NHS ENGLAND SPECIALISED SERVICES

CLINICAL PANEL REPORT

Date: November 2020

Intervention: Rituximab

Indication: nodal/paranodal antibody positive inflammatory/autoimmune neuropathy in adults and post-pubescent children

URN: 2001

Gateway: 2, 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 rituximab, a therapeutic monoclonal antibody which targets the CD20 surface marker present on B cell subsets, as a primary or secondary treatment option for nodal/paranodal antibody positive inflammatory/autoimmune neuropathy in adults and post-pubescent children.

This progressive condition causes autoantibody mediated damage at the nodes of Ranvier on the axons of neurons. Although typically considered a variant of Chronic Inflammatory Demyelinating Polyradiculopathy (CIDP), the condition is considered distinguishable from CIDP without detectable nodal/paranodal auto-antibodies in causing more aggressive and severe disease with more rapid onset and a different disease mechanism. This is based on four criteria. There is a not for routine commissioning policy statement published for CIPD. The current main treatments are intravenous immunoglobulin (IVIg) and/or corticosteroids. Rituximab is proposed first line for people with more severe disease and first line or second line to steroid treatment for people with less severe disease. Approximately 10-20 people newly identified per year would be considered eligible for this treatment.

Clinical Panel was presented with the evidence review which comprised of three studies – one multicentre prospective case series and two retrospective case series with small relevant study

populations. It was noted that nodal/paranodal antibody positive inflammatory/autoimmune neuropathy is extremely rare and the evidence base presented reflects this. Panel members debated the evidence base at length. Overall Neuropathy Limitations Scale (ONLS) demonstrated a clinically meaningful change likely to result in improved ability to perform activities of daily living. The Inflammatory Neuropathy Rasch-built Overall Disability Scale (R-DOS) demonstrated a clinically meaningful change likely to result in some reduction in disability. There was no evidence presented for improved strength or quality of life.

It was raised that a study was published in April 2020 which maybe material to this proposition. This should be identified through stakeholder testing and for Public Health England to review and report a recommendation.

Clinical Panel considered the proposition. Within the inclusion criteria it was not clear why the ONLS score of 6 was identified as a marker to start rituximab. This differs with that stated in the evidence base.

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

It was raised that the conclusion of the evidence review was worded negatively given the proposition is recommended for routine commissioning. It was explained that the evidence review is commissioned independently and states the quality and strength of the evidence. The proposition is written by the Policy Working Group. It is the role of Clinical Panel to debate the evidence base and whether the proposition progresses with the recommended commissioning position or not. This then gets recorded briefly in the committee discussion section of the proposition.

Within the starting criteria – It was not clear if those patients, for example, who were HIV or Hepatitis C positive would be included or not.

The Panel agreed that the SPC should be referenced rather than adding all the information into the proposition.

It was raised whether subcutaneous injection would be a route for delivery, noting that the device base referred only to intravenous injection.

Errors were noted within the Blueteq® form that need addressing.

EHIA considered – no comments received.

Patient Impact Form considered – no comments received.

Recommendation

Clinical Panel recommends that this proposition progresses as a for routine commissioning policy proposition.

Why the panel made these recommendations

The Panel debated the evidence base at length and as to whether this should progress as for routine commissioning or not, understanding the rarity of the condition. Nine versus seven members voted in favour hence the proposition progresses as for routine commissioning.

Documentation amendments required

Policy Proposition:

- Explanation about antibodies related to the condition needs to be moved to nearer the beginning of the proposition.

- Inclusion criteria – check why the ONLS score as written is identified as the marker to give rituximab as this differs from that stated in the evidence base
- Inclusion criteria – 2nd, 3rd and 4th bullet points – language used doesn't make sense as currently written
- Starting criteria – Policy Working Group to review wording and make it clearer what would happen to such patients e.g. HIV or Hepatitis positive – would they be included or excluded
- Reference to the SPC and remove the information in the proposition that is directly taken from it
- Flowchart of patient pathway– starts with newly diagnosed patients rather than those on regular treatment. Policy Working Group to review if that group of patients needs to be also added

Blueteq® Form:

- The stopping criteria in the proposition explains patients who have progressive multifocal leukoencephalopathy but this is not explained in this form
- The form in general needs reviewing as not written as a typical Blueteq® form. Pharmacy Lead to help review
- Ivacaftor is referred to which is an error and needs removing

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Declarations of Interest of Panel Members: A member of the Panel is also a member of the Policy Working Group for this proposition.

Panel Chair: James Palmer, Medical Director Specialised Services

Post Meeting Note 15/12/2020

The following have been amended:

Policy Proposition:

- Explanation about antibodies related to the condition needs to be moved to nearer the beginning of the proposition; *the explanation about antibodies related to the condition has now been included under the executive summary on page 2*.
- Inclusion criteria – check why the ONLS score as written is identified as the marker to give rituximab as this differs from that stated in the evidence base; *ONLS>=5 is stated in the evidence base on page 8. The ONLS score has been changed from ONLS>=6 to ONLS>= 5 on page 10 under inclusion criteria and in the patient pathway on page 12.*
- Inclusion criteria – 2nd, 3rd and 4th bullet points – language used doesn't make sense as currently written; *the bullet points have been amended on page 10 under inclusion criteria so that they make sense.*
- Starting criteria – Policy Working Group to review wording and make it clearer what would happen to such patients e.g. HIV or Hepatitis positive – would they be included or excluded; *2 paragraphs have been inserted at the bottom of page 10 to address this point.*
- Reference to the SPC and remove the information in the proposition that is directly taken from it; *information taken from the SPC has been removed from the implementation section starting on page 9.*
- Flowchart of patient pathway– starts with newly diagnosed patients rather than those on regular treatment. Policy Working Group to review if that group of patients needs to be also added; *patients who are already established on IVIg have been added to the patient pathway on page 12.*

Blueteq® Form:

- The stopping criteria in the proposition explains patients who have progressive multifocal leukoencephalopathy but this is not explained in this form; *a footnote has been added to explain the meaning of progressive multifocal leukoencephalopathy.*
- The form in general needs reviewing as not written as a typical Blueteq® form. Pharmacy Lead to help review; *the PWG pharmacy lead and the NHSE pharmacy lead have both reviewed and edited the form.*
- Ivacaftor is referred to which is an error and needs removing; *reference to Ivacaftor has been removed.*

In addition to the above one of the PWG members queried the meaning of the sentence 'It is expected that new funding will be required to commission rituximab for the treatment adults and post-pubescent children with nodal/paranodal antibody positive inflammatory/autoimmune neuropathy*.' Following discussion with the NHS England pharmacy lead, the sentence was removed.*