National Institute for Health and Clinical Excellence

Adalimumab, etanercept and infliximab for the treatment of rheumatoid arthritis after failure of a previous TNF-α inhibitor

Royal College of Nursing

With a membership of over 400,000 registered nurses, midwives, health visitors, nursing students, health care assistants and nurse cadets, the Royal College of Nursing (RCN) is the voice of nursing across the UK and the largest professional union of nursing staff in the world. RCN members work in a variety of hospital and community settings in the NHS and the independent sector. The RCN promotes patient and nursing interests on a wide range of issues by working closely with the Government, the UK parliaments and other national and European political institutions, trade unions, professional bodies and voluntary organisations.

The RCN welcomes the opportunity to review the Final Appraisal Determination (FAD) on the sequential use of Anti-TNFs for the treatment of Rheumatoid Arthritis. The RCN Rheumatology Forum has reviewed the FAD. The recommendations are discriminatory and perverse and are not in the interest of patients requiring these health technologies. The RCN therefore wishes to appeal against the FAD.

IN THE MATTER OF THE RCN's APPEAL AGAINST NICE'S FINAL APPRAISAL DETERMINATION (FAD) IN RESPECT OF ADALIMUMAB, ETANERCEPT & INFLIXIMAB.

The Royal College of Nursing appeal against the FAD under grounds 2 and 3 of NICE's appeal procedure. The bases for the appeal are set out below:

Ground 2: The Institute has prepared guidance that is perverse in the light of the evidence submitted.

The Recommendations are perverse on account of NICE not taking account of "offset costs" in analysing sequential use of adalimumab, etanercept or infliximab:

1. Paragraph 4.3.11 of the July 2008 FAD states in the analysis of the cost effectiveness of sequential use of adalimumab, etanercept or infliximab that "The Committee noted that the offset costs of avoiding or delaying joint replacement, outpatient visits and impatient stays had not been included in the analysis of sequential use."

2. This is despite the Birmingham Rheumatoid Arthritis Model (BRAM) making an assumption (in the absence of adequate data) that "people incurred an annual cost of £880 per unit of HAQ score ...), FAD, para. 4.2.2.

3. In this regard it is important to note that in the October 2006 FAD it is recorded that NICE "was persuaded that the inclusion of benefits related to reduction in hospitalisations and longer-term requirements for joint replacement, although based on as yet unproven assumptions, was important in the economic modelling and an important factor to be taken into account in the costs associated with the treatment of RA."

4. It is not controversial that there are costs which will fall on the NHS if treatment for RA is not provided. These costs go further than hip replacement and include the costs resulting from for example osteoporosis and increase in cardiovascular disease. What is contentious is the quantification of these costs. Where such figures are not available it is perverse to ignore the relevant costs as to do so is to undermine the credibility of the cost effectiveness exercise. In the absence of empirical evidence NICE should have sought advice so as to make sensible estimates of likely cost to factor into its calculations.

5. As the process is rendered perverse by this error this ground of appeal falls within Ground 2 of the prescribed grounds of appeal.

The Recommendations provide for the arbitrary provision of adalimumab, etanercept or infliximab and are therefore perverse:

6. Which of the three drugs under consideration by NICE is prescribed for a particular patient in the first instance is arbitrary. Apart from a preference on the part of the patient as to whether they would rather have intravenous or subcutaneous injected medication there is no way of distinguishing between the drugs at this stage. Which drug they are prescribed is a "roll of the dice".

   In practice a patient is monitored for six months and if there is no clinical benefit for the patient the prescription is stopped. Absent this FAD at this point one of the other TNFα inhibitors may be tried.

7. The NICE recommendations provide at para. 2.6 of the FAD that if a patient has an adverse event within six months of taking the first TNFα inhibitor a second TNFα inhibitor may be tried. An "adverse event" is taken to mean a toxic reaction or similar. It does not mean that the patient has not benefited from the drug. However the lack of clarity as to what is meant by "adverse reaction" is open to differing interpretation and lacks the precision necessary to avoid arbitrary decision-making.

8. The six months referred to in para 2.6 of the FAD is presumably referable to the clinical practice of six monthly reviews.

