Belimumab (Benlysta®) for the treatment of adult patients with auto-antibody-positive systemic lupus erythematosus (SLE)

Summary of recommendations by *Zorginstituut Nederland* (National Health Care Institute, the Netherlands) dated 29 March 2018

Zorginstituut Nederland has carried out an assessment of the medicinal product subcutaneous belimumab (Benlysta®) and a re-assessment of intravenous belimumab, the latter of which is subject to Conditional Inclusion in the insured standard package, whereby they came to the following conclusion.

In 2012 *Zorginstituut Nederland* assessed that the intravenous formulation of belimumab does not comply with established medical science and medical practice. The reason for this was a shortcoming in the pivotal phase 3 study with intravenous belimumab. Independent confirmation of the effect of belimumab was therefore necessary in a new study with a comparable, explicitly defined population. For that purpose the Minister of Health, Welfare and Sport decided to start a trajectory of conditional inclusion in the insured package for the intravenous formulation of belimumab, accompanied by an observational study (DAiRE-register). Belimumab is a medicine that is part of treatment provided by a medical specialist.
In response to a new dossier submitted in 2017 by the marketing authorisation holder, the *Zorginstituut* carried out an assessment of subcutaneous and intravenous delivery formulations of the medicinal product belimumab (Benlysta®) for the treatment of adult patients with auto-antibody-positive systemic lupus erythematosus (SLE) with a high level of disease activity (e.g. positive anti-dsDNA and low complement), despite receiving standard treatment. The dossier included data resulting from a new phase 3 study for subcutaneous belimumab. The question is whether belimumab is covered by health insurance described in articles 2.1 and 2.4 of the Health Insurance Decision. Specifically, this is about whether belimumab complies with established medical science and medical practice.

The *Zorginstituut* has completed its assessment. Based on the outcomes of the assessment, the *Zorginstituut* concludes:
- For the treatment of active SLE with a high level of disease activity (despite standard treatment), the addition of belimumab in a subcutaneous delivery formulation has added value in comparison with placebo;
- an indirect comparison, based on pharmacokinetic data, between the subcutaneous formulation and the intravenous formulation of belimumab suggests that the two delivery formulations have the same therapeutic value;
- For the treatment of active SLE with a high level of disease activity, both the subcutaneous and the intravenous delivery formulations of belimumab comply with established medical science and medical practice;
- Because belimumab was exempt from supplying cost-effectiveness data based on the expected costs of belimumab, this leads to the conclusion that belimumab is an insured provision.

Budget impact of treatment with belimumab
The use of belimumab, added to the usual treatment of adult patients with auto-antibody-positive SLE with a high level of disease activity (e.g. positive anti-dsDNA and low complement) despite standard care, will be accompanied by additional costs estimated at approximately €1.5 million per year after three years. Based on this estimation, exemption was granted from supplying cost-

effectiveness data on belimumab. The *Zorginstituut* will continue to monitor developments in the costs of belimumab. It is possible that, based on new information, including actual costs incurred, the *Zorginstituut* may eventually initiate a cost-effectiveness assessment.

Outcome of assessment of belimumab
The *Zorginstituut* establishes that the addition of both the subcutaneous and the intravenous delivery formulations of belimumab to the usual treatment of adult patients with auto-antibody-positive SLE with a high level of disease activity (e.g. positive anti-dsDNA and low complement), despite standard care, complies with 'established medical science and medical practice'. In combination with exemption from supplying cost-effectiveness data, this leads to the conclusion that both delivery formulations of belimumab fall within the basic package of the Health Insurance Act (Zvw).
The full report describes the considerations that resulted in this outcome of assessment of the *Zorginstituut*. The Zorginstituut was advised by the Scientific Advisory Board (WAR).

Terminating the trajectory of conditional inclusion of intravenous belimumab
Intravenous belimumab was granted *Conditional Inclusion* into the basic package of care. The current outcome of assessment on the insured status of belimumab means that, henceforth, the intravenous delivery formulation of belimumab is also covered by the basic package of the Zvw. This means it is no longer necessary to continue the trajectory of conditional inclusion of the intravenous delivery formulation of belimumab. For this reason, the *Zorginstituut* advised the Ministry of Health, Welfare and Sport to terminate this trajectory prematurely. Naturally, the professional group is at liberty to continue to follow patients via the DAiRE-register.

Lastly
Care provided by medical specialists that is covered by the basic package has an open definition in the policies of health care insurers. Outcome of assessments issued by the *Zorginstituut* are explicit statements about the contents of the basic package, so no adjustments are needed in the policies of the health care insurers. The Dutch Healthcare Authority (NZa), which issues descriptions of care provided by medical specialists and expensive medicinal products, has established a care activity in the form of an add-on for belimumab.

This outcome of assessment of the *Zorginstituut* acts as a guideline in practice. No administrative appeal can be submitted against this outcome of assessment. Its implementation takes place via the health care insurers in their policies which are subject to private law.

For further information, please contact: JBoer@zinl.nl; warcg@zinl.nl

The original text of this excerpt from advice of Zorginstituut Nederland was in Dutch. Although great care was taken in translating the text from Dutch to English, the translation may nevertheless have resulted in discrepancies. Rights may only be derived on the basis of the Dutch version of Zorginstituut Nederland's advice. Furthermore, Zorginstituut Nederland points out that only the summary of this report was translated. A proper understanding of all relevant considerations and facts would require familiarity with the Dutch version of this report, including all appendices.