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

URN	2001
POLICY TITLE	Rituximab for the treatment of nodal/paranodal antibody positive inflammatory/autoimmune neuropathy in adults and post-pubescent children
CRG:	Neurosciences
NPOC:	Trauma
Date	21/03/2021

Description of comments during consultation (If studies have been suggested please provide a list of references)	1) "There is a request to review further recent evidence contained in the following paper: Pascual-Goni E, Fehmi J, Lleixa M, Martin-Aguilar L, Devaux J, Delmon E, Doppler K, Sommer C, Radunovic A, Carvajal A, Smyth S, Williams L, Mazanec R, Potockova V, Hinds N, Cassereau J, Viala K, Lefilliatre M, Nicolas G, Foley P, Leypoldt S, Keddie S, Lunn M, Zimprich F, Nunkoo VS, Loscher W, Martinez-Martinez L, Diaz-Manera J, Rojas-Garcia R, Illa I, Rinaldi S, Querol. *Antibodies to the Caspr1/contactin-1 complex in chronic inflammatory demyelinating polyneuropathy*. Brain, accepted for publication, 2021." The PWG proposed that the following paper should also be reviewed: 2) Desiree De Simoni, Gerda Ricken, Michael Winklehner, Inga Koneczny, Michael Karenfort, Ulf Hustedt, Ulrich Seidel, Omar Abdel-Mannan, Pinki Munot, Simon Rinaldi, Claudia Steen, Michael Freilinger, Markus Breu, Rainer Seidl, Markus Reindl, Julia Wanschitz, Cinta Lleixà, Günther Bernert, Klaus-Peter Wandinger, Ralf Junker, Luis Querol, Frank Leypoldt, Kevin Rostásy, Romana Höftberger. *Antibodies to nodal/paranodal proteins in paediatric immune-mediated neuropathy.* Neurol Neuroimmunol Neuroinflamm Jul 2020, 7 (4) e763; DOI: 10.1212/NXI.0000000000000763

Action taken by Public Health lead	The public health lead reviewed the abstract of the Pascual-Goni et al. 2021 paper and the full De Simoni 2020 paper.
Outcome for studies suggested during consultation	
1. Evidence already identified during the evidence review	None
2.New evidence identified by stakeholders that does not fall within PICO and search methodology	Pascual-Goni et al (accepted for publication 2021). As this paper has not yet been published it does not meet the evidence review criteria. However, also the paper does not expand the range of antibodies currently considered within the policy/evidence review and does not provide a higher quality of evidence than currently within the evidence review. It is a further case series (albeit slightly larger in sample size) that shows a generally good response to rituximab.
3.New evidence identified by stakeholders that falls within PICO and search methodology but does not materially affect the conclusions of the existing evidence review	De Simoni et al, 2020. 54 children with GBS (n = 42) and CIDP (n = 12) and retrospectively screened for antibodies against neurofascin155 (NF155), NF186, NF140, contactin-1 (CNTN1), contactin associated protein1 (CASPR1), and glycine-receptor (GlyR) using cell-based assays2,3; 1 patient was additionally tested with CNTN1-ELISA Five of 12 children, who met the EFNS/PNS criteria for CIDP, had nodal/paranodal antibodies: 2 pan-neurofascin (NF155/NF186/140 triple positive), 1 NF155, and 2 CNTN1-antibodies. Of those 5 patients, 3 received rituximab following unsuccessfully being treated with IVIG and corticosteroids. All are stated to have a made a significant improvement as measure by mRS scores (although the baseline scores aren't included, only the outcome scores). We don't know the specific ages of the 3 treated with rituximab, but we do know that the 5 CIDP patients that were nodal/paranodal positive had an age range of 3-11 so we can confidently say all 3 were pre-pubescent and within that age range. No safety data is reported. But it is a small group of prepubescent children treated with rituximab with a reported positive outcome. Any GRADE assessment of the evidence would likely class it as very low quality/certainty. But it is some evidence of use and outcome in this age group and the small numbers of patients are not inconsiderable when

	compared the small numbers currently reported within the evidence review. This new evidence is helpful in providing some evidence of effectiveness for pre-pubescent children and therefore may allow a wider age range for the policy, but it does not materially change the evidence on effectiveness from the evidence review, it supports it and enhances the age range.
4.New evidence identified by stakeholders that falls within PICO and search methodology, that does materially affect the conclusions of the existing evidence review. Updated evidence review to be undertaken (agreed with CET)	None.