

AMERICAN COLLEGE OF RHEUMATOLOGY

POSITION STATEMENT

SUBJECT: Biologic Agents for Rheumatic Diseases

PRESENTED BY: Committee on Rheumatologic Care

FOR DISTRIBUTION TO: Members of the American College of Rheumatology
Medical Societies
Members of Congress
Centers for Medicare and Medicaid Services
Managed Care organizations/Third-Party Carriers
Arthritis Foundation

1 BACKGROUND:

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3 A group of DMARDS (disease modifying anti-rheumatic drugs) has been developed with the
4 purpose of interfering with inflammatory cytokine biology. They represent a significant advance
5 in the treatment of rheumatic diseases and block specific pathways and signals of inflammation.
6 These so-called "biologics" or biologic response modifying agents have proved to be
7 revolutionary and offer the possibility of controlling rheumatic diseases to an extent not
8 previously possible.

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10 Currently approved biologic DMARDs are anakinra, etanercept, infliximab, adalimumab,
11 golimumab, certolizumab pegol, rituximab and abatacept; and, there are more in development.
12 These agents are considered by the FDA to inhibit the progression of structural damage and
13 improve physical function in rheumatoid arthritis (RA). Biologics also have applications among
14 a growing list of diseases including, psoriasis, psoriatic arthritis, ankylosing spondylitis, juvenile
15 arthritis, sarcoidosis, reactive arthritis, inflammatory eye conditions, ulcerative colitis, and
16 Crohn's disease, although FDA approval is lacking in some of these clinical situations.

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18 Although they all are categorized under the label "biologics", many of these medications work
19 on different arms of the immune system, providing alternative ways to control inflammation.
20 For example, anakinra inhibits the effects of interleukin-1, etanercept, infliximab, and
21 adalimumab block tumor necrosis factor, abatacept blocks an interaction between T cells and
22 macrophages, and rituximab effectively eliminates B cells for several months. Even the three
23 available medications which block tumor necrosis factor (TNF) have clinically important
24 differences in mechanism, method of delivery, and side effects, and are not biologically
25 equivalent. For reasons which are not well understood, a patient may respond better to one TNF
26 inhibitor than another. Therefore, it may be appropriate to try another TNF inhibitor if the
27 response has been lost or there was no improvement with the first or second TNF inhibitor.

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29 The clinical improvement with these medications is often quite dramatic and long-term data
30 show that these responses persist. However, the production of these medications is significantly
31 more complicated because they are bioengineered proteins rather than small molecules, and their

32 cost is significantly higher. Because of cost, access to these medications has become increasingly
33 difficult for our patients. The policy of the American College of Rheumatology regarding these
34 medications is herein clarified and updated from the 2003 statement.

35 36 **Policy:**

37 We believe that all patients with serious rheumatic disease must have these "biologic"
38 medications available when clinically appropriate.

39 40 **Access**

41 Attempts to restrict the use of biologics by non evidence-based guidelines or criteria that are
42 outside the patient-physician relationship should be discouraged, and cost based substitutions
43 within this group are inappropriate. The differences in mechanism of action, response rates, route
44 and frequency of administration, antigen target and possible side effect profiles prevent any
45 consideration of these medications as equivalent agents.

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47 The health assessment questionnaire (HAQ) and the gathering of ACR or disease activity (DAS)
48 scores are useful within the context of clinical trials but are not measurements in general use in
49 clinical practice. Therefore, the request for these measures in pre-certification or recertification
50 of biologic medication use may be inappropriate. They may not reflect all relevant information
51 for an individual patient influencing therapeutic decisions.

52 53 54 **Decision Making**

55 In the absence of validated clinical guidelines, the choice for any individual patient should be
56 determined by the treating rheumatologist who, as an expert in the field of inflammatory
57 diseases, the immune system, and the biologics, will take into consideration not only the above
58 medication differences but logistics, patient willingness or aversion to various medication
59 delivery systems, contraindications, co-morbidities, concomitant medications, susceptibility to
60 infection, and other factors which are unique for each patient. Third party payers should not
61 attempt to mandate the use of one medication over another based on cost alone. To do so ignores
62 the complexity of decision making by the rheumatologist, preempts the expertise of the physician
63 and blindly intrudes on the patient-physician relationship.

64 65 **Cost Considerations**

66 Because these newer medications are costly, the rheumatologist has added responsibility in
67 selecting appropriate treatment for rheumatic patients. Financial considerations are not limited to
68 the direct cost of medication, however. A growing body of evidence suggests that by slowing
69 disease progression, these medications may reduce some costly disease-related complications
70 such as long term disability, joint replacement surgery, and cardiovascular complications. The
71 optimal management for a given patient may be complex, and these decisions should be made
72 within the confines of the patient-physician relationship. Although the ACR recognizes that cost
73 is a factor in health care, it believes that medication access restrictions may adversely affect
74 patients and outcomes, as all drugs are not bioequivalent. It is not justifiable for third party
75 payers to attempt to influence these medication selections solely by burdensome pre-
76 authorization requirements, "preferred drug status" (such as cost discounts negotiated by third

77 party payers) or tiered levels of co-pays, without concern for the right drug for the right patient at
78 the right time.

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80 **Spectrum of Use**

81 Etanercept, infliximab, adalimumab, anakinra, golimumab, certolizumab pegol, rituximab and
82 abatacept are currently FDA approved for the treatment of rheumatoid arthritis. Etanercept,
83 infliximab, and adalimumab are indicated for psoriatic arthritis. Alefacept, etanercept, ,
84 adalimumab and infliximab are FDA approved for psoriasis. Etanercept, adalimumab and
85 infliximab are FDA approved for ankylosing spondylitis. Etanercept and adalimumab are also
86 approved for the treatment of juvenile idiopathic arthritis. The clinical applications and FDA
87 approved indications for many of these medications are expected to expand with time and further
88 study. Furthermore, many new biologic medications including tocilizumab show significant
89 promise in the treatment of rheumatic diseases including lupus and rheumatoid arthritis. It must
90 be recognized that many adult and pediatric rheumatic diseases may never have FDA approval
91 for biologic treatment but have adequate evidence-based data published in the medical literature
92 to justify such treatment. Third party payers should not deny payment for treatments for which
93 there is good evidence in published medical literature even though such treatment may not yet
94 have FDA approval. Many established, routinely used, and effective drugs for the treatment of
95 rheumatic diseases are not specifically FDA approved for such uses. Rheumatologists have a
96 responsibility to provide what they consider to be the safest and most effective treatment option
97 for the patient's illness, even where full FDA approval may never be obtained.

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100 Approved by the Board of Directors: 03/03 08/09