LOUISIANA BLUE

upadacitinib (Rinvoq®, Rinvoq LQ®)

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Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

Investigational or experimental services are not covered. This includes any drug, device, procedure, or service provided under the investigational arm of a clinical trial or clinical study. These services are excluded from coverage under benefits.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Rheumatoid Arthritis

Based on review of available data, the Company may consider the use of upadacitinib (Rinvoq®)‡ for the treatment of patients with rheumatoid arthritis to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for upadacitinib (Rinvoq) will be considered when ALL of the following criteria are met:

Initial

- Patient has a diagnosis of moderately to severely active rheumatoid arthritis; AND
- Patient is 18 years of age or older; AND
- Patient has failed treatment with one or more traditional disease modifying anti-rheumatic drugs (DMARDs), such as methotrexate, unless there is clinical evidence or patient history that suggests the use of these products will be ineffective or cause an adverse reaction to the patient; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
- Requested drug is NOT being used in combination with biologic DMARDs, such as adalimumab (Humira®, biosimilars)‡ or etanercept (Enbrel®)‡, OR potent immunosuppressants such as azathioprine and cyclosporine, OR drugs such as apremilast (Otezla®/XR)‡ or tofacitinib (Xeljanz/XR®)‡; AND
- Patient has failed treatment with etanercept (Enbrel) OR adalimumab (Simlandi®, adalimumab-adaz, adalimumab-adbm [manufactured by Quallent Pharmaceuticals])‡ after at least TWO months of therapy unless there is clinical evidence or patient history that suggests the use of these products will be ineffective or cause an adverse reaction to the patient. A failure of a different tumor necrosis factor (TNF) inhibitor would also count towards this criterion (e.g., certolizumab pegol [Cimzia®]‡, golimumab [Simponi® or Simponi Aria®]‡, infliximab [Remicade®, Renflexis®, etc.]‡); AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met).*

- Patient has a negative TB (tuberculosis) test (e.g., purified protein derivative [PPD], blood test) prior to treatment.

Continuation

- Patient has received an initial authorization; AND
- Patient has experienced a beneficial clinical response from baseline (prior to therapy with Rinvoq) as evidenced by improvement in clinical signs and symptoms such as decreased joint pain, morning stiffness, or fatigue; improved function or activities of daily living; decreased soft tissue swelling in joints or tendon sheaths; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
- Requested drug is NOT used in combination with other biologic DMARDs, such as adalimumab (Humira, biosimilars) or etanercept (Enbrel), OR potent immunosuppressants such as azathioprine and cyclosporine, OR other drugs such as apremilast (Otezla/XR) or tofacitinib (Xeljanz/XR).

Psoriatic Arthritis

Based on review of available data, the Company may consider the use of upadacitinib (Rinvoq, Rinvoq LQ®)‡ for the treatment of patients with psoriatic arthritis to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for upadacitinib (Rinvoq, Rinvoq LQ) will be considered when ALL of the following criteria are met:

Initial

- Patient has a diagnosis of active psoriatic arthritis; AND
- Patient is 2 years of age or older; AND
- If the request is for Rinvoq LQ, the patient is less than 18 years of age; AND
- If the request is for Rinvoq, the patient is 30 kilograms or greater; AND
- Patient has failed treatment with one or more traditional DMARDs, such as methotrexate, unless there is clinical evidence or patient history that suggests the use of these products will be ineffective or cause an adverse reaction to the patient; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
- Requested drug is NOT used in combination with other biologic DMARDs, such as adalimumab (Humira, biosimilars) or etanercept (Enbrel), OR potent immunosuppressants such as azathioprine and cyclosporine, OR other drugs such as apremilast (Otezla/XR) or tofacitinib (Xeljanz/XR); AND
- Patient has failed treatment with etanercept (Enbrel) OR adalimumab (Simlandi, adalimumab-adaz, adalimumab-adbm [manufactured by Quallent Pharmaceuticals]) after at least TWO months of therapy unless there is clinical evidence or patient history that suggests the use of these products will be ineffective or cause an adverse reaction to the patient. A failure of a different TNF inhibitor would also count towards this criterion (e.g., certolizumab pegol [Cimzia], golimumab [Simponi or Simponi Aria], infliximab [Remicade, Renflexis, etc.]); AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met).*

- Patient has a negative TB test (e.g., PPD, blood test) prior to treatment.

Continuation

- Patient has received an initial authorization; AND
- Patient has experienced a beneficial clinical response from baseline (prior to therapy with Rinvoq) as evidenced by improvement in clinical signs and symptoms such as decreased joint pain, morning stiffness, or fatigue; improved function or activities of daily living; decreased soft tissue swelling in joints or tendon sheaths; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
- Requested drug is NOT used in combination with other biologic DMARDs, such as adalimumab (Humira, biosimilars) or etanercept (Enbrel), OR potent immunosuppressants such as azathioprine and cyclosporine, OR other drugs such as apremilast (Otezla/XR) or tofacitinib (Xeljanz/XR).

