**Clinical Policy: Upadacitinib (Rinvoq)**
Reference Number: CP.PHAR.443
Effective Date: 12.01.19
Last Review Date: 11.19
Line of Business: Medicaid

See Important Reminder at the end of this policy for important regulatory and legal information.

**Description**
Upadacitinib (Rinvoq™) is a Janus kinase (JAK) inhibitor.

**FDA Approved Indication(s)**
Rinvoq is indicated for treatment of adults with moderately to severely active rheumatoid arthritis (RA) who have had an inadequate response or intolerance to methotrexate.

**Policy/Criteria**
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Rinvoq is medically necessary when the following criteria are met:

I. **Initial Approval Criteria**
   A. **Rheumatoid Arthritis** (must meet all):
      1. Diagnosis of RA;
      2. Prescribed by or in consultation with a rheumatologist;
      3. Age ≥ 18 years;
      4. Member meets one of the following (a or b):
         a. Failure of a ≥ 3 consecutive month trial of methotrexate (MTX) at up to maximally indicated doses;
         b. Member has intolerance or contraindication to MTX (see Appendix D), and failure of a ≥ 3 consecutive month trial of at least ONE conventional DMARD (e.g., sulfasalazine, leflunomide, hydroxychloroquine) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effect are experienced;
      5. Failure of at least TWO of the following, each used for ≥ 3 consecutive months, unless contraindicated or clinically significant adverse effects are experienced: Enbrel®, Kevzara®, Xeljanz®/Xeljanz XR®;
         *Prior authorization is required for Enbrel, Kevzara, and Xeljanz/Xeljanz XR*
      6. Dose does not exceed 15 mg (one tablet) per day.

   **Approval duration:** 6 months
B. Other diagnoses/indications
   1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.PMN.53 for Medicaid.

II. Continued Therapy
   A. Rheumatoid Arthritis (must meet all):
      1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
      2. Member is responding positively to therapy;
      3. If request is for a dose increase, new dose does not exceed 15 mg (one tablet) per day.
         Approval duration: 12 months
   
   B. Other diagnoses/indications (must meet 1 or 2):
      1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
         Approval duration: Duration of request or 6 months (whichever is less); or
      2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:
   A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policy – CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information
   Appendix A: Abbreviation/Acronym Key
   DMARD: disease-modifying antirheumatic drug
   MTX: methotrexate
   RA: rheumatoid arthritis
   FDA: Food and Drug Administration

   Appendix B: Therapeutic Alternatives
   This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.
<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dosing Regimen</th>
<th>Dose Limit/ Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>azathioprine (Azasan®, Imuran®)</td>
<td>RA 1 mg/kg/day PO QD or divided BID</td>
<td>2.5 mg/kg/day</td>
</tr>
<tr>
<td>Cuprimine® (d-penicillamine)</td>
<td>RA* Initial dose: 125 or 250 mg PO QD Maintenance dose: 500 – 750 mg/day PO QD</td>
<td>1,500 mg/day</td>
</tr>
<tr>
<td>cyclosporine (Sandimmune®, Neoral®)</td>
<td>RA 2.5 – 4 mg/kg/day PO divided BID</td>
<td>4 mg/kg/day</td>
</tr>
<tr>
<td>hydroxychloroquine (Plaquenil®)</td>
<td>RA* Initial dose: 400 – 600 mg/day PO QD Maintenance dose: 200 – 400 mg/day PO QD</td>
<td>600 mg/day</td>
</tr>
<tr>
<td>leflunomide (Arava®)</td>
<td>RA 100 mg PO QD for 3 days, then 20 mg PO QD</td>
<td>20 mg/day</td>
</tr>
<tr>
<td>methotrexate (Rheumatrex®)</td>
<td>RA 7.5 mg/week PO, SC, or IM or 2.5 mg PO Q12 hr for 3 doses/week</td>
<td>30 mg/week</td>
</tr>
<tr>
<td>Ridaura® (auranofin)</td>
<td>RA 6 mg PO QD or 3 mg PO BID</td>
<td>9 mg/day (3 mg TID)</td>
</tr>
<tr>
<td>sulfasalazine (Azulfidine®)</td>
<td>RA 2 g/day PO in divided doses</td>
<td>3 g/day</td>
</tr>
<tr>
<td>Enbrel® (etanercept)</td>
<td>RA 25 mg SC twice weekly or 50 mg SC once weekly</td>
<td>50 mg/week</td>
</tr>
<tr>
<td>Kevzara® (sarilumab)</td>
<td>RA 200 mg SC once every two weeks</td>
<td>200 mg/2 weeks</td>
</tr>
<tr>
<td>Xeljanz® (tofacitinib)</td>
<td>RA 5 mg PO BID</td>
<td>10 mg/day</td>
</tr>
<tr>
<td>Xeljanz XR® (tofacitinib extended-release)</td>
<td>RA 11 mg PO QD</td>
<td>11 mg/day</td>
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</tbody>
</table>

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

*Off-label

Appendix C: Contraindications/Boxed Warnings
- Contraindication(s): none reported
- Boxed warning(s): serious infections, malignancy, and thrombosis

Appendix D: General Information
CLINICAL POLICY
Upadacitinib

• Definition of MTX or DMARD Failure
  o Child-bearing age is not considered a contraindication for use of MTX. Each drug has risks in pregnancy. An educated patient and family planning would allow use of MTX in patients who have no intention of immediate pregnancy.
  o Social use of alcohol is not considered a contraindication for use of MTX. MTX may only be contraindicated if patients choose to drink over 14 units of alcohol per week. However, excessive alcohol drinking can lead to worsening of the condition, so patients who are serious about clinical response to therapy should refrain from excessive alcohol consumption.

• Examples of positive response to therapy may include, but are not limited to:
  o Reduction in joint pain/swelling/tenderness
  o Improvement in ESR/CRP levels
  o Improvements in activities of daily living

V. Dosage and Administration

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>RA</td>
<td>15 mg PO QD</td>
<td>15 mg/day</td>
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</table>

VI. Product Availability
Tablets, extended-release: 15 mg

VII. References

Reviews, Revisions, and Approvals

<table>
<thead>
<tr>
<th>Date</th>
<th>P&amp;T Approval Date</th>
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<tbody>
<tr>
<td>Policy created</td>
<td>10.15.19</td>
</tr>
<tr>
<td>Removed HIM-TBD line of business; updated preferred redirections based on SDC recommendation and prior clinical guidance: for RA, removed redirection to adalimumab and added redirection to 2 of 3 agents (Enbrel, Kevzara, Xeljanz/Xeljanz XR).</td>
<td>12.13.19</td>
</tr>
</tbody>
</table>

Important Reminder
This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and
accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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Note:

For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.