



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

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Committee for Orphan Medicinal Products

## Public summary of opinion on orphan designation

L-Pyr-L-Glu-L-Gln-L-Leu-L-Glu-L-Arg-L-Ala-L-Leu-L-Asn-L-Ser-L-Ser for the prevention of graft loss in pancreatic islet transplantation

On 29 August 2016, orphan designation (EU/3/16/1721) was granted by the European Commission to Araim Pharma Europe Ltd, United Kingdom, for L-Pyr-L-Glu-L-Gln-L-Leu-L-Glu-L-Arg-L-Ala-L-Leu-L-Asn-L-Ser-L-Ser (also known as ARA 290) for the prevention of graft loss in pancreatic islet transplantation.

### What is graft loss in pancreatic islet transplantation?

Pancreatic islets are clusters of cells (beta cells) in the pancreas which produce insulin. Pancreatic islet transplantation can be used to treat patients with type 1 diabetes that is difficult to control.

Graft loss occurs when the recipient's body rejects the transplanted pancreatic islets (the 'graft'). It is caused by the patient's immune system (the body's natural defences) recognising the transplanted cells as 'foreign' and reacting against them. This results in inflammation and damage to the graft.

Graft rejection in pancreatic islet transplantation is debilitating in the long term because it can lead to failure to cure type 1 diabetes.

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

At the time of designation, patients at risk of graft loss in pancreatic islet transplantation were less than 0.01 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 500 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).

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\*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 513,700,000 (Eurostat 2016).



## **What methods of prevention are available?**

At the time of designation, no satisfactory methods were authorised in the EU for the prevention of graft loss in pancreatic islet transplantation.

## **How is this medicine expected to work?**

The medicine is a short chain of amino acids that is able to attach to and activate a receptor in the body called the innate repair receptor (IRR). The IRR is produced at high levels in cells, including pancreatic islet cells, when there is tissue damage or inflammation. When the medicine attaches to the receptor, it stimulates repair processes in the cells and tissues which help to control inflammation and apoptosis (programmed cell death). This is expected to reduce the loss of islet cells from the graft following transplantation.

## **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 the medicine in patients who had undergone pancreatic islet transplantation had been started.

At the time of submission, the medicine was not authorised anywhere in the EU for prevention of graft loss in pancreatic islet transplantation. Orphan designation of the medicine had been granted in the USA for prevention of delayed graft function following kidney transplant.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 13 July 2016 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:

Contact details of the current sponsor for this orphan designation can be found on EMA website, on the medicine's [rare disease designations page](#).

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<sup>1</sup>, Norwegian and Icelandic

