Evidence-based Management of Rheumatoid Arthritis (2009)

CPLD reviews its distance learning programmes every twelve months to ensure currency. This update has been produced by an expert and should be read in conjunction with the Evidence-based Management of Rheumatoid Arthritis (2009) distance learning course. Where updated information has been provided, we have indicated the relevant section and page number in the Evidence-based Management of Rheumatoid Arthritis (2009) for your reference. All updated information is available to download from www.nicpld.org

Pharmacists are reminded that information contained in this addendum is correct at the time of publication (January 2015) but it is their responsibility to keep up-to-date with any changes in practice.

Section 1: Incidence, aetiology and pathophysiology

P13 Should read human leucocyte antigens (HLAs) rather than human lymphocyte antigens.

P20 Exercise 1 review. Question 2 answer: True - During an inflammatory response, many cytokines are produced by a wide range of cells including macrophages, T-cells and B-cells.

Section 2: Clinical features and diagnosis

P30 The 1987 American College of Rheumatology (ACR; formerly, the American Rheumatism Association) classification criteria for rheumatoid arthritis (RA) have been criticised for their lack of sensitivity in early disease. A joint working group from the ACR and the European League Against Rheumatism (EULAR) have developed a new approach to classifying RA - The 2010 Rheumatoid Arthritis Classification Criteria.

In the new criteria set classification as “definite RA” is based on the confirmed presence of synovitis in at least 1 joint, absence of an alternative diagnosis that better explains the synovitis, and achievement of a total score of 6 or greater (of a possible 10) from the individual scores in 4 domains:
1. number and site of involved joint (score range 0-5)
2. serologic abnormality (score range 0-3)
3. elevated acute-phase response (score range 0-1)
4. symptom duration (2 levels; 0-1)

P36 Figure 12. Calculation of the disease activity score (DAS28). Delete the DAS reference values and refer to the text on P35 for the correct values.

Section 3: Initial management of rheumatoid arthritis

Since publication of this course, a paper entitled “EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs (2010)” has become available, to access the paper visit the following website http://ard.bmj.com/. In this paper recommendations for the treatment of RA with synthetic and biological DMARDs and glucocorticoids are made, based on evidence from five systematic literature reviews. The recommendations need to be considered when reading this section and Section 4 of this course.

P46/47 NICE Clinical Guideline 79 (Rheumatoid arthritis: The management of rheumatoid arthritis in adults. February 2009) provides guidance on the management of RA. One of the key priorities for implementation in this document is in people with newly diagnosed active RA, a combination of disease modifying antirheumatic drugs (DMARDs) (including methotrexate and at least one other DMARD, plus short-term glucocorticoids) should be offered as first-line treatment as soon as possible, ideally within 3 months of the onset of persistent symptoms. Amend Figure 15. Early rheumatoid arthritis management pathway, to reflect these guidelines.

P48 NICE Clinical Guideline 79 states that when offering treatment with an oral NSAID/COX-2 inhibitor, the first choice should be either a standard NSAID or a COX-2 inhibitor. In either case, these should be co-prescribed with a proton pump inhibitor (PPI)

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P48 In June 2013, the MHRA produced a drug safety update on 'Diclofenac: new contraindications and warnings after a Europe-wide review of cardiovascular safety'. The MHRA summary highlighted that: Available data indicate that the cardiovascular risk with diclofenac is similar to that of the selective COX-2 inhibitors. Consistent with COX-2 inhibitors, diclofenac is now contraindicated in those with: ischaemic heart disease; peripheral arterial disease; cerebrovascular disease; or established congestive heart failure (New York Heart Association [NYHA] classification II–IV). The new treatment advice applies to systemic formulations (ie, tablets, capsules, suppositories, and injection available both on prescription and via a pharmacy, P); it does not apply to topical (ie, gel or cream) formulations of diclofenac. Further information available at: http://www.mhra.gov.uk/Safetyinformation/DrugSafetyUpdate/CON286975.

However, in practice having considered the risk/benefit ratio, diclofenac may still be most effective for some patients.

