

National Institute for Health and Care Excellence

Single technology Appraisal (STA)

**Slow-release potassium bicarbonate and potassium citrate for treating distal renal tubular acidosis
Response to consultee and commentator comments on the draft remit and draft scope (pre-referral)**

Please note: Comments received in the course of consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees.

Comment 1: the draft remit

Section	Consultee/ Commentator	Comments [sic]	Action
Appropriateness	Advicenne	Yes, as dRTA is sub optimally treated it potentially presents a severe health impact to patients	Thank you for your comment. No action needed.
	Renal Association	Yes	Thank you for your comment. No action needed.
Wording	Advicenne	The most accurate wording reflecting the new technology of Sibnaya is prolonged release	Thank you for your comment. The wording has been updated.
	Renal Association	Yes	Thank you for your comment. No action needed.

Section	Consultee/ Commentator	Comments [sic]	Action
Timing Issues	Advicenne	[REDACTED]	Comment noted. NICE aims to provide draft guidance to the NHS within 6 months from the date when marketing authorisation for a technology is granted. NICE has scheduled this topic into its work programme. No action needed.
	Renal Association	1-2 years	Comment noted. NICE aims to provide draft guidance to the NHS within 6 months from the date when marketing authorisation for a technology is granted. NICE has scheduled this topic into its work programme. No action needed.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	Advicenne	<p>There is a grammatical error in the sentence where it reads 'prevents the build of up acids in the blood'.</p> <p>dRTA varies in severity. Some patients experience elevated acid levels but are asymptomatic. For others, dRTA presents a severe health impact that should be considered: metabolic</p>	<p>Thank you for your comments.</p> <p>The error has been corrected and deafness was added to the background.</p>

Section	Consultee/ Commentator	Comments [sic]	Action
		emergency (due to hypokalemia or severe acidosis or both) in 25% of patients (McSherry 1981); hypokalemia 63.12% (Zhang et al 2015), that could lead to arrhythmia and paralysis (32%) which can affect respiratory muscles; Chronic Kidney Disease in 82% of patients (López García 2019), including end stage CKD in up to 5% of patients (Reddi A 2020); osteoporosis in adults (90%) and in children (43%), Zhang et al 2015 and Caldas et al 1992; osteomalacia in adults 9.6 to 23.3% (Jha et al 2011 and Nilwarangkur S et al, 1990); pathological fractures in 6.3% of these patients (Zhang et al 2015); clinically relevant deafness in 31% of patients. Additionally, a mortality rate of 11.1% has been reported in some paediatric dRTA patients (Sharifian M et al 2010.)	The background section is intended to provide a brief summary of the condition. More details will be discussed during the appraisal. No further action is needed.
	Renal Association	Worth detailing that treatment is required long term and some preparations are unpleasant to take (see outcomes below)	Thank you for your comment. The background section is intended to provide a brief summary of the condition. More details will be discussed during the appraisal. No action needed.
The technology/ intervention	Advicenne	SIBNAYAL is a fixed-dose combination of potassium citrate and potassium bicarbonate as prolonged-release granules. The pivotal study B21CS uses the standard of care alkalinising treatments as comparators, not placebo. Products used as standard of care include one product regimens: potassium bicarbonate, potassium citrate, modified shohl's solution, sodium bicarbonate, and two product combinations: potassium bicarbonate+ potassium citrate, potassium bicarbonate+ sodium bicarbonate, potassium citrate+ sodium bicarbonate, modified shohl's solution.	Thank you for your comments. The wording has been updated.
	Renal Association	Yes	Thank you for your comment. No action needed.

