NHS ENGLAND SPECIALISED SERVICES

CLINICAL PANEL REPORT

Date: January 2021

Intervention: Rituximab

Indication: IgM paraproteinaemic demyelinating peripheral neuropathy (PDPN) in adults

URN: 1910

Gateway: 1, Round 1

Programme: Trauma

CRG: Neurosciences

Information provided to the Panel

Policy Proposition

Evidence review completed by Solutions for Public Health

Equality and Health Inequalities Assessment (EHIA) Report

Clinical Priorities Advisory Group (CPAG) Summary Report

Patient Impact Form

Policy Working Group Appendix

Blueteq® Form

Key elements discussed

This policy proposition recommends the routine commissioning of rituximab as a primary or secondary treatment option for PDPN, a condition in which paraproteins produced by white blood cells bind to the myelin sheath surrounding the body's nerve fibres and affects their structure and function. The resulting neuropathy manifests as sensory disturbance, imbalance, tremor and weakness of muscles. The current standard treatment for PDPN focuses on suppressing the blood cancer which is the underlying cause of PDPN. It is approximated that 50 newly identified patients per year would be eligible for this treatment.

There is an existing published policy concerning rituximab for three conditions, of which this is one, which is not for routing commissioning. The evidence was considered per condition, not altogether, in the review supporting this policy.

PDPN is a rare condition which means that the evidence base is limited. Clinical Panel was presented with the evidence review which comprised of one paper which was a systematic review and meta-analysis, presenting efficacy and safety data in adults. No comparative studies were identified concerning immunoglobulin or other treatments. Rituximab was compared to placebo. The patient populations studied was too small to identify specific cohorts.

Panel discussed the significance of improvement against the critical and important outcomes identified in the review. There is studies reported a statistically significant improvement in the

critical outcomes of disability, global impression of change and haematological response and the important outcome of quality of life (physical subscale). However, the clinical benefit and meaningfulness of these improvements was not clear and some Panel members were not convinced by the findings. There was no statistically significant difference between rituximab and placebo on the important outcomes of sensory impairment, 10 metre walk test or motor impairment. There was no statistically significant difference between rituximab and placebo for any adverse events or serious adverse events.

No cost-effectiveness reported.

Intravenous immunoglobulin (IVIg) was discussed and the need to reduce usage is important.

Clinical Panel considered the proposition. Comments were made about the flow diagram as it is not currently thought to be clear on the pathway. For patients being treated with IVIg and symptoms not worsening, it is not clear what then happens. The flow chart refers to rituximab if the patient has worsening symptoms with IVIg. If the answer is 'no' it doesn't read as if rituximab necessarily replaces IVIg. It was discussed that if a newly diagnosed patient is prescribed rituximab and is already receiving IVIg, then they would not necessarily stop IVIg – clarity needed to understand if this is an alternative or addition.

Clinical Panel commented that reference to antibodies reacting to myelin-associated glycoprotein (anti-MAG antibodies) does not appear in the existing policy. Panel considered this could demonstrate a more targeted use of rituximab in these patients.

Blueteq® form – no comments received.

Panel decided not to review the EHIA at this point but will when the proposition is resubmitted to a future meeting.

Patient Impact Form – no comments received.

The way the policy proposition is currently written is not clear as to why it is recommended to use rituximab as first line as the outcomes reported are similar. The proposition needs to be strengthened if this remains the recommendation.

Recommendation

Clinical Panel recommends that this proposition is returned to a future meeting once the Policy Working Group has considered feedback and made revisions to the proposition.

Why the panel made these recommendations

The Panel debated the evidence base, understanding the rarity of the condition. Further clarity is needed regarding the positioning of rituximab in the treatment pathway if this is to be considered for a routine commissioning recommendation.

Documentation amendments required

Policy Proposition:

- Clarity needed in the proposition as to why it is recommended to use rituximab as first line as the outcomes reported are similar.
- Page 5 – last sentence in the second paragraph - the usage of the terms 'sustained and permanent' are considered to be overstated and need to be amended.
- Flowchart of patient pathway – Comments were made about the flow diagram as it is not currently thought to be clear on the pathway. For patients being treated with IVIg and symptoms not worsening, it is not clear what then happens. It is also not clear if/when

IVIg would be stopped. The Policy Working Group need to review the flowchart and revise to ensure the pathway is clearer.

Declarations of Interest of Panel Members: None received.

Panel Chair: James Palmer, Medical Director Specialised Services

Post Meeting Note 03/02/2021

The following have been amended:

- Clarity needed in the proposition as to why it is recommended to use rituximab as first line as the outcomes reported are similar. *Paragraph 2 on page 5 has been amended to explain why rituximab should be the first line treatment for PDPN.*
- Page 5 – last sentence in the second paragraph - the usage of the terms 'sustained and permanent' are considered to be overstated and need to be amended. *The last sentence of paragraph 2 on page 5 has been amended and the words 'sustained and permanent' have been removed.*
- Flowchart of patient pathway – Comments were made about the flow diagram as it is not currently thought to be clear on the pathway. For patients being treated with IVIg and symptoms not worsening, it is not clear what then happens. It is also not clear if/when IVIg would be stopped. The Policy Working Group need to review the flowchart and revise to ensure the pathway is clearer. *The flowchart on page 11 has been amended to illustrate when IVIg should be stopped.*