What is the estimated number of patients at risk of developing the condition?

At the time of designation, the number of patients at risk of ischaemia/reperfusion injury associated with solid organ transplantation was estimated to be approximately 0.6 people in 10,000 in the European Union (EU). This was equivalent to a total of around 31,000 people*, and is below the ceiling

*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 511,100,000 (Eurostat 2014).

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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 methods of prevention are available?

At the time of designation, methods used to reduce the effects of ischaemia, and thereby prevent ischaemia/reperfusion injury, included storage of the organ in cold conditions in special preservation solutions or in special machines that help to preserve them. Several preservation solutions were authorised for organ preservation in some countries of the EU at the time of designation.

The sponsor has provided sufficient information to show that this medicine might be of significant benefit for patients at risk of ischaemia/reperfusion injury associated with solid organ transplantation because early studies in experimental models show improved survival of transplanted organs when this product was used. 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 is made of many units of heparin, a blood thinner, linked together by a backbone of inert material. Heparin works by blocking certain enzymes involved in the process of blood clotting and since the formation of blood clots is part of the complex process leading to ischaemia, this medicine is expected to reduce the risk of ischaemia in the graft. As clotting and inflammation are closely related, this medicine may also reduce the inflammation associated with ischaemia and reperfusion. This is expected to reduce the risk of reperfusion injury following an organ transplant.

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, no clinical trials with this medicine in patients at risk of ischaemia/reperfusion injury associated with solid organ transplantation had been started.

At the time of submission, this medicine was not authorised anywhere in the EU for the prevention of ischaemia/reperfusion injury associated with solid organ transplantation 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 10 July 2014 recommending the granting of this designation.

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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 languages[1], Norwegian and Icelandic

Language	Active ingredient	Indication
English	Macromolecular conjugate of heparin sodium on a polymer backbone	Prevention of ischaemia reperfusion injury associated with solid organ transplantation
Bulgarian	Макромолекулен конюгат на хепарин натрий на полимерен гръбнак	Превенция на исхемия реперфузия увреда, свързана с трансплантация на плътни органи
Croatian	Makromolekularni konjugat heparinnatrija na polimernu okosnicu	Prevencija ozljede zbog ishemije i reperfuzije povezane s transplantacijom solidnih organa
Czech	Makromolekulární konjugát heparinu sodn ého na polymerním řetězci	Prevence ischemie reperfuzního poškození u transplantace solidních orgánů
Danish	Makromolekylært konjugat af heparinnatrium på et polymerskelet	Forebyggelse af iskæmisk reperfusionsskade forbundet med transplantation af solide organer
Dutch	Macromoleculaire conjugaat van heparine natrium op een polymeerskelet	Preventie van ischemie - reperfusieletsel geassocieerd aan soliede orgaantransplantatie
Estonian	Naatriumhepariini makromolekulaarne konjugaat polümeersel alusstruktuuril	Soliidorganite siirdamisega seotud isheemia reperfusioonvigastuse ennetamine
Finnish	Makromolekulaarinen konjugaatti, jossa hepariininatrium on liitetty polymeerirunkoon	Iskemia-reperfuusiovaurion esto elinsiirtoleikkauksessa
French	Conjugué macromoléculaire d'héparine sodique sur un squelette de polymère	Prévention des lésions d'ischémie-reperfusion associées aux transplantations d'organes solides
German	Makromolekulares Konjugat von Heparin-Natrium auf einer Polymerhauptkette	Prävention von Ischämie-Reperfusions-Syndromen bei Transplantation solider Organe
Greek	Μακρομοριακό σύμπλοκο νατριούχου ηπαρίνης επί ενός πολυμερούς άξονα	Πρόληψη τουτραυματισμού ισχαιμίας/επαναιμάτωσης που συσχετίζεται με τη μεταμόσχευση συμπαγών οργάνων
Hungarian	Polimer vázra épült heparin-nátrium makromolekuláris konjugátuma	Szervátültetéssel összefüggő ischemiás reperfúziós károsodás megelőzése
Italian	Coniugato macromolecolare di eparina sodica in una struttura polimerica	Prevenzione del danno da ischemia da riperfusione associato al trapianto di organi solidi
Latvian	Heparīna nātrija sāls lielmolekulu konjugāts uz polimēra bāzes	Išēmisku reperfūzijas bojājumu profilakse saistībā ar orgānu transplantāciju
Lithuanian	Natrio heparino makromolekulinis konjugatas ant polimerinio karkaso	Išemijos Reperfuzijos pažeidimo sąlygotos išemijos prevencija, sietina su parenchiminių organų transplantacija

[1] At the time of designation

Language	Active ingredient	Indication
Maltese	Heparin sodium konjugat b'mod makromolekulari fuq sinsla ta' polimer	Prevenzjoni tad-dannu minn riperfusjoni wara iskemija assoċjat mat-trapjant ta' organi solidi
Polish	Wielkocząsteczkowy koniugat heparyny sodowej w szkielecie polimerowym	Zapobieganie uszkodzeniu narządu spowodowanego niedokrwieniem/reperfuzją związanym z przeszczepem narządów litych
Portuguese	Conjugado macromolecular de heparina de sódio num esqueleto de polímero	Prevenção da lesão de isquémia reperfusão associada ao transplante de órgãos sólidos
Romanian	Conjugat macromolecular de heparină sodică pe un schelet polimeric	Prevenirea leziunilor de ischemie-reperfuzie asociate cu transplantul de organe solide
Slovak	Makromolekulárny konjugát heparínu sodného na polymérnom reťazci	Prevencia ischemicko-reperfúzneho poškodenia súvisiaceho s transplantáciou solídneho orgánu
Slovenian	Makromolekularni konjugat heparin natrija na polimernem ogrodju	Preprečevanje ishemične reperfuzijske poškodbe, povezane s presaditvijo parenhimskih organov
Spanish	Conjugado macromolecular de heparina sódica en una cadena principal de polímero	Prevención del daño por isquemia/reperfusión asociado al transplante de órganos sólidos
Swedish	Makromolekylärt konjugat av heparin-natrium på en polymerryggrad	Förebyggande av ischemisk reperfusionsskada i samband med solid organtransplantation
Norwegian	Makromolekylært konjugat av heparinnatrium på et polymerskjelett	Forebygging av iskemi-reperfusjonsskade forbundet med solid organ-transplantasjon
Icelandic	Makrómolekúlar samtengi af natríumheparíni á fjölliðu grunnkeðju	Forvörn gegn blóðþurrðar blóðendurvæðingar skaða í tengslum við líffæraígræðslu