P52 Shared care guidelines are available for: azathioprine, ciclosporin (oral), cyclophosphamide (oral), hydroxychloroquine, leflunomide, methotrexate (subcutaneous), methotrexate (oral), mycophenolate mofetil, penicillamine, sodium aurothiomalate and sulfasalazine.

P54/63 The Interface Pharmacist Network Specialist Medicines web address has been updated to http://www.ipnsm.hscni.net/. Shared care guidelines can be accessed at this web address.

P55 Methotrexate: Dosage. Subcutaneous methotrexate is now available as Metoject® and is widely prescribed, shared care guidelines are available.

P64 Antimalarials.
Hydroxychloroquine is used not chloroquine.

P65 Oral gold (auranofin). The use of oral gold is almost obsolete

P66 NICE Clinical Guideline 79 (Rheumatoid arthritis: The management of rheumatoid arthritis in adults. February 2009) is available, superseding the draft NICE guidelines for the management of RA (2008) and providing more detail on combination therapy as follows: In people with newly diagnosed active RA, a combination of DMARDs (including methotrexate and at least one other DMARD, plus short-term glucocorticoids) should be offered as first-line treatment as soon as possible, ideally within 3 months of the onset of persistent symptoms. Once satisfactory levels of disease control have been achieved, drug doses should be cautiously reduced to levels that still maintain disease control. For those whom combination DMARD therapy is not appropriate (for example, because of co-morbidities or pregnancy, during which certain drugs would be contraindicated) DMARD monotherapy should be commenced, placing greater emphasis on fast escalation to a clinically effective dose rather than on the choice of DMARD. You can download the guidelines from www.nice.org.uk/CG79.

P67/68 NICE Clinical Guideline 79 (February 2009) has replaced the draft NICE guidelines for the management of rheumatoid arthritis (2008) and recommends the use of short-term glucocorticoids plus combination DMARD therapy as first-line treatment as soon as possible, ideally within 3 months of the onset of persistent symptoms in people with newly diagnosed active RA. Short-term treatment with glucocorticoids for managing flares in people with recent-onset or established disease to rapidly decrease inflammation should be offered. In people with established RA, long-term treatment with glucocorticoids should only be continued when the long-term complications of glucocorticoid therapy have been fully discussed, and all other treatment options (including biological drugs) have been offered. You can download the guidelines from www.nice.org.uk/CG79

P73 Exercise 6 review. The answers have changed according to the updated recommendations. Refer to the Clinical Knowledge Summaries (http://cks.nice.org.uk/nsaids-prescribing-issues#!topicsummary website for up-to-date information)

P74 Exercise 7 review. Question 3 answer: True - DMARDs are used in RA, psoriasis, psoriatic arthritis as well as the connective tissues diseases and vasculitis.

P78 Alopecia should be further down this list of side-effects as it is not the most frequent side-effect of leflunomide

P78 Female patients of childbearing age should not be started on methotrexate without effective contraception being in place.

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Section 4: New therapies for Rheumatoid Arthritis and future developments

The Royal College of Nursing (RCN) have produced guidelines on assessing, managing and monitoring biologic therapies for inflammatory arthritis (2009). The guidelines can be downloaded from RCN publications website available at http://www.rcn.org.uk/development/publications. The guidelines should be considered when reading this section.

The British Society for Rheumatology (BSR) and British Health Professionals in Rheumatology (BHPR) have published RA guidelines on eligibility criteria for the first biological therapy (2010). You can download the guidelines from http://www.rheumatology.org.uk/includes/documents/cm_docs/2010/r/2_ra_ guidelines_on_eligibility_criteria_for_the_first_biological_therapy.pdf These guidelines suggest a lower value for DAS28 score however NICE guidelines for DAS have not changed yet. NICE recommendations for the management of rheumatoid arthritis can be found in NICE clinical guideline 79 (Rheumatoid arthritis: The management of rheumatoid arthritis in adults. February 2009) available at www.nice.org.uk/CG79