Section	Consultee/ Commentator	Comments [sic]	Action
Population	Advicenne	SIBNAYAL is indicated for the treatment of distal renal tubular acidosis (dRTA) in adults, adolescents and children aged one year and older .	Thank you for your comment. The wording has been updated.
	Renal Association	Yes	Thank you for your comments. No action needed.
Comparators	Advicenne	There is currently no licensed medicine indicated specifically for dRTA and therefore clinicians rely on unlicensed alkalisating therapies to treat the disease. Products used as standard of care include one product regimens: potassium bicarbonate, potassium citrate, modified shohl's solution, sodium bicarbonate, and two product combinations: potassium bicarbonate+ potassium citrate, potassium bicarbonate+ sodium bicarbonate, potassium citrate+ sodium bicarbonate, modified shohl's solution.	Thank you for your comments. The comparators section was updated after consultation.
	Renal Association	They are, but many patients will be receiving combined sodium bicarbonate and potassium citrate therapy – how will this be addressed	Thank you for your comment. The comparators section was updated after consultation. Combined sodium bicarbonate and potassium citrate therapy (not Sibnaya) is included in the list of comparators.
Outcomes	Advicenne	The additional outcome of life-years gained was assessed. Responder rate with SoC compared to Sibnaya in terms of bicarbonatemia normalisation. Bone mineral density (BMD) at the start of B21CS and after 2 years of treatment with Sibnaya (results pending yet to be published)	Thank you for your comments. The outcomes section was updated after consultation.

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	Renal Association	Palatability and adherence to treatment should be considered. I would also favour including development of kidney stones / nephrocalcinosis, as well as onset of CKD (although suspect interpretation of such studies may be difficult)	Thank you for your comments. The outcomes section was updated after consultation.
Economic analysis	Advicenne	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of the primary outcome , incremental cost per quality-adjusted life year. The secondary outcome observed in the economic analysis is cost per life-year gained. 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.	Thank you for your comments. No action needed.
	Renal Association	Agree with approach	Thank you for your comment. No action needed.
Equality and Diversity	Advicenne	Advicenne aims to comply fully with all legal obligations to: promote race and disability equality and equality of opportunity between men and women, eliminate unlawful discrimination on grounds of race, disability, age, sex, gender reassignment, marriage and civil partnership, pregnancy and maternity (including women post-delivery), sexual orientation, and religion or belief (these are protected characteristics under the Equality Act 2010). Advicenne cannot see any equality issues with the use of SIBNAYAL.	Thank you for your comments. No action needed.

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	Renal Association	Please confirm that products being assessed are licensed for CYP <16 years (or that, if appropriate, recommendations for their use off-licence can be made)	Thank you for your comment. Fixed-dose prolonged-release potassium citrate and potassium bicarbonate (Sibnaya) will be assessed within its marketing authorisation. No action needed.
Innovation	Advicenne	<p>SIBNAYAL is innovative, and has fulfils the need for:</p> <ul style="list-style-type: none"> • one specific product containing an alkalisng product and potassium supplement • one single product with no sodium intake • a BID dosing with no intake during school or at night • a product easy to swallow whatever the age and tasteless • a product allowing dose adjustment whatever the age • a product with an improved gastrointestinal tolerability • a product with a positive benefit/risk profile to control metabolic acidosis. <p>All of which have not been achieved until the development of this therapy.</p>	Thank you for your comments. The innovative nature of the technology will be considered throughout the course of the appraisal. No action needed.
	Renal Association	Could improve QOL and adherence if more palatable	Thank you for your comments. The innovative nature of the technology will be considered throughout the course of the appraisal. No action needed.

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Questions for consultation	Advicenne	<p>Treatment pathway: Primary dRTA is diagnosed by paediatric nephrologists even in newborns or in the first 1-3 years of life, depending on severity of the disease and genes affected. Treatment follow up is done by paediatric nephrologists 1-2 times a year. If renal stones appeared patients are referred to urologists. Acquired dRTA is usually diagnosed by adult nephrologists as mainly affects patients over the age of 18.</p> <p>Products used as standard of care include one product regimens: potassium bicarbonate, potassium citrate, modified shohl's solution, sodium bicarbonate, and two product combinations: potassium bicarbonate+ potassium citrate, potassium bicarbonate+ sodium bicarbonate, potassium citrate+ sodium bicarbonate, modified shohl's solution.</p>	<p>Thank you for your comments.</p> <p>The comparators section was updated after consultation.</p> <p>No further action is needed.</p>

The following consultees/commentators indicated that they had no comments on the draft remit and/or the draft scope

Neonatal and Paediatric Pharmacists Group (NPPG)