Atopic Dermatitis

Based on review of available data, the Company may consider the use of upadacitinib (Rinvoq) for the treatment of patients with atopic dermatitis to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for upadacitinib (Rinvoq) will be considered when ALL of the following criteria are met:

Initial:

- Patient has a diagnosis of moderate to severe atopic dermatitis; AND
- Patient is 12 years of age or older; AND
- Patient has had chronic atopic dermatitis for at least 6 months; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
- Patient has atopic dermatitis involvement estimated to be greater than or equal to 10% of the body surface area (BSA) according to the prescribing physician; AND
  *(Note: This specific patient selection criterion is an additional Company requirement, based on clinical trials, for coverage eligibility and will be denied as not medically necessary** if not met.)*
- Patient has tried and failed (e.g., intolerance or inadequate response) at least one prescription generic topical corticosteroid or calcineurin inhibitor (tacrolimus ointment, pimecrolimus cream) unless there is clinical evidence or patient history that suggests the use of these products will be ineffective or cause an adverse reaction to the patient; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
- Patient has tried and failed at least one systemic therapy for at least 3 months OR tried but couldn't tolerate systemic therapy for at least 3 months unless there is clinical evidence or patient history that suggests the use of these products will be ineffective or cause an adverse reaction to the patient. Note that systemic therapies include: methotrexate, azathioprine, cyclosporine, and mycophenolate mofetil. A failure of dupilumab (Dupixent®)‡ or tralokinumab-ldrm (Adbry™)‡ would count towards this criterion; AND

*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*

- Requested drug is NOT being used in combination with other JAK (janus kinase) inhibitors (e.g., tofacitinib [Xeljanz/XR], ruxolitinib [Opzelura™]‡, abrocitinib [Cibinqo®]‡), monoclonal antibodies (e.g., tralokinumab-ldrm [Adbry™]‡, dupilumab [Dupixent]), or other systemic immunosuppressants (such as methotrexate or cyclosporine); AND
- Patient has a negative TB test (e.g., PPD, blood test) prior to treatment.

Continuation:

- Patient has received an initial authorization; AND
- Patient has received at least 6 months of therapy with the requested drug; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
- Patient has been adherent to the requested drug and other medications for the condition being treated; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
- Patient has had a clinically meaningful beneficial response to Rinvoq therapy as compared to their baseline status (before Rinvoq therapy) as evidenced by TWO or more of the following:
  - Reduction in disease severity (e.g., erythema, dryness, edema/papulation, excoriations, lichenification, oozing/crusting)
  - Reduction in the frequency or intensity of pruritus
  - Reduction in the frequency of disease exacerbations/flares
  - Reduction in the BSA with atopic dermatitis involvement (a 20% reduction in percent BSA involved over baseline)
  - Improvement in overall patient quality of life (e.g., improved sleep, less depression or anxiety, etc.); AND

  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
- Requested drug is NOT being used in combination with other JAK (janus kinase) inhibitors (e.g., tofacitinib [Xeljanz/XR], ruxolitinib [Opzelura], abrocitinib [Cibinqo]), monoclonal antibodies (e.g., tralokinumab-ldrm [Adbry], dupilumab [Dupixent]), or other systemic immunosuppressants (such as methotrexate or cyclosporine).

Ulcerative Colitis

Based on review of available data, the Company may consider the use of upadacitinib (Rinvoq) for the treatment of patients with ulcerative colitis to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for upadacitinib (Rinvoq) will be considered when ALL of the following criteria are met:

Initial

- Patient has a diagnosis of moderately to severely active ulcerative colitis; AND
- Patient is 18 years of age or older; AND

- Patient meets one of the following:
  - Patient has failed treatment with a TNF inhibitor such as adalimumab (Simlandi, adalimumab-adaz, adalimumab-adbm [manufactured by Quallent Pharmaceuticals]) after at least TWO months of therapy unless there is clinical evidence or patient history that suggests the use of a TNF inhibitor will be ineffective or cause an adverse reaction to the patient. A failure of a different TNF inhibitor would also count towards this criterion (e.g., golimumab [Simponi] or infliximab [Remicade, Renflexis, etc.]); OR
  - Patient has failed treatment with at least one conventional therapy such as a corticosteroid, azathioprine, or 6-mercaptopurine (6-MP) if the use of a TNF inhibitor is clinically inadvisable; AND
- Requested drug is NOT used in combination with other biologic DMARDs, such as adalimumab (Humira, biosimilars), OR potent immunosuppressants such as azathioprine and cyclosporine, OR other drugs such as apremilast (Otezla/XR) or tofacitinib (Xeljanz/XR); AND
- Patient has a negative TB test (e.g., PPD, blood test) prior to treatment.

Continuation

- Patient has received an initial authorization; AND
- Patient has experienced a beneficial clinical response from baseline (prior to therapy with Rinvoq) as evidenced by improvement in objective measures (e.g., fecal or serum inflammatory markers, endoscopic findings, reduced corticosteroid use) or in symptoms such as pain, fatigue, stool frequency, or rectal bleeding; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
- Requested drug is NOT used in combination with other biologic DMARDs, such as adalimumab (Humira, biosimilars) or etanercept (Enbrel), OR potent immunosuppressants such as azathioprine and cyclosporine, OR other drugs such as apremilast (Otezla/XR) or tofacitinib (Xeljanz/XR).