In August 2010, NICE published technology appraisal guidance 195 "Adalimumab, etanercept, infliximab, rituximab and abatacept for the treatment of rheumatoid arthritis after the failure of a TNF inhibitor". This replaces TA126 Rheumatoid arthritis (refractory) - rituximab and TA141 Rheumatoid arthritis (refractory) – abatacept. It also replaces the remaining recommendations in NICE technology appraisal guidance 36 issued in March 2002. The guidance should be considered when reading this section. Please see TA195 Rheumatoid arthritis - drugs for treatment after failure of a TNF inhibitor for the updated recommendations available at www.nice.org.uk/Guidance/TA195

P81 Unlike systemic drugs that affect the whole body, biologic therapies are protein molecules engineered to target specific cells or other molecules. The biologic drugs now available to treat rheumatoid arthritis include:

- five anti-tumour necrosis factor alpha (TNF) agents (adalimumab, certolizumab, etanercept, golimumab and infliximab)
- one anti-interleukin-1 agent (anakinra)
- one anti-interleukin-6 agent (tocilizumab)
- one agent that targets B-cells (rituximab)
- one agent that targets T-cells (abatacept).

Visit the most recent version of the BNF for further information on new therapies.

P88 NICE technology appraisal guidance 195 (August 2010) states that rituximab in combination with methotrexate is still recommended as an option for the treatment of adults with severe active RA who have had an inadequate response to, or have an intolerance of, other DMARDs, including at least one TNF inhibitor. Additional treatment options including adalimumab, etanercept, infliximab and abatacept, each in combination with methotrexate are now recommended for these adults if rituximab therapy is contraindicated or withdrawn because of an adverse event. If rituximab therapy cannot be given because methotrexate is contraindicated or withdrawn because of an adverse event, adalimumab and etanercept, each as monotherapy, are now recommended as treatment options. The updated recommendations are available at www.nice.org.uk/Guidance/TA195

P88 Abatacept is now available for use as first line treatment; available as IV and sc.

Oral agent Tofacitinib is licensed for use in the United States

NICE published technology appraisal guidance 280 'Abatacept for treating rheumatoid arthritis after the failure of conventional disease-modifying anti-rheumatic drugs (rapid review of TA234)'. Guidance can be accessed at: http://publications.nice.org.uk/abatacept-for-treating-rheumatoid-arthritis-after-the-failure-of-conventional-disease-modifying-ta280

P88 Anakinra is not approved for use and only used rarely

P89 NICE technology appraisal guidance 195 (August 2010) recommends abatacept as a treatment option for people with moderate to severe active RA who have already tried DMARDs (including a 'TNF inhibitor' drug), which didn't work or weren't suitable. This replaces NICE technology appraisal guidance 141 issued in April 2008.

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P92 Tocilizumab is now available and is recommended in combination with methotrexate for the treatment of moderate to severe active RA in people whose RA has responded inadequately to one or more tumour necrosis factor alpha (TNF) inhibitors and: whose RA has responded inadequately to rituximab or in whom rituximab is contraindicated or when rituximab is withdrawn because of an adverse effect (NICE TA198).

P92 NICE TA247 updates and replaces NICE TA198 and now recommends tocilizumab in combination with DMARDs for two populations:

- people whose rheumatoid arthritis had responded inadequately to previous DMARDs but before treatment with a TNF-α inhibitor (the 'DMARD-IR' population) and
- people whose rheumatoid arthritis had responded inadequately to previous TNF-α inhibitors but before treatment with rituximab (the 'TNG-IR' population).

The manufacturer also presented evidence on the clinical effectiveness of tocilizumab as monotherapy. For more information, see https://www.nice.org.uk/guidance/TA247

P92 Certolizumab pegol is now available and recommended as an option for the treatment of people with RA only if it is used as described for other tumour necrosis factor (TNF) inhibitor treatments in NICE technology appraisal guidance 130. Further information can be found in NICE Technology Appraisal 186 (Issue date: February 2010; Review date: September 2010) 'Certolizumab pegol for the treatment of rheumatoid arthritis" available at www.nice.org.uk/guidance/TA186 and in the SPC for certolizumab pegol available at http://www.medicines.org.uk/EMC/

