
LUPUS UK would like its submission to be considered at an oral hearing.

LUPUS UK wishes to appeal to the Committee’s final decision on Ground 2 and 3

2.1 *Ground two: The Institute has formulated guidance which cannot reasonably be justified in the light of evidence submitted*

2.2 LUPUS UK considers that the Institute has formulated guidance on Belimumab (BMB) which cannot reasonably be justified in the light of evidence submitted. The Final Appeal Determination (FAD) contains exceptionally frequent references to uncertainty and lack of clarity: we consider that the Institute is premature in issuing its decision until it has satisfied itself on the majority of points needing clarification.

2.3 In particular support of this we would cite

3.43 “a substantial degree of uncertainty over whether the effects observed in the data would translate into longer term benefits”,

4.4 “...concluded that in clinical practice BMB might be used in the same intermittent way as RTX although no efficacy data that reflects this use of BMB is available”

4.8 “...currently the effect of BMB on the full range of manifestations of systemic lupus erythematosus was uncertain”

4.25 “...could not be considered in the absence of any clinical and cost-effectiveness data”
2.4 Other paragraphs highlighting the uncertainties are

3.36: “lack of clarity”,
3.43: (“lack of clarity” cited earlier in this para, as well as the point made in 2.3),
3.44:  i) “maximum duration of BMB was uncertain”,
    ii) “substantial degree of uncertainty”,
3.46: “was uncertain”,
4.10: “number of uncertainties”,
4.11: “not definitive proof”,
4.12: “no reliable data”,
4.13: “uncertainty”,
4.14: “underestimated”,
4.16: “did not consider sufficiently robust”,
4.18: “uncertainty”
4.20: “considerable uncertainty”
4.23: “some inconsistencies”
4.27: “no reliable data”
4.28: “...not adequately captured”

2.5 This may result in a time delay whilst further data are collected, but we believe it is imperative for NICE to ensure that all evidence has been considered, as well as being in the interests of patients and their clinicians, in order to ensure the clinical effectiveness of this biologic. The committee recognised several times (3.9, 3.31, 4.2) that any medication which may be a very appropriate treatment to reduce steroid and immunosuppressive dosage is very much to the benefit of patients.

2.6 Clinical opinion has been heard and received both during the meetings and by submission: but LUPUS UK is very concerned that some of the points made have not been given sufficient weight by the committee in reaching their conclusions, in particular comments by:
LUPUS UK believes that, if NICE are not persuaded by this and considers that more data are needed, they should not be making any definitive decision until they have received and reviewed it.

2.7 In its pre-meeting briefing (PB) the committee listed a number of key issues for consideration (pp2-4). LUPUS UK is of the opinion that several of these questions have still not been answered:

   “Can inferences be made about the effectiveness of BMB in the target population based on the clinical trial data?”

   “Can the effect of BMB be applied to all SLE manifestations?”

   “What inferences can be drawn about the relative effectiveness of BMB in comparison with RTX?”

Until data are available to answer these questions the Appraisal Committee should not be making their final decision on this treatment.

2.8 This would provide data for a longer period than is currently available (6 years), and would involve members of the UK population, thus creating meaningful information for NICE’s authorised population.

2.9 There seems to have been confusion about the 6 years of use of BMB: the manufacturer’s submission of evidence from 6 years use has become confused with an intention to treat patients continuously for 6 years. Clinical opinion on this has been clearly stated in 4.3 and item 7 (letter from Prof D Isenberg, and in responses from health professionals:

   British Renal Society: p2

   British Sociey of Rheumatologist: bullet pts 2 and 5.

   Royal College of Nursing: p3, 1st para
2.10 LUPUS UK’s opinion is that the Institute should ensure that it has all relevant data necessary before it makes a final decision and that by making a decision at this point it will leave some lupus patients who have the most difficult manifestations of the illness paying a very heavy physical price, without effective treatment.

2.11 LUPUS UK also consider that the comments which the FAD has made on Rituximab have caused considerable confusion and increased the uncertainty about treatment of lupus patients. A direct comparison with this drug cannot be made as is frequently referred to (paras...........) because the measured outcomes are different from the BLISS trials.

**Ground 3: The institute has exceeded its powers**

3.1 The technology appraisal was for Belimumab. NICE implies that Rituximab has a useful clinical benefit in selected patients. If it believes this then access to rituximab should be formalised and facilitated.

3.2 Rituximab was put forward to the committee in terms of another biologic which has shown some benefit to lupus patients. The committee seem to have missed the point that it is not the treatment of choice for lupus: some clinician’s opinion is that when patients do not respond to RTX, BMB may well offer an appropriate new choice for those who have the highest unmet need.

3.3 However IFRs are necessary for Rituximab and this has created severe delays in access to treatment and a ‘postcode lottery’ in terms of refusals by PCTs to allow funding:

   British Association of Dermatologist submission, para 4,

   British Health Professionals in Rheumatology submission para 5,

   item 7 in July 2012 meeting, letter from Prof D Isenberg para 5.

Whilst this may not be in the remit of the Appraisal committee, these problems do need urgent consideration by NICE.
4.1 LUPUS UK welcomes Recommendation 6 which calls on the manufacturer to carry out more research on Belimumab as it considers these studies would be of value: LUPUS UK would take this further and calls for more research to be carried out into effective treatments of Systemic Lupus Erythematosus.

4.2 LUPUS UK notes Recommendation 7 which states that there is no related guidance for this technology and would call on NICE to ensure that Guidelines on treating lupus are made available (see 4.5). Currently the British Society of Rheumatology is taking the lead on preparing such guidelines, and we would encourage NICE to adopt these on completion.

5.1 In conclusion we ask NICE to agree to limited use of Belimumab and would suggest the following stipulations:

- Belimumab is used only in specialist lupus centre on patients for whom no other treatment has proved effective and who are on high dose steroids or other medications which have a high attrition rate
- Data on all of these patients should be collected using the S/S scores so that meaningful comparisons could be reached
- Details of all patients receiving the treatment should be submitted to the British Biologics Register to ensure safety and consistency of outcomes

5.2 This would provide data for a longer period than is currently available (6 years), and would involve members of the UK population, thus creating meaningful information for NICE’s authorised population. We note (8.1) that “guidance will be considered for review in August 2014”: further research from a variety of sources is imperative during that period of time (the manufacturer is not in a position to conduct all the research necessary), otherwise the position will remain uncertain for future appraisal.

5.3 We appeal to the Appraisal Committee to reconsider its position and allow limited use under strict criteria, so that patients who have severe lupus which is not responding to other medications will have some quality of life during the intervening period, rather than descend into unrelieved attrition and seriously life-limiting

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