9. It is arbitrary whether a patient receives an effective treatment under this proposed regime. It may of course be the case that the first drug is not effective and that one of the other two drugs would be. Not only is which drug is chosen first arbitrary but it is also arbitrary whether a patient has a toxic reaction to the first prescribed drug and is then prescribed another of the TNFα inhibitors. Such a patient may switch from a non-beneficial drug to a drug that provides clinical benefit. A patient who does not have a toxic or other reaction will not be able to do so. It is accordingly arbitrary whether a patient falls within the criteria for a switch from one TNFα inhibitor to another.

10. As the process is rendered perverse by this arbitrariness this ground of appeal falls within Ground 2 of the prescribed grounds of appeal.

Ground 3: The Institute has exceeded its powers

The Recommendations are Discriminatory:

11. The recommendation that sequential treatment with adalimumab, etanercept or infliximab should be restricted to patients who are taking part in research is discriminatory in that access to such research programmes is likely to be less readily available to patients with learning disabilities or from ethnic or minority backgrounds. Research shows that ethnic minority people are frequently under-represented in clinical trials, see 'Ethnic minority under-representation in clinical trials: Whose responsibility is it anyway?'; Mahvash Hussain-Gambles: Journal of Health Organisation and Management (2003) vol.17 pages 138-143.

12. In this regard the recommendations fall foul of the duty found in section 71 of the Race Relations Act 1976 to eliminate unlawful discrimination and promote equality of opportunity. There is also a breach of the duty imposed by section 19B of the Race Relations Act 1976 to not discriminate.

13. The requirement for research participation to be the only option for patients who have failed on one drug assumes that there is sufficient nursing resource to collect the data required for research in routine clinical practice, particularly if patients have equity of access throughout the country for these therapies. It is not reasonable in the circumstances outlined in the FAD for patients to have to travel distances to research units to participate in research as a requirement for access to a further clinical treatment. Nor is it reasonable that there should be an additional demand for nurses to collect additional data for research purposes on top of the already heavy burden of collecting data for the British Society for Rheumatology Biologics Register.

14. Additionally the recommendation to restrict sequential prescription of adalimumab, etanercept or infliximab is contrary to the duty found in sections 20 and 21 of the Disability Discrimination Act 1995 in that under this policy disabled people will be treated less favourably than non-disabled people.

15. With respect to the above discrimination the recommendations are in breach of the NICE's positive obligations found in article 14 of the European Convention on Human Rights read together with article 8 of the said Convention.

16. In this regard NICE has acted unlawfully and exceeded its powers. Ground 3 of the prescribed grounds of appeal applies.

The Recommendation that sequential treatment with adalimumab, etanercept or infliximab is an effective ban on the NHS use of these drugs for most patients and as such is in breach of EC Directive 89/105/EEC:

17. Paragraph 2 of Article 7 of Directive 89/105/EEC provides that "... Member States shall publish in an appropriate publication and communicate to the Commission the criteria which are to be taken into account by the competent authorities in deciding whether or not to exclude an individual medicinal product from the coverage of the national health insurance system."

18. Paragraph 3 of Article 7 of Directive 89/105/EEC provides that "any decision to exclude an individual medicinal product from the coverage of the national health insurance system shall contain a statement of reasons based on objective and verifiable criteria."

19. The criteria provided pursuant to Article 7 of Directive 89/105/EEC provides that "a medicinal product or a category of medicinal products may be excluded entirely from supply on NHS prescription. It may alternatively be excluded except in specified circumstances or except in relation to specified conditions or categories of condition, or specified categories of patient. A medicinal product or category of them may be so excluded when the forecast aggregate cost to the NHS of allowing the product (or category of products) to be supplied on NHS prescription, or to be supplied more widely than the permitted exceptions, could not be justified having regard to all the relevant circumstances including in particular the Secretary of State's duties pursuant to the NHS Act 1977 and the priorities for expenditure of NHS resources."

20. The criteria provided by the UK government as being the criteria that they may apply in deciding whether to exclude drugs do not include NICE appraisals. A recommendation that works as an effective ban for significant numbers of patients of the prescription of such drugs is accordingly contract to Directive 89/105/EEC and is unlawful.

21. Grounds 3 of the prescribed grounds of appeal applies.