Ankylosing Spondylitis

Based on review of available data, the Company may consider the use of upadacitinib (Rinvoq) for the treatment of patients with active ankylosing spondylitis to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for upadacitinib (Rinvoq) will be considered when ALL of the following criteria are met:

Initial

- Patient has a diagnosis of active ankylosing spondylitis; AND
- Patient is 18 years of age or older; AND
- Patient has failed treatment with non-steroidal anti-inflammatory drugs (NSAIDs) unless there is clinical evidence or patient history that suggests these products will be ineffective or cause an adverse reaction to the patient; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*

- Requested drug is NOT used in combination with other biologic DMARDs, such as adalimumab (Humira, biosimilars) or etanercept (Enbrel), OR potent immunosuppressants such as azathioprine and cyclosporine, OR other drugs such as apremilast (Otezla/XR) or tofacitinib (Xeljanz/XR); AND
- Patient has failed treatment with etanercept (Enbrel) OR adalimumab (Simlandi, adalimumab-adaz, adalimumab-adbm [manufactured by Quallent Pharmaceuticals]) after at least TWO months of therapy unless there is clinical evidence or patient history that suggests the use of these products will be ineffective or cause an adverse reaction to the patient. A failure of a different TNF inhibitor would also count towards this criterion (e.g., certolizumab pegol [Cimzia], golimumab [Simponi or Simponi Aria], infliximab [Remicade, Renflexis, etc.]); AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met).*
- Patient has a negative TB test (e.g., PPD, blood test) prior to treatment.

Continuation

- Patient has received an initial authorization; AND
- Patient has experienced a beneficial clinical response from baseline (prior to therapy with Rinvoq) as evidenced by improvement in objective measures (e.g., Ankylosing Spondylitis Disease Activity Score [ASDAS], Bath Ankylosing Spondylitis Disease Activity Index [BASDAI], inflammatory serum markers) or in clinical signs and symptoms such as reduced pain, stiffness, or improved daily functioning; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
- Requested drug is NOT used in combination with other biologic DMARDs, such as adalimumab (Humira, biosimilars) or etanercept (Enbrel), OR potent immunosuppressants such as azathioprine and cyclosporine, OR other drugs such as apremilast (Otezla/XR) or tofacitinib (Xeljanz/XR).

Non-Radiographic Axial Spondyloarthritis

Based on review of available data, the Company may consider the use of upadacitinib (Rinvoq) for the treatment of non-radiographic axial spondyloarthritis to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for the use of upadacitinib (Rinvoq) will be considered when ALL of the following criteria are met:

Initial

- Patient has active non-radiographic axial spondyloarthritis as confirmed by the presence of sacroiliitis on magnetic resonance imaging (MRI); AND
- Patient has failed at least TWO months of current continuous therapy with at least TWO different oral NSAIDs (at prescription strength dosages) unless there is clinical evidence or patient history that suggests these products will be ineffective or cause an adverse reaction to the patient; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met).*

- Patient has failed treatment with certolizumab pegol (Cimzia) after at least TWO months of therapy unless there is clinical evidence or patient history that suggests the use of certolizumab pegol (Cimzia) will be ineffective or cause an adverse reaction to the patient; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met).*
- Patient is 18 years of age or older; AND
- Requested drug is NOT used in combination with other biologic DMARDs, such as adalimumab (Humira, biosimilars) or etanercept (Enbrel), OR potent immunosuppressants such as azathioprine and cyclosporine, OR other drugs such as apremilast (Otezla/XR) or tofacitinib (Xeljanz/XR); AND
- Patient has a negative TB test (e.g., PPD, blood test) prior to treatment.

Continuation

- Patient has received an initial authorization; AND
- Patient has experienced a beneficial clinical response from baseline (prior to therapy with Rinvoq) as evidenced by improvement in objective measures (e.g., ASDAS, BASDAI, inflammatory serum markers) or in clinical signs and symptoms such as reduced pain, stiffness, or improved daily functioning; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
- Requested drug is NOT used in combination with other biologic DMARDs, such as adalimumab (Humira, biosimilars) or etanercept (Enbrel), OR potent immunosuppressants such as azathioprine and cyclosporine, OR other drugs such as apremilast (Otezla/XR) or tofacitinib (Xeljanz/XR).

Crohn's Disease

Based on review of available data, the Company may consider the use of upadacitinib (Rinvoq) for the treatment of patients with Crohn's disease to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for upadacitinib (Rinvoq) will be considered when ALL of the following criteria are met:

Initial

- Patient has a diagnosis of moderately to severely active Crohn's disease; AND
- Patient is 18 years of age or older; AND
- Patient meets one of the following:
  - Patient has failed treatment with a TNF inhibitor such as adalimumab (Simlandi, adalimumab-adaz, adalimumab-adbm [manufactured by Quallent Pharmaceuticals]) after at least TWO months of therapy unless there is clinical evidence or patient history that suggests the use of a TNF inhibitor will be ineffective or cause an adverse reaction to the patient. A failure of a different TNF inhibitor would also count towards this criterion (e.g., golimumab [Simponi] or infliximab [Remicade, Renflexis, etc.]); OR

  - Patient has failed treatment with at least one conventional therapy such as a corticosteroid, azathioprine, or 6-mercaptopurine (6-MP) if the use of a TNF inhibitor is clinically inadvisable; AND
- Requested drug is NOT used in combination with other biologic DMARDs, such as adalimumab (Humira, biosimilars), OR potent immunosuppressants such as azathioprine and cyclosporine, OR other drugs such as apremilast (Otezla/XR) or tofacitinib (Xeljanz/XR); AND
- Patient has a negative TB test (e.g., PPD, blood test) prior to treatment.