| Language   | Active ingredient   | Indication   |
|------------|---|--|
| English    | L-Pyr-L-Glu-L-Gln-L-Leu-L-Glu-L-Arg-L-Ala-L-Leu-L-Asn-L-Ser-L-Ser | Prevention of graft loss in pancreatic islet transplantation                                 |
| Bulgarian  | L-Pyr-L-Glu-L-Gln-L-Leu-L-Glu-L-Arg-L-Ala-L-Leu-L-Asn-L-Ser-L-Ser | За предотвратяване на отхвърляне на присадката при трансплантация на парче от панкреаса      |
| Croatian   | L-Pyr-L-Glu-L-Gln-L-Leu-L-Glu-L-Arg-L-Ala-L-Leu-L-Asn-L-Ser-L-Ser | Prevenција odbacivanja presatka kod transplantacije otočica pankreasa                        |
| Czech      | L-Pyr-L-Glu-L-Gln-L-Leu-L-Glu-L-Arg-L-Ala-L-Leu-L-Asn-L-Ser-L-Ser | Prevence rejekce štěpu během transplantace Langeransových ostrůvků pankreatu                 |
| Danish     | L-Pyr-L-Glu-L-Gln-L-Leu-L-Glu-L-Arg-L-Ala-L-Leu-L-Asn-L-Ser-L-Ser | Forebyggelse af implantatafstødning ved transplantation af langerhanske øer                  |
| Dutch      | L-Pyr-L-Glu-L-Gln-L-Leu-L-Glu-L-Arg-L-Ala-L-Leu-L-Asn-L-Ser-L-Ser | Preventie van transplantaatafstoting bij transplantatie van de eilandjes van Langerhans.     |
| Estonian   | L-Pyr-L-Glu-L-Gln-L-Leu-L-Glu-L-Arg-L-Ala-L-Leu-L-Asn-L-Ser-L-Ser | Implantaadi äratõuke vältimiseks pankrease rakkude siirdamisel                               |
| Finnish    | L-Pyr-L-Glu-L-Gln-L-Leu-L-Glu-L-Arg-L-Ala-L-Leu-L-Asn-L-Ser-L-Ser | Siirteen hylkimisen esto haiman osittaissiirossa   |
| French     | L-Pyr-L-Glu-L-Gln-L-Leu-L-Glu-L-Arg-L-Ala-L-Leu-L-Asn-L-Ser-L-Ser | Prévention du rejet de greffe lors d'une transplantation d'îlots de Langerhans pancréatiques |
| German     | L-Pyr-L-Glu-L-Gln-L-Leu-L-Glu-L-Arg-L-Ala-L-Leu-L-Asn-L-Ser-L-Ser | Zur Prävention der Abstoßungsreaktion bei Inselzelltransplantationen                         |
| Greek      | L-Pyr-L-Glu-L-Gln-L-Leu-L-Glu-L-Arg-L-Ala-L-Leu-L-Asn-L-Ser-L-Ser | Για την πρόληψη απόρριψης των μοσχευμάτων κατά τη μεταμόσχευση παγκρεατικών νησίδων          |
| Hungarian  | L-Pyr-L-Glu-L-Gln-L-Leu-L-Glu-L-Arg-L-Ala-L-Leu-L-Asn-L-Ser-L-Ser | Beültetési kilöködés megakadályozására hasnyálmirigy testecske transzplantációnál            |
| Italian    | L-Pyr-L-Glu-L-Gln-L-Leu-L-Glu-L-Arg-L-Ala-L-Leu-L-Asn-L-Ser-L-Ser | Prevenzione delle crisi di rigetto dopo trapianto di isole pancreatiche                      |
| Latvian    | L-Pyr-L-Glu-L-Gln-L-Leu-L-Glu-L-Arg-L-Ala-L-Leu-L-Asn-L-Ser-L-Ser | Transplantāta atgrūšanas novēršanai aizkuņģa dziedzera saliņu transplantācijas gadījumā      |
| Lithuanian | L-Pyr-L-Glu-L-Gln-L-Leu-L-Glu-L-Arg-L-Ala-L-Leu-L-Asn-L-Ser-L-Ser | Transplantato atmetimo reakcijos prevencija kasos salelių transplantacijos metu              |
| Maltese    | L-Pyr-L-Glu-L-Gln-L-Leu-L-Glu-L-Arg-L-Ala-L-Leu-L-Asn-L-Ser-L-Ser | Prevenzjoni ta' rigettar ta' l-organu waqt trapjant tal-islets tal-frixa                     |
| Polish     | L-Pyr-L-Glu-L-Gln-L-Leu-L-Glu-L-Arg-L-Ala-L-Leu-L-Asn-L-Ser-L-Ser | Zapobieganie odrzuceniu przeszczepu podczas transplantacji wysp trzustkowych                 |

<sup>1</sup> At the time of designation

| Language   | Active ingredient   | Indication   |
|------------|---|--|
| Portuguese | L-Pyr-L-Glu-L-Gln-L-Leu-L-Glu-L-Arg-L-Ala-L-Leu-L-Asn-L-Ser-L-Ser | Prevenção da rejeição de enxertos no decurso de transplantes de ilhéus pancreáticos  |
| Romanian   | L-Pyr-L-Glu-L-Gln-L-Leu-L-Glu-L-Arg-L-Ala-L-Leu-L-Asn-L-Ser-L-Ser | Prevenirea rejetului de grefă în cazul transplantului de celule insulare pancreatice |
| Slovak     | L-Pyr-L-Glu-L-Gln-L-Leu-L-Glu-L-Arg-L-Ala-L-Leu-L-Asn-L-Ser-L-Ser | Prevenia odmietnutia štepů pri transplantácii Langerhansových ostrovčeků pankreasu   |
| Slovenian  | L-Pyr-L-Glu-L-Gln-L-Leu-L-Glu-L-Arg-L-Ala-L-Leu-L-Asn-L-Ser-L-Ser | Preprečevanje zavrnitve presadka med presajanjem pankreasnih otočkov                 |
| Spanish    | L-Pyr-L-Glu-L-Gln-L-Leu-L-Glu-L-Arg-L-Ala-L-Leu-L-Asn-L-Ser-L-Ser | Prevención del rechazo del injerto en el trasplante de islotes pancreáticos          |
| Swedish    | L-Pyr-L-Glu-L-Gln-L-Leu-L-Glu-L-Arg-L-Ala-L-Leu-L-Asn-L-Ser-L-Ser | Förebyggande av avstötning vid transplantation av ö-celler från pancreas             |
| Norwegian  | L-Pyr-L-Glu-L-Gln-L-Leu-L-Glu-L-Arg-L-Ala-L-Leu-L-Asn-L-Ser-L-Ser | Forebygging av transplantatrefeksjon ved transplantasjon av øyceller fra pancreas    |
| Icelandic  | L-Pyr-L-Glu-L-Gln-L-Leu-L-Glu-L-Arg-L-Ala-L-Leu-L-Asn-L-Ser-L-Ser | Til að koma í veg fyrir höfnun græðlings við ígræðslu briseyja                       |