Muscle

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Rheumatoid arthritis is caused by the immune system attacking the body. It affects around 1% of people in the UK and is now treated with a variety of biologic drugs that dampen the immune system in different ways. By Janna Lawrence.

BLOCKING THE IMMUNE SYSTEM IN RHEUMATOID ARTHRITIS

Rheumatoid arthritis treatment was methotrexate. Since then, numerous biologics have been approved by the National Institute for Health and Care Excellence (NICE) for use within the NHS.

### Drug Targets

Oral disease-modifying anti-rheumatic drugs (DMARDs), the mainstay of rheumatoid arthritis treatment, were the first drugs available that affected the immune system. But over the past 15 years, a multitude of new biologic therapies have hit the market, which target specific parts of the immune system. New small molecules are also in development that target intracellular immune signalling.

### Drug Development

The first breakthrough in rheumatoid arthritis treatment was methotrexate. Since then, numerous biologics have been approved by the European Medicines Agency for use in combination with methotrexate. The prices are high but efficacy is good for patients who have failed on methotrexate and other oral DMARDs alone. The first biologics were approved in 2003, introducing more price competition to the biologics market.

### Treatment Pathway

Early targeted therapy to rapidly control disease activity in rheumatoid arthritis (RA) is crucial to limiting long-term joint damage. A range of drugs are approved by the National Institute for Health and Care Excellence (NICE) for use within the NHS.

1. **Diagnosis**
   - Person diagnosed with rheumatoid arthritis.

2. **Initial Treatment**
   - Prescribe a combination of methotrexate and one other anti-TNF drug (e.g., adalimumab, etanercept, certolizumab pegol, golimumab, infliximab or adalimumab). Use the least expensive drug first, taking account of administration and drug costs and patient access schemes. Analysis is not approving NICE.

3. **Second Line Biologic**
   - Prescribe a combination on with methotrexate (e.g., adalimumab, etanercept, certolizumab pegol, golimumab, infliximab or adalimumab). Use the least expensive drug first, taking account of administration and drug costs and patient access schemes. Analysis is not approving NICE.

4. **Third Line Biologic**
   - There is an inadequate number of responsive other drugs, including at least one TNF inhibitor, prescribers may consider including combination with a JAK inhibitor. It is contraindicated, prescribe another biologic that has not been used (e.g., adalimumab, etanercept, certolizumab pegol, golimumab, inefliximab or adalimumab).

### Small Molecules

A range of drugs are approved by the National Institute for Health and Care Excellence (NICE) for use within the NHS.

- **Cyclophilins**
  - Enfuvirtide (Crixivan)
  - Avidity (Aprozol)
  - Daratumumab (Darzalex)

- **Janus kinase (JAK) inhibitors** block JAK enzymes, part of the signal transduction and activation of transcription (STAT) pathway, which is activated in cells that respond to cytokines.

### TREATMENT PATHWAY

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