

SPECIALISED COMMISSIONING – RESPONSE TO AMENDMENTS REQUESTED TO EVIDENCE REVIEW DURING ENGAGEMENT OR CONSULTATION

URN	170094P
POLICY TITLE	Trientine dihydrochloride for Wilson disease
CRG:	Metabolic Disorders
NPOC:	Women and Children
PUBLIC HEALTH LEAD:	██████████

Description of comments during consultation	<p>The policy proposition does not currently include a new medicinal product for Wilson disease (WD) patients which was approved in all EU member states on 9th September 2017. This product is Cuprior which contains a new trientine salt (trientine tetrahydrochloride) and is indicated for the treatment of WD in adults, adolescents and children ≥ 5 years intolerant to D-penicillamine therapy.</p>
Action taken by Public Health lead	<p>Reviewed articles submitted by stakeholder and European Medicines Agency application studies. Comments for each are noted below:</p> <p>1. Ala A, Walker AP, Ashkan K et al. Wilson's disease. Lancet. 2007 Feb 3;369(9559):397-408.</p> <p>This is a review on Wilson disease and treatment care pathways. The policy proposition recognises the variation in disease genetic pool and its presentation and takes account of similar studies which are pertinent to the target population.</p> <p>2. Dzieżyc K, Karliński M, Litwin T, et al. Eur J Neurol. 2014 Feb;21(2):332-7.</p> <p>Compliant treatment with anti-copper agents prevents clinically overt Wilson disease in pre-symptomatic patients. This study focuses on pre-symptomatic patients (which was not the focus of the policy proposition) and looks at treatment with zinc sulphate (apart from zinc acetate dehydrate which is included in the proposition, zinc sulphate is not licensed in the UK for this condition). Thus for both reasons this was excluded from the evidence review and the proposition.</p>

	<p>3. Todd S. Refrigerated medicinal products: what pharmacists need to know. The Pharmaceutical Journal, 1 October 2008. Not relevant as it describes how Trientine needs to be refrigerated and this is well understood in clinical practice including how it effects compliance with treatment, hence it does not change current policy proposition.</p> <p>4. Specialist Pharmacy Service (SPS). Refrigerated storage trientine (Univar) capsules. Published 26th Jan 2016, updated 2nd Feb 2018. Available at: https://www.sps.nhs.uk/medicines/trientine/ Accessed 18 September, 2018.</p> <p>This review relates to article number 4. The proposition states that Trientine will be prescribed as per indication and it is recognised that the product needs refrigeration. This evidence does not add or differ from existing knowledge.</p> <p>5. European Medicines Agency – Cuprior post Evidence review completion. The EMA evidence considers trientine dihydrochloride (TETA 4HCL) and trientine tetrahydrochloride (TETA 2HCL) as the same product based on mechanism of action. The evidence acknowledges that abortion of TETA 4HCL is better than TETA 2HCL and other differences between products in relation to dissolution requiring dosage adjustments across the range pending further pharmacokinetic studies. Whilst this product appears to be easier to comply with, there are gaps in the data on special populations, e.g. WD patients with renal/hepatic impairment. The Lariboisière study comparing hepatic and neurological outcomes of patients taking TETA 4HCL over 12 months is evidence of a low grade as it is a retrospective survey, not blinded over a small group of patients with WD who presented with an imbalance of phenotype at baseline. In addition, clinical laboratory evaluation was performed only at the start of each treatment sequence and when a treatment sequence was stopped, and only in some patients. The overall amount of patients with WD on the TETA 4HCL “alone” group was small (2).</p>
<p>Outcome</p>	<p><u>Low grade evidence identified by stakeholders that does not materially affect the conclusions of the existing evidence reviews</u></p>