NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Slow-release potassium bicarbonate and potassium citrate for treating distal renal tubular acidosis

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of slow-release potassium bicarbonate and potassium citrate within its marketing authorisation for treating distal renal tubular acidosis.

Background

Distal renal tubular acidosis (dRTA) is a disorder of impaired acid removal from the blood.The kidneys filter acids from the blood and remove them from the body in urine, this prevents the build of up acids in the blood. dRTA occurs when the kidneys do not properly remove acids from the blood into the urine, which causes a person's blood to be too acidic[1]. DRTA may be hereditary (primary dRTA) or acquired (secondary dRTA) caused by autoimmune diseases such as Sjögren syndrome or secondary to other conditions like sickle cell anaemia, systemic lupus erythematosus, chronic obstructive uropathy, or post-renal transplantation) [2].

Distal renal tubular acidosis is a rare condition with a prevalence in the UK of between the company reported a prevalence 0.46 to 1.6 per 10,000 people [3], which means between 3066 and 10664 people are currently living with the condition. The incidence of the disease seems to be unknown

Primary dRTA is a highly variable disorder and can affect people very differently some people have slightly elevated acid levels and no accompanying symptoms (and are asymptomatic) and others can experience kidney stones, growth failure or rickets (bowing of the bones) [4].

There is no NICE guidance on the treatment of dRTA. Standard management includes the use of alkali replacement therapy is given to correct metabolic acidosis and to maintain serum potassium levels in the normal range, this can vary slightly in dosages and exact treatment dependent on the form of dRTA.

The technology

Potassium citrate and potassium bicarbonate (Sibnayal, Advicenne) is in a prolonged-release formulation, designed to maintain sustained release over a twelve-hour period. It is expected to both neutralise excess acid in the blood and restore levels of potassium. It is administered orally.

Potassium citrate and potassium bicarbonate does not have marketing authorisation in the UK for dRTA. It has been studied in clinical trials compared with placebo in people aged 6 months and over with hereditary (primary) and acquired (secondary) dRTA.

Intervention(s)	Potassium citrate and potassium bicarbonate (Sibnayal)
Population(s)	People with primary and secondary distal renal tubular acidosis aged 6 months and older
Comparators	Alkali therapy, sodium bicarbonate or sodium citrate
Outcomes	The outcome measures to be considered include: • Blood bicarbonate level • Mean change in blood bicarbonate level • Reduction of excess calcium in the urine • Correction of low citrate levels in the urine • Adverse effects of treatment • Health-related quality of life.
Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective.
Other considerations	Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.
Related NICE recommendations and NICE Pathways	None
Related National Policy	NHS England (2019) The NHS long term plan NHS England (2018) NHS England Funding and Resource 2018/19: Supporting 'Next Steps for the NHS Five Year Forward View' NHS England (2017) Next steps on the five year forward view NHS England (2014) NHS Five year forward view

	National Service Frameworks Renal Services - archived **Other policies** Department of health (2016) NHS outcomes framework 2016 to 2017

Questions for consultation

What is the treatment pathway for dRTA?

Have all relevant comparators for potassium citrate and potassium bicarbonate been included in the scope? Which treatments are considered to be established clinical practice in the NHS for treating primary distal renal tubular acidosis?

Are the outcomes listed appropriate? Are there any other outcomes that should be considered such as e.g. Kidney stone formation, onset of chronic kidney disease, kidney failure, hearing loss?

Are there any subgroups of people in whom potassium citrate and potassium bicarbonate is expected to be more clinically effective and cost effective or other groups that should be examined separately?

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which it potassium citrate and potassium bicarbonate will be licensed.
- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology.
- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts.

Do you consider potassium citrate and potassium bicarbonate to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of potassium citrate and potassium bicarbonate can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.

To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/article/pmg19/chapter/1-Introduction).

References

1. Rehman HU; A woman with generalised weakness, hypokalaemia, and metabolic acidosis. BMJ. 2012 Apr 12344:e2545. doi: 10.1136/bmj.e2545.

2. Both T, Zietse R, Hoorn EJ, et al; Everything you need to know about distal renal tubular acidosis in autoimmune disease. Rheumatol Int. 2014 Aug34(8):1037-45. doi: 10.1007/s00296-014-2993-3. Epub 2014 Mar 29

3. ISPOR poster, Advicenne, 2019, link, https://advicenne.com/2019/wp-content/uploads/2019/06/20190613_Advicenne_PR_Poster-presentation-at-ISPOR.pdf, accessed 03/12/2020

4. National Organization for Rare Disorders. Primary Distal Renal Tubular Acidosis, link, https://rarediseases.org/rare-diseases/primary-distal-renal-tubular-acidosis/, accessed 03/12/2020

5. National clinical trials website, A Phase 3 Multicenter, Randomized, Double-Blinded, Placebo-Controlled Withdrawal Study Evaluating ADV7103 In Pediatric and Adult Subjects With Distal Renal Tubular Acidosis (dRTA), Link; https://clinicaltrials.gov/ct2/show/NCT03644706?term=ADV7103&cond=Distal+Renal+Tubular+Acidosis&phase=2&draw=2&rank=1, accessed 27/11/2020

6. National clinical trials website, A Phase 3B Open-Label Extension Of Study B23CS (ARENA 2) Evaluating The Continued Safety And Efficacy Of ADV7103 In Subjects With Primary Distal Renal Tubular Acidosis, link, https://clinicaltrials.gov/ct2/show/NCT03831152?term=ADV7103&cond=Distal+Renal+Tubular+Acidosis&phase=2&draw=2&rank=2, accessed 27/11/2020

7. EU Clinical Trials Register website, A multicentre, open-label, non-inferiority sequential study, evaluating the efficacy, safety, tolerability and acceptability of ADV7103 compared to standard of care in distal renal tubular acidosis patients, link, https://www.clinicaltrialsregister.eu/ctr-search/trial/2013-002988-25/SK#A, accessed 27/11/2020

8. BMJ best practice website, Distal renal tubular acidosis, link https://bestpractice.bmj.com/topics/en-gb/239/treatment-algorithm#patientGroup-0-0

Appendix B