ACD on Belimumab for the Treatment of active autoantibody-positive systemic lupus erythematosus
Response by [Redacted] on behalf of the Renal Association

- Has all of the relevant evidence been taken into account?
  
  The evidence has been well considered in particular the lack of availability of a direct comparison with Rituximab.

- Are the summaries of clinical and cost effectiveness reasonable interpretations of the evidence?
  
  The summaries of clinical effectiveness have erred on the side of caution.
  
  a) The ACD highlights that the population in BLISS-76 reflects the England and Wales population more closely than that in BLISS-52. However, patients with lupus in England and Wales are not representative of the population as a whole as they tend to be much more ethnically varied and hence BLISS-52 may be as appropriate as BLISS-76. As the committee noted, more outcomes were significantly improved with Belimumab in BLISS-52 than BLISS-76.
  
  b) There are several comments about the arbitrary nature of a SELENA-SLEDAI score of >10 being significant and of stopping at 24 weeks if improvement in SELENA-SLEDAI score being not greater than 4. However, current clinical practice is much more arbitrary and scoring systems are not in routine use in most lupus clinics. Ensuring that responses are documented with scoring would be a huge improvement in the management of patients with lupus and the inclusion of the BILAG and PGA scores (as used in the SRI) would improve this further. The BLISS trials are to be commended for including formal scoring and the recommendation of a target population and the use of scoring to assess the benefit of therapy would be advantageous. Patients often remain on treatments that are ineffective for prolonged periods and responses are often poorly judged. Whilst a score of 10 is fairly arbitrary it does require significant clinical disease that would be noticeable to patients and therefore is meaningful.
  
  c) Standard of care is not standard in England and Wales – treatment approaches vary by unit and individual clinician and reflect the lack of trial data in the “target” population described in the manufacturer’s submission. Patients could be on a range of treatments though for musculoskeletal and skin involvement are less likely to be on Rituximab but are likely to be on steroid sparing agents if severe. Hence the SOC treatments in both trials are reasonable representations of the SOC likely to be given to different lupus patients in England and Wales.

In the economic analysis more consideration should be given to:

a) consideration that in practice Belimumab is likely to be discontinued e.g. after a maximum of 2 years. The manufacturer’s suggestion that it might be a lifelong treatment is surprising and not in keeping with current approaches to treatment, especially with biologicals. It is very
likely that clinicians would plan a course of treatment and then either
to increase dosage intervals or simply stop and see how patients
fared. This would significantly reduce costs.
b) If review at 6 months is mandated, the scoring could be more
rigorous (though this is not based on the data available) and for
instance insistence on an improvement of at least 6 rather than 4 in
SELENA-SLEDAI score being a guide to stopping treatment (or a
failure of trend to improvement might be clinically more meaningful).
This would reduce the numbers of patients being treated and reduce
costs.
c) Cost effectiveness based on mortality is not hugely relevant in the
early phase of lupus as the mortality rates, although hugely elevated
compared to a normal population, are not absolutely high. The
clinical issues are those that allow maintenance of normal life (being
able to work, look after children, have safe pregnancies) with
minimum short and long term adverse events. Any drug which
reduces the exposure to steroids is likely to be cost effective both to
the individual and to the NHS.

- **Are the provisional recommendations sound and a suitable basis
  for guidance to the NHS?**
  On the basis of the comments above, there is room to reconsider cost
effectiveness. There is a desperate need for new licensed therapies for
lupus and whilst Belimumab may not be a perfect agent, there is
evidence for its effectiveness. Skin and musculoskeletal problems in
lupus can be hugely debilitating and often require very large doses of
steroids – abhorrent drugs for a young, predominantly female population
and associated with increased damage and premature mortality in the
long term. It is not clear that this has been adequately considered in the
cost effectiveness appraisal and will be a major issue for patients.

- **Are there any aspects of the recommendations that need particular
  consideration to ensure we avoid unlawful discrimination against
  any group of people on the grounds of gender, race, disability, age,
  sexual orientation, religion or belief?**
  Lupus predominantly affects women of child bearing age from ethnic
minority groups – by failing to recommend Belimumab, it is these groups
that will be predominantly affected.

21/10/2011