Continuation

- Patient has received an initial authorization; AND
- Patient has experienced a beneficial clinical response from baseline (prior to therapy with Rinvoq) as evidenced by improvement in objective measures (e.g., fecal or serum inflammatory markers, endoscopic findings, reduced corticosteroid use) or in symptoms such as pain, fatigue, stool frequency, or blood in stool; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
- Requested drug is NOT used in combination with other biologic DMARDs, such as adalimumab (Humira, biosimilars) or etanercept (Enbrel), OR potent immunosuppressants such as azathioprine and cyclosporine, OR other drugs such as apremilast (Otezla/XR) or tofacitinib (Xeljanz/XR).

Polyarticular Juvenile Idiopathic Arthritis

Based on review of available data, the Company may consider the use of upadacitinib (Rinvoq, Rinvoq LQ) for the treatment of patients with polyarticular juvenile idiopathic arthritis to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for upadacitinib (Rinvoq, Rinvoq LQ) will be considered when ALL of the following criteria are met:

Initial

- Patient has a diagnosis of polyarticular juvenile idiopathic arthritis; AND
- Patient is 2 years of age or older; AND
- If the request is for Rinvoq LQ, the patient is less than 18 years of age; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
- If the request is for Rinvoq, the patient is 30 kilograms or greater; AND
- Patient has failed treatment with one or more traditional DMARDs, such as methotrexate, unless there is clinical evidence or patient history that suggests the use of these products will be ineffective or cause an adverse reaction to the patient; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
- Requested drug is NOT used in combination with other biologic DMARDs, such as adalimumab (Humira, biosimilars) or etanercept (Enbrel), OR potent immunosuppressants such as azathioprine and cyclosporine, OR other drugs such as apremilast (Otezla/XR) or tofacitinib (Xeljanz/XR); AND

- Patient has failed treatment with etanercept (Enbrel) OR adalimumab (Simlandi, adalimumab-adaz, adalimumab-adbm [manufactured by Quallent Pharmaceuticals]) after at least TWO months of therapy unless there is clinical evidence or patient history that suggests the use of these products will be ineffective or cause an adverse reaction to the patient. A failure of a different TNF inhibitor would also count towards this criterion (e.g., certolizumab pegol [Cimzia], golimumab [Simponi or Simponi Aria], infliximab [Remicade, Renflexis, etc.]); AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met).*
- Patient has a negative TB test (e.g., PPD, blood test) prior to treatment.

Continuation

- Patient has received an initial authorization; AND
- Patient has experienced a beneficial clinical response from baseline (prior to therapy with Rinvoq) as evidenced by improvement in clinical signs and symptoms such as improved range of motion, reduced joint pain or tenderness, decreased duration of morning stiffness or fatigue, improved function or activities of daily living, reduced corticosteroid dosage, or improvement in inflammatory serum markers; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
- Requested drug is NOT used in combination with other biologic DMARDs, such as adalimumab (Humira, biosimilars) or etanercept (Enbrel), OR potent immunosuppressants such as azathioprine and cyclosporine, OR other drugs such as apremilast (Otezla/XR) or tofacitinib (Xeljanz/XR).

Giant Cell Arteritis

Based on review of available data, the Company may consider the use of upadacitinib (Rinvoq) for the treatment of patients with giant cell arteritis to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for upadacitinib (Rinvoq) will be considered when ALL of the following criteria are met:

Initial

- Patient has a diagnosis of giant cell arteritis; AND
- Patient is 18 years of age or older; AND
- Patient is using the requested drug in combination with a tapering course of corticosteroids; AND
- Requested drug is NOT used in combination with other biologic DMARDs, such as adalimumab (Humira, biosimilars) or etanercept (Enbrel), OR potent immunosuppressants such as azathioprine and cyclosporine, OR other drugs such as apremilast (Otezla/XR) or tofacitinib (Xeljanz/XR); AND
- Patient has failed treatment with systemic corticosteroid therapy unless there is clinical evidence or patient history that suggests the use of these products will be ineffective or cause an adverse reaction to the patient; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*

- Patient has a negative TB test (e.g., PPD, blood test) prior to treatment.

Continuation

- Patient has received an initial authorization; AND
- Patient has experienced a beneficial clinical response from baseline (prior to therapy with Rinvoq) as evidenced by improvement in clinical signs and symptoms such as decreased headache, scalp, or jaw pain, reduced fatigue, improved vision, reduced corticosteroid dosage, or improvement in inflammatory serum markers; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
- Requested drug is NOT used in combination with other biologic DMARDs, such as adalimumab (Humira, biosimilars) or etanercept (Enbrel), OR potent immunosuppressants such as azathioprine and cyclosporine, OR other drugs such as apremilast (Otezla/XR) or tofacitinib (Xeljanz/XR).

