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Public summary of opinion on orphan designation

Tripotassium citrate monohydrate and potassium hydrogen carbonate for the treatment of cystinuria

On 9 January 2020, orphan designation EU/3/19/2239 was granted by the European Commission to Advicenne S.A, France, for tripotassium citrate monohydrate and potassium hydrogen carbonate (also known as ADV7103) for the treatment of cystinuria.

What is cystinuria?

Cystinuria is an inherited condition caused by a mutation (change) in the genes that produce the protein rBAT, which transports the amino acid cystine out of the urine and gut. Because the mutation means that rBAT does not work properly, people with the condition develop high concentrations of cystine in their urine. As cystine is poorly soluble, it crystallises in the urine inside the kidney, forming kidney stones that can damage the kidneys and block passage of urine. The condition is long-term debilitating due to the pain, bleeding, obstruction and risk of infection and kidney damage caused by the stones.

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

At the time of designation, cystinuria affected approximately 1 in 10,000 people in the European Union (EU). This was equivalent to a total of around 52,000 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, patients were managed with increased fluid intake, restriction of sodium and protein in the diet, and with substances such as potassium citrate to make the urine more alkaline and so improve the amount of cystine it can dissolve, reducing the risk of stones. In some EU countries the medicines penicillamine and tiopronin were authorised for treatment in patients who could not be managed with other measures.

*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).

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The sponsor has provided sufficient information to show that the medicine might be of significant benefit for patients with cystinuria. Early data in patients showed that the medicine kept the urine more alkaline throughout the night and for longer than other medicines that work in the same way. 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 contains tripotassium citrate monohydrate and potassium hydrogen carbonate, which are substances that can make urine more alkaline, allowing cysteine to be dissolved and preventing stone formation. The substances are included in granules designed to slow down the release of the substances over several hours. After the medicine is taken by mouth, the slow release of the substances in the body is expected to maintain the medicine's effect throughout the day and especially during the night.

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 cystinuria were ongoing.

At the time of submission, the medicine was not authorised anywhere in the EU for the treatment of cystinuria 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 5 December 2019, 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.

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	Tripotassium citrate monohydrate and potassium hydrogen carbonate	Treatment of cystinuria
Bulgarian	Трикалиев цитрат монохидрат и калиев хидроген бикарбонат	Лечение на цистинурия
Croatian	Trikalijski citrat monohidrat i kalijev hidrogen karbonat	Liječenje cistinurije
Czech	Citrát draselný a hydrogenuhličitan draselný	Léčba cystinurie
Danish	Trikaliumcitratmonohydrat og kaliumhydrogencarbonat	Behandling af cystinuri
Dutch	Trikaliumcitraatmonohydraat en kaliumbicarbonaat	Behandeling van cystinurie
Estonian	Tri-Kaalium tsitraat monohüdraat ja kaaliumvesinikkarbonaat	Tsüstiinuria ravi
Finnish	Trikaliumsitraatti monohydraatti ja kaliumvetykarbonaatti	Kystinurian hoito
French	Citrate de potassium monohydrate et bicarbonate de potassium	Traitement de la cystinurie
German	Tr-Kaliumcitrat Monohydrat und Kaliumhydrogencarbonat	Behandlung von Cystinurie
Greek	Μονοϋδρικό κιτρικό κάλιο και όξινο ανθρακικό κάλιο	Θεραπεία της κυστινουρίας
Hungarian	Trikálium-citrátmonohidrát és kálium-hidrogén-karbonát	Cystinuria kezelése
Italian	Citrato di potassio monoidrato e bicarbonato di potassio	Trattamento della cistinuria
Latvian	Trikālija citrāta monohidrāts un kālija hidrogēnkarbonāts	Cistinūrijas ārstēšana
Lithuanian	Trikalio citrato monohidratas su kalio hidrogeno karbonatu	Cistinurijos gydymas
Maltese	Ċitrat monoidrat tat-tripotassju u karbonat idroġenat tal-potassju	Trattament taċ-ċistinurja
Polish	Monohydrat cytrynianu potasu oraz węglan wodorowęglanu potasu	Leczenie cystynurii
Portuguese	Citrato tripotássico mono-hidratado e Hidrogenocarbonato de potássio	Tratamento da cistinúria
Romanian	Citrat de potasiu monohidrat şi bicarbonat de potasiu	Tratamentul cistinuriei
Slovak	Monohydrát citrátu draselného a hydrogénuhličitan draselný	Liečba cystinúrie
Slovenian	Trikalijev citrat monohidrat in kalijev hidrogenkarbonat	Zdravljenje cistinurije
Spanish	Citrato de potasio monohidratado y bicarbonato de potasio	Tratamiento de la cistinuria
Swedish	Kaliumcitrat och monohydrate kaliumbikarbonat	Behandling av cystinuri
Norwegian	Trikaliumsitratmonohydrat og kaliumbikarbonat	Behandling av cystinuri
Icelandic	Kalíum sítrat og kalíum bíkarbónat	Meðferð á cystinmigu

[1] At the time of designation