



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Public summary of opinion on orphan designation

Tripotassium citrate monohydrate and potassium hydrogen carbonate for the treatment of distal renal tubular acidosis

On 20 June 2017, orphan designation (EU/3/17/1888) was granted by the European Commission to Advicenne Pharma SA, France, for tripotassium citrate monohydrate and potassium hydrogen carbonate (also known as ADV7103) for the treatment of distal renal tubular acidosis.

What is distal renal tubular acidosis?

Distal renal tubular acidosis is a kidney disease in which the kidneys do not remove acid through the urine well enough. This results in a build-up of acid in the blood, which leads to a range of symptoms including hearing and growth problems, vomiting, kidney stones and lack of alertness.

The disease also causes levels of potassium in the blood to fall, which can lead to muscle weakness and paralysis. One type of distal renal tubular acidosis, usually first detected in babies, is caused by mutations (changes) in certain genes. A second type, usually seen in adults, can be caused by several other diseases including some autoimmune diseases (diseases caused by the body's defence system attacking normal tissue).

Distal renal tubular acidosis is debilitating due to the problems it causes with hearing, growth, the kidneys and bone development and can be life-threatening in some patients.

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

At the time of designation, distal renal tubular acidosis affected approximately 2.1 in 10,000 people in the European Union (EU). This was equivalent to a total of around 108,000 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 28), Norway, Iceland and Liechtenstein. This represents a population of 515,700,000 (Eurostat 2017).



What treatments are available?

At the time of designation, treatments containing salts, such as potassium/sodium citrate and potassium/sodium bicarbonate, used on their own or in different combinations, were used in patients with distal renal tubular acidosis.

The sponsor has provided sufficient information to show that the medicine might be of significant benefit for patients with distal renal tubular acidosis because preliminary data show that it stops the blood becoming too acidic, and its effects compare well with currently 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?

The medicine is a combination of two salts, tripotassium citrate monohydrate (also known as potassium citrate) and potassium hydrogen carbonate (also known as potassium bicarbonate), that are taken by mouth and released slowly into the body over a few hours. Because the combination is alkaline and contains potassium, it is expected to both neutralise excess acid in the blood and restore levels of potassium.

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, clinical trials with the medicine in patients with distal renal tubular acidosis were ongoing.

At the time of submission, the medicine was not authorised anywhere in the EU for distal renal tubular acidosis 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 12 May 2017 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:

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 languages¹, Norwegian and Icelandic

Language	Active ingredient	Indication
English	Tripotassium citrate monohydrate and potassium hydrogen carbonate	Treatment of distal renal tubular acidosis
Bulgarian	Трикалийв цитрат монохидрат и калиев хидроген бикарбонат	Лечение на дистална тубулна ацидоза
Croatian	Trikalijski citrat monohidrat i kalijev hidrogen karbonat	Liječenje distalne renalne tubularne acidoze
Czech	Citrát draselný a hydrogenuhlíčan draselný	Léčba distální renální tubulární acidózy
Danish	Trikaliumcitratmonohydrat og kaliumhydrogencarbonat	Behandling af distal renal tubulær acidose
Dutch	Trikaliumcitraatmonohydraat en kaliumbicarbonaat	Behandeling van distale renale tubulaire acidose
Estonian	Tri-Kaalium tsitraat monohüdraat ja kaalumvesinikkarbonaat	Neeru distaalse e tubulaaratsidoosi ravi
Finnish	Trikaliumsitraatti monohydraatti ja kaliumvetykarbonaatti	Distaalisen renaalisen tubulaarisen asidoosin hoito
French	Citrate de potassium monohydrate et bicarbonate de potassium	Traitement de l'acidose tubulaire rénale distale
German	Tr-Kaliumcitrat Monohydrat und Kaliumhydrogencarbonat	Behandlung der distalen renalen tubulären Azidose
Greek	Μονοϋδρικό κίτρικό κάλιο και όξινο ανθρακικό κάλιο	Θεραπεία της άπω νεφρικής σωληναριακής οξέωσης
Hungarian	Trikálium-citrátmonohidrát és kálium-hidrogén-karbonát	Distalis renális tubuláris acidózis kezelése
Italian	Citrato di potassio monoidrato e bicarbonato di potassio	Trattamento dell' acidosi tubulare renale distale
Latvian	Trikālija citrāta monohidrāts un kālija hidrogēnkarbonāts	Distālās nieru tubulārās acidozes ārstēšana
Lithuanian	Trikalio citrato monohidratas su kalio hidrogeno karbonatu	Distalinės inkstų kanalėlių acidozės gydymas
Maltese	Ċitrat monoidrat tat-tripotassju u karbonat idroġenat tal-potassju	Trattament ta' aċidożi tubulari renali distali
Polish	Monohydrat cytrynianu potasu oraz węglan wodorowęglanu potasu	Leczenie dystalnej kwasicy kanalików nerkowych
Portuguese	Citrato tripotássico mono-hidratado e Hidrogenocarbonato de potássio	Tratamento da acidose tubular renal distal
Romanian	Citrat de potasiu monohidrat și bicarbonat de potasiu	Tratamentul acidozei tubulare renale distale
Slovak	Monohyrát citrátu draselného a hydrogenuhlíčan draselný	Liečba distálnej renálnej tubulárnej acidózy

¹ At the time of designation

Language	Active ingredient	Indication
Slovenian	Trikalijev citrat monohidrat in kalijev hidrogenkarbonat	Zdravljenje distalne ledvične tubulne acidoze
Spanish	Citrato de potasio monohidratado y bicarbonato de potasio	Tratamiento de la acidosis tubular renal distal
Swedish	Kaliumcitrat och monohydrate kaliumbikarbonat	Behandling av distal njurkanalsacidosis
Norwegian	Trikaliumsitratmonohydrat og kaliumbikarbonat	Behandling av distal renal tubulær acidose
Icelandic	Kalíum sítrat og kalíum bíkarbónat	Meðferð distal nýrnápíplablóðsýring