When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of upadacitinib (Rinvoq) when any of the following criteria for their respective disease state listed below (and denoted in the patient selection criteria above) are NOT met to be **not medically necessary**:**

- For rheumatoid arthritis or psoriatic arthritis:
  - Patient has failed treatment with ONE or more traditional DMARDs
  - Patient has failed treatment with etanercept (Enbrel) OR adalimumab (Simlandi, adalimumab-adaz, adalimumab-adbm [manufactured by Quallent Pharmaceuticals]) after at least TWO months of therapy
  - For continuation requests: Patient has experienced a beneficial clinical response from baseline (prior to therapy with Rinvoq) as evidenced by improvement in clinical signs and symptoms such as decreased joint pain, morning stiffness, or fatigue; improved function or activities of daily living; decreased soft tissue swelling in joints or tendon sheaths
- For atopic dermatitis:
  - Patient has had chronic atopic dermatitis for at least 6 months
  - Patient has atopic dermatitis involvement estimated to be greater than or equal to 10% of the body surface area (BSA) according to the prescribing physician
  - Patient has tried and failed at least one prescription generic topical corticosteroid or calcineurin inhibitor (tacrolimus ointment, pimecrolimus cream)
  - Patient has tried and failed at least ONE systemic therapy for at least 3 months OR tried but couldn't tolerate systemic therapy for at least 3 months.
  - For continuation requests: Patient has received at least 6 months of therapy with the requested drug
  - For continuation requests: Patient has been adherent to the requested drug and other medications for the condition being treated

  - For continuation requests: Patient has had a clinically meaningful beneficial response to Rinvoq therapy as compared to their baseline status (before Rinvoq therapy) as evidenced by TWO or more of the following:
    - Reduction in disease severity (e.g., erythema, dryness, edema/papulation, excoriations, lichenification, oozing/crusting)
    - Reduction in the frequency or intensity of pruritus
    - Reduction in the frequency of disease exacerbations/flares
    - Reduction in the BSA with atopic dermatitis involvement (a 20% reduction in percent BSA involved over baseline)
    - Improvement in overall patient quality of life (e.g., improved sleep, less depression or anxiety, etc.).
- For ulcerative colitis:
  - For continuation requests: Patient has experienced a beneficial clinical response from baseline (prior to therapy with Rinvoq) as evidenced by improvement in objective measures (e.g., fecal or serum inflammatory markers, endoscopic findings, reduced corticosteroid use) or in symptoms such as pain, fatigue, stool frequency, or rectal bleeding
- For active ankylosing spondylitis:
  - Patient has failed treatment with ONE or more NSAIDs
  - Patient has failed treatment with etanercept (Enbrel) OR adalimumab (Simlandi, adalimumab-adaz, adalimumab-adbm [manufactured by Quallent Pharmaceuticals]) after at least TWO months of therapy
  - For continuation requests: Patient has experienced a beneficial clinical response from baseline (prior to therapy with Rinvoq) as evidenced by improvement in objective measures (e.g., ASDAS, BASDAI, inflammatory serum markers) or in clinical signs and symptoms such as reduced pain, stiffness, or improved daily functioning
- For active non-radiographic axial spondyloarthritis:
  - Patient has failed at least TWO months of current continuous therapy with at least TWO different oral NSAIDs (at prescription strength dosages)
  - Patient has failed treatment with certolizumab pegol (Cimzia) after at least TWO months of therapy
  - For continuation requests: Patient has experienced a beneficial clinical response from baseline (prior to therapy with Rinvoq) as evidenced by improvement in objective measures (e.g., ASDAS, BASDAI, inflammatory serum markers) or in clinical signs and symptoms such as reduced pain, stiffness, or improved daily functioning
- For Crohn's disease:
  - For continuation requests: Patient has experienced a beneficial clinical response from baseline (prior to therapy with Rinvoq) as evidenced by improvement in objective measures (e.g., fecal or serum inflammatory markers, endoscopic findings, reduced corticosteroid use) or in symptoms such as pain, fatigue, stool frequency, or blood in stool
- For polyarticular juvenile idiopathic arthritis:
  - If the request is for Rinvoq LQ, the patient is less than 18 years of age; AND
  - Patient has failed treatment with ONE or more traditional DMARDs

    - Patient has failed treatment with etanercept (Enbrel) OR adalimumab (Simlandi, adalimumab-adaz, adalimumab-adbm [manufactured by Quallent Pharmaceuticals]) after at least TWO months of therapy
    - For continuation requests: Patient has experienced a beneficial clinical response from baseline (prior to therapy with Rinvoq) as evidenced by improvement in clinical signs and symptoms such as improved range of motion, reduced joint pain or tenderness, decreased duration of morning stiffness or fatigue, improved function or activities of daily living, reduced corticosteroid dosage, or improvement in inflammatory serum markers
- For giant cell arteritis:
    - Patient has failed treatment with systemic corticosteroid therapy
    - For continuation requests: Patient has experienced a beneficial clinical response from baseline (prior to therapy with Rinvoq) as evidenced by improvement in clinical signs and symptoms such as decreased headache, scalp, or jaw pain, reduced fatigue, improved vision, reduced corticosteroid dosage, or improvement in inflammatory serum markers

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of upadacitinib (Rinvoq, Rinvoq LQ) when the patient selection criteria are not met to be **investigational*** (with the exception of those denoted above as **not medically necessary****).

