



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Executive Director

Letter of support for the development of a needs-based quality of life Patient Reported Outcome (PRO) measure specific to adults with plexiform neurofibromas

On 1 March 2017 the Applicant Galen Research Ltd requested qualification opinion for a plexiform neurofibromas quality of life scale (the PlexiQoL), as biomarker for use as a secondary endpoint in clinical studies pursuant to Article 57(1)(n) of Regulation (EC) 726/2004 of the European Parliament and of the Council.

During its meeting held on 29 August – 1 September 2017, the SAWP agreed on the Qualification Advice to be given to the Applicant. During its meeting held on 11 – 14 September 2017, the CHMP adopted the Qualification Advice to be given to the Applicant.

On the basis of the qualification advice, the Agency is issuing this letter of support to facilitate the design of studies aimed at eventual qualification for the novel methodology under evaluation.

Background and context of use of the novel methodology

The Neurofibromatosis Therapeutic Acceleration Program (NTAP) funded the development of a patient-reported outcome (PRO) measure specific to adults with Neurofibromatosis type 1 (NF1) associated plexiform neurofibromas (pNFs). The measure was developed with expertise from three organisations; Galen Research Ltd, Manchester UK; the Department of Genetic Medicine, St Mary's Hospital, Manchester, UK; and Johns Hopkins Comprehensive Neurofibromatosis Center, Baltimore, US.

The PlexiQoL is a patient-centric PRO measure, based on the needs-based model of QoL (Hunt & McKenna, 1992). The measure is intended to be suitable for determining whether interventions improve the QoL of patients with NF1-associated pNFs, in addition to any improvement in their clinical status. The needs-based model of QoL is embedded in a wider body of theoretical work on human motivation (Maslow 1970; Max-Neef et al., 1991; Kenrick et al., 2010). The approach postulates that individuals are driven by their needs and that fulfilment of these provides satisfaction. It is intended that the PRO, as a unidimensional measure, will be able to assess the impact of stigma, pain, organ compression, neurologic dysfunction and other effects of the disease on need fulfilment. It is proposed for use as a secondary endpoint in pNF volume reduction and symptom management trials with patients aged 18 years or above. The work was conducted in parallel in the US and UK meaning the scale would be valid for use in both countries individually or combined.

The results of further validation work were presented to the Agency to obtain feedback on the adequacy of the PlexiQoL as a valid secondary endpoint in interventional clinical trials for the treatment of patients aged 18 years or above with neurofibromatosis type 1 associated plexiform neurofibromas.



Available data

The Agency considered the methodology for establishing the psychometric and scaling properties of the PlexiQoL to be acceptable. The validation work conducted was thorough, of a high-standard and is endorsed by the Agency. The PlexiQoL demonstrated sensitivity to differences in patient-perceived pNF severity and general health and to the use of pain medication; however, sensitivity to change needs to be demonstrated in interventional trials. Since there are currently no treatments available, a minimum threshold for a clinically important change has yet to be established.

Continuing and future investigations

The Neurofibromatosis Clinical Trials Consortium (NFCTC) has included the PlexiQoL in a Phase II Study of Binimetinib in Children and Adults with NF1 associated Plexiform Neurofibromas.

The Agency encourages collaboration with research groups/consortia to generate additional responsiveness data for a final qualification opinion on the use of the PlexiQoL scale as an endpoint in plexiform volume reduction and symptom management trials with patients aged 18 years and above.

It is envisaged that the PlexiQoL might be of value as a relevant endpoint in clinical trials. It is envisaged that the PlexiQoL may be a suitable endpoint for a wide range of interventions since it assesses need fulfilment so is not limited by measuring particular symptoms or functional limitations. It could be used to measure the effect of medicines, surgical interventions, the use of devices or even counselling or exercise programmes.

Any groups that would like to join in this effort can contact Professor Stephen P McKenna (smckenna@galen-research.com) or Dr Jaishri Blakeley (jblake13@jhmi.edu).

Sincerely,

Guido Rasi
Executive Director