10th October 2011

National Institute for Health and Clinical Excellence

Dear Ms Moore

RE: Belimumab for the treatment of active autoantibody-positive systemic lupus erythematosus

On behalf of Commissioning Support, Appraisals Service (CSAS), Solutions for Public Health, I would like to submit our comments on the appraisal consultation document for belimumab for the treatment of active autoantibody-positive systemic lupus erythematosus.

We are in agreement with the recommendations in the ACD not to recommend belimumab for this indication as on the basis of the evidence considered it is unlikely that this treatment can be considered clinically and cost effective.

- **Belimumab is not a cost effective use of NHS resources compared to standard care.** The ICER without the patient access scheme (PPRS) was between £64,400 and £71,000 per QALY, and with the PPRS applied the ICER still remained above the threshold range usually considered an acceptable use of NHS resources.

- **Belimumab is not considered a cost effective use of NHS resources compared to rituximab.** No sound case was presented on the cost effectiveness of belimumab compared to rituximab.

- **No direct comparison of efficacy was made between belimumab and rituximab.** Rituximab is used increasingly in patients with severe disease and is therefore a relevant comparator which should have been considered.

- **Generalisability of findings from the BLISS studies to the UK population is uncertain.** Approximately 50% of patients enrolled in both BLISS trials were receiving an immunosuppressant whereas standard therapy in the UK for most SLE patients would include an immunosuppressant. Patients enrolled in the BLISS-52 study were recruited from South America, Asia and Eastern Europe and so are not representative of a UK population. Most patients included in the BLISS trials had mucocutaneous and musculoskeletal manifestations of SLE. The effect of belimumab on the full range of possible manifestations of SLE is therefore unknown.

- **There were numerous uncertainties about the plausibility of assumptions in the manufacturer’s economic model.** The manufacturer’s model may have underestimated the ICER: it was uncertain whether the equations derived from a longer term cohort of patients with less active disease could be applied to the trial population; the number of patients discontinuing treatment at 24 weeks may have been overestimated; it was assumed that treatment effect would be maintained over time; it was unclear whether the modelled gains survival were valid; and cost
data was derived from various sources which may have given inconsistent estimates.

- **Belimumab did not demonstrate improved health-related quality of life benefits compared to standard care.** Functional assessment of chronic illness therapy (FACIT)-fatigue scores were not significantly better at week 52 in people receiving belimumab compared to standard care.

If you require any further information please contact me directly.

Yours sincerely