Based on review of available data, the Company considers the use of upadacitinib (Rinvoq) 30 mg tablets for rheumatoid arthritis, psoriatic arthritis, active non-radiographic axial spondyloarthritis, active ankylosing spondylitis, juvenile idiopathic arthritis, or giant cell arteritis to be **investigational*.**

Based on review of available data, the Company considers the use of upadacitinib (Rinvoq) 45 mg tablets for any indication other than ulcerative colitis or Crohn's disease induction therapy to be **investigational*.**

Based on review of available data, the Company considers the use of upadacitinib (Rinvoq LQ) oral solution for any indication other than psoriatic arthritis or polyarticular juvenile idiopathic arthritis to be **investigational*.**

Background/Overview

Rinvoq is indicated for the treatment of adults with moderately to severely active rheumatoid arthritis who have had an inadequate response or intolerance to one or more tumor necrosis factor (TNF) blockers, the treatment of adults and pediatric patients 2 years of age and older with active psoriatic arthritis who have had an inadequate response or intolerance to one or more TNF blockers, the treatment of adults and pediatric patients 12 years of age and older with refractory, moderate to

severe atopic dermatitis whose disease is not adequately controlled with other systemic drug products, including biologics, or when use of those therapies are inadvisable, the treatment of adults with moderately to severely active ulcerative colitis who have had an inadequate response or intolerance to one or more TNF blockers, the treatment of adults with active ankylosing spondylitis who have had an inadequate response or intolerance to one or more TNF blockers, the treatment of adults with active non-radiographic axial spondyloarthritis with objective signs of inflammation who have had an inadequate response or intolerance to TNF blocker therapy, for the treatment of adults with moderately to severely active Crohn's disease who have had an inadequate response or intolerance to one or more TNF blockers, for the treatment of patients 2 years of age and older with active polyarticular juvenile idiopathic arthritis who have had an inadequate response or intolerance to one or more TNF blockers, and for the treatment of adults with giant cell arteritis. Its latest formulation, Rinvoq LQ, which is an oral solution, is indicated for the treatment of adults and pediatric patients 2 years of age and older with active psoriatic arthritis who have had an inadequate response or intolerance to one or more TNF blockers and for the treatment of patients 2 years of age and older with active polyarticular juvenile idiopathic arthritis who have had an inadequate response or intolerance to one or more TNF blockers. Rinvoq is a Janus kinase (JAK) inhibitor. JAKs are intracellular enzymes which transmit signals arising from cytokine or growth factor-receptor interactions on the cellular membrane to influence cellular processes of hematopoiesis and immune cell function. Within the signaling pathway, JAKs phosphorylate and activate Signal Transducers and Activators of Transcription (STATs) which modulate intracellular activity including gene expression. Rinvoq modulates the signaling pathway at the point of JAKs, preventing the phosphorylation and activation of STATs. The recommended dose of Rinvoq for rheumatoid arthritis, psoriatic arthritis in adults, active non-radiographic axial spondyloarthritis, active ankylosing spondylitis, and giant cell arteritis is 15 mg once daily. Atopic dermatitis dosing can range from 15 mg to 30 mg once daily. Ulcerative colitis dosing includes an 8-week 45 mg once daily induction dose, followed by a maintenance dose of 15 mg to 30 mg once daily. Crohn's disease dosing includes a 12-week 45 mg once daily induction dose, followed by a maintenance dose of 15 mg to 30 mg once daily. The recommended dose for Rinvoq LQ in pediatric patients with psoriatic arthritis is based on weight. For those who are 10 kg to less than 20 kg, the recommended dose is 3 mg twice daily. For those who are 20 kg to less than 30 kg, the recommended dose of Rinvoq LQ is 4 mg twice daily. For those 30 kg or more, the recommended dose is 6 mg twice daily. Rinvoq LQ oral solution is not substitutable with Rinvoq extended release tablets.

Rheumatoid Arthritis
Rheumatoid Arthritis is a chronic (long-term) disease that causes inflammation of the joints and surrounding tissues. It can also affect other organs. It is considered an autoimmune disease. In an autoimmune disease, the immune system confuses healthy tissue for foreign substances. Typically, first line treatments such as traditional DMARDs are used to treat this condition. An example of a traditional DMARD would include methotrexate.

Psoriatic Arthritis
Psoriatic Arthritis is an arthritis that is often associated with psoriasis of the skin. Typically, first line treatments such as traditional DMARDs are used to treat this condition. An example of a traditional DMARD would include methotrexate.

Traditional Disease-Modifying Anti-Rheumatic Drugs (DMARDs)
Traditional disease-modifying anti-rheumatic drugs are used for the treatment of rheumatoid arthritis as well as other inflammatory conditions. These drugs slow the disease process by modifying the immune system.

- methotrexate
- cyclosporine
- sulfasalazine
- mercaptopurine
- gold compounds

Atopic Dermatitis
There are various treatment options for atopic dermatitis, including first line agents such as topical corticosteroids (many of which are in generic form) and topical immunomodulatory agents such as generic tacrolimus and generic pimecrolimus. For those that are refractory to topical therapies, systemic immunomodulatory agents are an option for therapy. Rinvoq has been addressed in guidelines published by the American Academy of Dermatology and the American Academy of Allergy, Asthma, and Immunology.

