Billing Code: 4160-90-M

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Agency for Healthcare Research and Quality

Supplemental Evidence and Data Request on Drug Therapy for Early Rheumatoid Arthritis in Adults – An Update

AGENCY: Agency for Healthcare Research and Quality (AHRQ), HHS.

ACTION: Request for Supplemental Evidence and Data Submissions

SUMMARY: The Agency for Healthcare Research and Quality (AHRQ) is seeking scientific information submissions from the public. Scientific information is being solicited to inform our review of *Drug Therapy for Early Rheumatoid Arthritis in Adults – An Update,* which is currently being conducted by the AHRQ's Evidence-based Practice Centers (EPC) Program. Access to published and unpublished pertinent scientific information will improve the quality of this review.

DATES: *Submission Deadline* on or before [INSERT DATE 30 DAYS AFTER DATE OF PUBLICATION IN THE FEDERAL REGISTER].

ADDRESSES:

E-mail submissions: SEADS@epc-src.org.

Print submissions:

Mailing Address:

Portland VA Research Foundation

Scientific Resource Center

ATTN: Scientific Information Packet Coordinator

PO Box 69539

Portland, OR 97239

Shipping Address (FedEx, UPS, etc.):

Portland VA Research Foundation

Scientific Resource Center

ATTN: Scientific Information Packet Coordinator
3710 SW U.S. Veterans Hospital Road
Mail Code: R&D 71
Portland, OR 97239

FOR FURTHER INFORMATION CONTACT: Ryan McKenna, Telephone: 503-220-8262 ext. 51723 or Email: SEADS@epc-src.org.

SUPPLEMENTARY INFORMATION: AHRQ is conducting this systematic review pursuant to Section 902(a) of the Public Health Service Act, 42 U.S.C. 299a(a). The Agency for Healthcare Research and Quality has commissioned the Evidence-based Practice Centers (EPC) Program to complete a review of the evidence for *Drug Therapy for Early Rheumatoid Arthritis in Adults – An Update*.

The EPC Program is dedicated to identifying as many studies as possible that are relevant to the questions for each of its reviews. In order to do so, we are supplementing the usual manual and electronic database searches of the literature by requesting information from the public (e.g., details of studies conducted). We are looking for studies that report on *Drug Therapy for Early Rheumatoid Arthritis in Adults – An Update*, including those that describe adverse events. The entire research protocol, including the key questions, is also available online at: https://effectivehealthcare.ahrq.gov/search-for-guides-reviews-and-reports/?pageaction=displayproduct&productID=2475

This is to notify the public that the EPC Program would find the following information on *Drug Therapy for Early Rheumatoid Arthritis in Adults – An Update* helpful:

- A list of completed studies that your organization has sponsored for this indication. In the list, please *indicate whether results are available on ClinicalTrials.gov along with the ClinicalTrials.gov trial number*.
    - *For completed studies that do not have results on ClinicalTrials.gov*, please provide a summary, including the following elements: study number, study period, design, methodology, indication and diagnosis,

proper use instructions, inclusion and exclusion criteria, primary and secondary outcomes, baseline characteristics, number of patients screened /eligible /enrolled /lost to follow-up /withdrawn /analyzed, effectiveness/efficacy, and safety results.

- *A list of ongoing studies that your organization has sponsored for this indication*. In the list, please provide the ClinicalTrials.gov trial number or, if the trial is not registered, the protocol for the study including a study number, the study period, design, methodology, indication and diagnosis, proper use instructions, inclusion and exclusion criteria, and primary and secondary outcomes.
- Description of whether the above studies constitute ALL Phase II and above clinical trials sponsored by your organization for this indication and an index outlining the relevant information in each submitted file.

Your contribution will be very beneficial to the EPC Program. Materials submitted must be publicly available or able to be made public. Materials that are considered confidential; marketing materials; study types not included in the review; or information on indications not included in the review cannot be used by the EPC Program. This is a voluntary request for information, and all costs for complying with this request must be borne by the submitter.

The draft of this review will be posted on AHRQ's EPC Program website and available for public comment for a period of 4 weeks. If you would like to be notified when the draft is posted, please sign up for the e-mail list at: https://www.effectivehealthcare.ahrq.gov/index.cfm/join-the-email-list1/.

The systematic review will answer the following questions. This information is provided as background. AHRQ is not requesting that the public provide answers to these questions.