P92 Golimumab in combination with methotrexate is recommended as an option for the treatment of rheumatoid arthritis in adults whose rheumatoid arthritis has responded inadequately to conventional DMARDs only, including methotrexate, if it is used as described for other tumour necrosis factor (TNF) inhibitor treatments in 'Adalimumab, etanercept and infliximab for the treatment of rheumatoid arthritis' (NICE technology appraisal guidance 130 available from: www.nice.org.uk/guidance/TA130) and if the manufacturer provides the 100-mg dose of golimumab at the same price as the 50-mg dose. Golimumab in combination with methotrexate is recommended as an option for the treatment of rheumatoid arthritis in adults whose rheumatoid arthritis has responded inadequately to other DMARDs, including a TNF inhibitor, if it is used as described for other TNF inhibitor treatments in 'Adalimumab, etanercept, infliximab, rituximab and abatacept for the treatment of rheumatoid arthritis after the failure of a TNF inhibitor' (NICE technology appraisal guidance 195 available from: www.nice.org.uk/guidance/TA195) and if the manufacturer provides the 100-mg dose of golimumab at the same price as the 50-mg dose.

Further information can be found in NICE Technology Appraisal TA225 (Issue date: June 2011) "Golimumab for the treatment of rheumatoid arthritis after the failure of previous disease-modifying anti-rheumatic drugs" available at www.nice.org.uk/guidance/TA225 and in the SPC for golimumab available at http://www.medicines.org.uk/EMC/

The NICE Rheumatoid arthritis overview pathway is available at: http://pathways.nice.org.uk/pathways/rheumatoid-arthritis

P94 Summary point 1. Updated to "The biologic drugs available to treat rheumatoid arthritis are adalimumab, etanercept, infliximab, anakinra, rituximab, abatacept, certolizumab, tocilizumab and golimumab."

P97 Case study 3 review. The answer to question 4 should read: Each patient has two baseline assessments:

- disease activity score (DAS28)
- health assessment questionnaire (HAQ)

Patients should also be assessed for the risk of tuberculosis at their initial assessment. These assessments are continued when the patient commences therapy. Patients are screened for previous exposure to tuberculosis, and treated if necessary before treatment.

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For information on pre-treatment screening and monitoring including specific screening and monitoring issues see the RCN guidelines on assessing, managing and monitoring biologic therapies for inflammatory arthritis (2009) available at http://www.rcn.org.uk/development/publications

References

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Reference 10. The guidance on the use of etanercept and infliximab after the failure of conventional DMARDs has been replaced by Adalimumab, etanercept and infliximab for the treatment of rheumatoid arthritis (TA130). The guidance in TA36 on the use of etanercept and infliximab after the failure of another TNF inhibitor has been replaced by Adalimumab, etanercept, infliximab, abatacept and rituximab for the treatment of rheumatoid arthritis after the failure of a TNF inhibitor (TA195).

Reference 18. Delete.

Reference 19. Update web address to http://www.ipnsm.hscni.net/library/RedAmberList.pdf

Reference 41. NICE technology appraisal guidance 126 has been updated and replaced by Rheumatoid arthritis – drugs for treatment after failure of a TNF inhibitor NICE technology appraisal guidance 195.

P102-105 Appendices. Monitoring parameters varies according to drug, monitor in accordance with shared care guidelines. Under Liver function tests: In practice LFTs would not be allowed to reach 2 – 3 times upper limit of normal (ULN) before intervention.

P105 (Appendix 2) Update bottom of table

** supplement with folic acid (normally 5mg of folic acid once weekly 24 - 48 hours post methotrexate).

BSR and BHPR guidelines on the use of rituximab in rheumatoid arthritis can be accessed at: http://www.rheumatology.org.uk/includes/documents/cm_docs/2013/r/rituximab_full_guidelines_2011.pdf

2012 Update of the 2008 American College of Rheumatology recommendations for the use of disease-modifying antirheumatic drugs and biologic agents in the treatment of rheumatoid arthritis. Arthritis Care and Research. Vol 64, Issue 5, pages 625 - 639.