Ulcerative Colitis
Ulcerative colitis is a chronic, episodic, inflammatory disease of the large intestine and rectum characterized by bloody diarrhea. This disease usually begins in the rectal area and may eventually extend through the entire large intestine. Repeated episodes of inflammation lead to thickening of the wall of the intestine and rectum with scar tissue. Death of colon tissue or sepsis may occur with severe disease. The goals of treatment are to control the acute attacks, prevent recurrent attacks and promote healing of the colon. Hospitalization is often required for severe attacks. Typically, first line treatments such as corticosteroids, 6-mercaptopurine and azathioprine are used to treat this condition.

Ankylosing Spondylitis
Ankylosing spondylitis is a chronic inflammatory disease that affects the joints between the vertebrae of the spine, and the joints between the spine and the pelvis. It eventually causes the affected vertebrae to fuse or grow together. Nonsteroidal anti-inflammatory drugs, such as ibuprofen or naproxen, are used to reduce inflammation and pain associated with the condition. Corticosteroid therapy or medications to suppress the immune system may be prescribed to control various symptoms.

Non-Radiographic Axial Spondyloarthritis.
Axial spondyloarthritis is an inflammatory arthritis of the spine. It often presents as chronic back pain, typically before the age of 45 and is often associated with one or more articular features (e.g., synovitis, enthesitis, and dactylitis) and/or non-articular features (e.g., uveitis, psoriasis, and inflammatory bowel diseases). Patients with this condition are classified as having one of two types of axial spondyloarthritis: either radiographic or non-radiographic. As supported by the name, the non-radiographic variety isn't evident on plain radiography and instead the diagnosis is supported by evidence of active inflammation of the sacroiliac joints via magnetic resonance imaging (MRI). Traditional pharmacologic therapy for the treatment of non-radiographic axial spondyloarthritis

includes oral NSAIDs. Approximately 70-80% of patients with this condition report substantial relief with NSAID therapy. The effect of an NSAID is typically seen within two to four weeks and multiple NSAIDs need to be tried as patient response to a particular NSAID isn't predictable. Currently Cimzia is the only TNF inhibitor product that is approved for non-radiographic axial spondyloarthritis. Taltz®‡ and Cosentyx®‡, both interleukin blockers, have gained approval for this indication. Most recently, Rinvoq gained an indication for this condition. If a response to two NSAIDs has not proven beneficial, a tumor necrosis factor (TNF) alpha inhibitor, such as Cimzia, an interleukin blocker, such as Taltz or Cosentyx, or a JAK inhibitor, such as Rinvoq, would be the next treatment options.

Crohn's Disease
Crohn's disease is a chronic autoimmune disease that can affect any part of the gastrointestinal tract but most commonly occurs in the ileum. As a result of the immune attack, the intestinal wall becomes thick, and deep ulcers may form. In addition to the bowel abnormalities, Crohn's disease can also affect other organs in the body. Typically, first line treatments such as corticosteroids, 6-MP and azathioprine are used to treat this condition.

Polyarticular Juvenile Idiopathic Arthritis
Polyarticular juvenile idiopathic arthritis includes the inflammation of joints and presence of arthritis in children. Polyarticular juvenile idiopathic arthritis typically occurs in a symmetrical manner with knees, wrists, and ankles most frequently affected. However certain subgroups of children do have predominantly asymmetrical involvement. Typically, first line treatments such as traditional DMARDs are used to treat this condition. An example of a traditional DMARD would include methotrexate.

Giant Cell Arteritis
Giant cell (temporal) arteritis is the most common of the systemic vasculitides and most often, occurs in those age 50 years or older. Typical presentation could include headache, abrupt visual disturbances, jaw claudication, unexplained fever or anemia, as well as elevated ESR and/or CRP. The gold standard for the diagnosis of giant cell arteritis is temporal biopsy. High dose corticosteroids are recommended as the first line treatment option. The corticosteroid dose is gradually reduced to establish a maintenance dose that controls disease activity.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)
Rinvoq is indicated for the treatment of adults with moderately to severely active rheumatoid arthritis who have had an inadequate response or intolerance to one or more tumor necrosis factor (TNF) blockers, the treatment of adults and pediatric patients 2 years of age and older with active psoriatic arthritis who have had an inadequate response or intolerance to one or more TNF blockers, the treatment of adults and pediatric patients 12 years of age and older with refractory, moderate to severe atopic dermatitis whose disease is not adequately controlled with other systemic drug products, including biologics, or when use of those therapies are inadvisable, the treatment of adults with moderately to severely active ulcerative colitis who have had an inadequate response or intolerance to one or more TNF blockers, the treatment of adults with active ankylosing spondylitis who have had an inadequate response or intolerance to one or more TNF blockers, the treatment of

adults with active non-radiographic axial spondyloarthritis with objective signs of inflammation who have had an inadequate response or intolerance to TNF blocker therapy, for the treatment of adults with moderately to severely active Crohn's disease who have had an inadequate response or intolerance to one or more TNF blockers, for the treatment of patients 2 years of age and older with active polyarticular juvenile idiopathic arthritis who have had an inadequate response or intolerance to one or more TNF blockers, and for the treatment of adults with giant cell arteritis. Rinvoq LQ is indicated for the treatment of adults and pediatric patients 2 years of age and older with active psoriatic arthritis who have had an inadequate response or intolerance to one or more TNF blockers and for the treatment of patients 2 years of age and older with active polyarticular juvenile idiopathic arthritis who have had an inadequate response or intolerance to one or more TNF blockers. In 2025, FDA labeling for Rinvoq was updated to clarify that, for ulcerative colitis and Crohn's disease, patients should have received at least one approved systemic therapy prior to treatment with Rinvoq when TNF blockers are not clinically appropriate.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to regulations, other plan medical policies, and accredited national guidelines.