The Key Questions

Key Question (KQ) 1

For patients with early Rheumatoid Arthritis (RA), do drug therapies differ in their ability to reduce disease activity, slow or limit the progression of radiographic joint damage, or induce remission?

KQ 2

For patients with early RA, do drug therapies differ in their ability to improve patient-reported symptoms, functional capacity, or quality of life?

KQ 3

For patients with early RA, do drug therapies differ in harms, tolerability, patient adherence, or adverse effects?

KQ 4

What are the comparative benefits and harms of drug therapies for early RA in subgroups of patients based on disease activity, prior therapy, demographics (e.g., women in their childbearing years), concomitant therapies, and presence of other serious conditions?

Contextual Questions (CQs)

Contextual questions are not systematically reviewed and use a "best evidence" approach. Information about the contextual questions may be included as part of the introduction or discussion section and related as appropriate to the Systematic Review.

CQ 1

Does treatment of early RA improve disease trajectory and disease outcomes compared with the trajectory or outcomes of treatment of established RA?

CQ 2

What barriers prevent individuals with early RA from obtaining access to indicated drug therapies?

PICOTS (Populations, Interventions, Comparators, Outcomes, Timing, Settings).

Populations:
Inclusion

I. All KQs: Adult outpatients ages 19 or older with an early RA diagnosis, defined as 1 year or less from disease diagnosis; we will include studies with mixed populations if >50% of study populations had an early RA diagnosis
II. KQ 4 only: Subpopulations by age, sex/gender, race/ethnicity, disease activity, prior therapies, concomitant therapies, and other serious conditions

Exclusion
Adolescents and adult patients with disease greater than 1 year from diagnosis

Intervention/Exposure:
Inclusion

I. FDA approved
A. Corticosteroids: methylprednisolone, prednisone, prednisolone
B. csDMARDs: hydroxychloroquine, leflunomide, methotrexate, sulfasalazine
C. TNF biologics: adalimumab, certolizumab pegol, etanercept, golimumab, infliximab
D. Non-TNF biologics: abatacept, rituximab, tocilizumab
E. tsDMARDs: tofacitinib
F. Biosimilars: adalimumab-atto, infliximab-dyyb, infliximab-abda, etanercept-szzs

II. Under review by FDA

A. Non-TNF biologics: sarilumab, sirukumab

Exclusion

Anakinra is excluded because, although it is approved for RA, clinically it is not used anymore for this population

Comparator:

Inclusion

I. For head-to-head RCTs, head-to-head nRCTs, and prospective, controlled cohort studies (all KQs): any active intervention listed above
II. For additional observational studies of harms (i.e., overall [KQ 3] and among subgroups [KQ 4]: any active intervention listed above or no comparator (e.g., postmarketing surveillance study of an active intervention with no comparison group)
III. For double-blinded, placebo-controlled trials for network meta-analysis (all KQs): placebo

Exclusion

All other comparisons, including active interventions not listed above

Outcomes:

Inclusion

I. KQs 1, 4: Disease activity, radiographic joint damage, remission
II. KQs 2, 4: Functional capacity, quality of life, patient-reported symptoms
III. KQs 3, 4: Overall risk of harms, overall discontinuation, discontinuation because of adverse effects, risk of serious adverse effects, specific adverse effects, patient adherence

Exclusion

All other outcomes not listed

Timing:

Inclusion

All KQs: At least 3 months of treatment

Exclusion

<3 months treatment

Settings:

Inclusion

All KQs: Outpatients

Exclusion

Inpatients

Country setting

Inclusion

All KQs: Any geographic area

Exclusion

None

Study designs

Inclusion

I. For all KQs (i.e., benefits and harms overall [KQs 1, 2, 3] and among subgroups [KQ 4]), we will include head-to head RCTs and nRCTs; prospective, controlled cohort studies (N ≥100); double-blinded, placebo-controlled trials for network meta-analysis; and SRs for identification of additional references only.
II. For studies of harms (i.e., overall [KQ 3] and among subgroups [KQ 4]), we will also include any other observational study (e.g., cohort, case-control, large case series, post marketing surveillance) (N ≥100).

Exclusion

All other designs not listed

Publication language

Inclusion

All KQs: English

Exclusion

Languages other than English

Sharon B. Arnold

Deputy Director

[FR Doc. 2017-13395 Filed: 6/26/2017 8:45 am; Publication Date: 6/27/2017]