Rheumatoid Arthritis

The efficacy and safety of Rinvoq 15 mg once daily were assessed in five Phase 3 randomized, double-blind, multicenter studies in patients with moderately to severely active rheumatoid arthritis and fulfilling the American College of Rheumatology/European League Against Rheumatism (ACR/EULAR 2010) classification criteria. Patients over 18 years of age were eligible to participate. Although other doses have been studied, the recommended dose of Rinvoq is 15 mg once daily.

Study RA-I was a 24-week monotherapy trial in 947 patients with moderately to severely active rheumatoid arthritis who were naïve to methotrexate. Patients received Rinvoq 15 mg or upadacitinib 30 mg once daily or methotrexate as monotherapy. At week 26, nonresponding patients on upadacitinib could be rescued with the addition of methotrexate, while patients on methotrexate could be rescued with the addition of blinded Rinvoq 15 mg or upadacitinib 30 mg once daily. The primary endpoint was the proportion of patients who achieved an ACR50 (50% or greater improvement) response at week 12. For the primary endpoint at week 12, 28% of patients achieved an ACR50 in the methotrexate group vs. 52% of patients in the Rinvoq group.

Study RA-II was a 14-week monotherapy trial in 648 patients with moderately to severely active rheumatoid arthritis who had an inadequate response to methotrexate. Patients received Rinvoq 15 mg or upadacitinib 30 mg once daily monotherapy or continued their stable dose of methotrexate monotherapy. At week 14, patients who were randomized to methotrexate were advanced to Rinvoq 15 mg or upadacitinib 30 mg once daily monotherapy in a blinded manner based on pre-determined

assignment at baseline. The primary endpoint was the proportion of patients who achieved an ACR20 (20% or greater improvement) response at week 14. For the primary endpoint at week 14, 41% of patients achieved an ACR20 in the methotrexate group vs. 68% of patients in the Rinvoq group.

Study RA-III was a 12-week trial in 661 patients with moderately to severely active rheumatoid arthritis who had an inadequate response to traditional disease modifying anti-rheumatic drugs (DMARDs). Patients received Rinvoq 15 mg or upadacitinib 30 mg once daily or placebo added to background traditional DMARD therapy. At week 12, patients who were randomized to placebo were advanced to Rinvoq 15 mg or upadacitinib 30 mg once daily in a blinded manner based on predetermined assignment at baseline. The primary endpoint was the proportion of patients who achieved an ACR20 response at week 12. For the primary endpoint at week 12, 36% of patients achieved an ACR20 in the placebo group vs. 64% of patients in the Rinvoq group.

Study RA-IV was a 48-week trial in 1,629 patients with moderately to severely active rheumatoid arthritis who had an inadequate response to methotrexate. Patients received Rinvoq 15 mg once daily, active comparator, or placebo added to background methotrexate. From week 14, non-responding patients on Rinvoq 15 mg could be rescued to active comparator in a blinded manner, and nonresponding patients on active comparator or placebo could be rescued to Rinvoq 15 mg in a blinded manner. At week 26, all patients randomized to placebo were switched to Rinvoq 15 mg once daily in a blinded manner. The primary endpoint was the proportion of patients who achieved an ACR20 response at week 12 versus placebo. For the primary endpoint at week 12, 36% of patients achieved an ACR20 in the placebo group vs. 71% of patients in the Rinvoq group.

Study RA-V was a 12-week trial in 499 patients with moderately to severely active rheumatoid arthritis who had an inadequate response or intolerance to biologic DMARDs. Patients received Rinvoq 15 mg or upadacitinib 30 mg once daily or placebo added to background traditional DMARD therapy. At week 12, patients who were randomized to placebo were advanced to Rinvoq 15 mg or upadacitinib 30 mg once daily in a blinded manner based on pre-determined assignment at baseline. The primary endpoint was the proportion of patients who achieved an ACR20 response at week 12. For the primary endpoint at week 12, 28% of patients achieved an ACR20 in the placebo group vs. 65% of patients in the Rinvoq group.

Treatment with Rinvoq 15 mg, alone or in combination with traditional DMARDs, resulted in a greater improvement in physical function at week 12/14 compared to all comparators as measured by HAQ-DI (Health Assessment Questionnaire Disability Index).

In all studies except for Study RA-V, patients receiving Rinvoq 15 mg had greater improvement from baseline in physical component summary (PCS) score, mental component summary (MCS) scores, and in all 8 domains of the Short Form Health Survey (SF-36) compared to placebo in combination with traditional DMARDs or methotrexate monotherapy at week 12/14.

Fatigue was assessed by the Functional Assessment of Chronic Illness Therapy-Fatigue score (FACITF) in Studies RA-I, RA-III, and RA-IV. Improvement in fatigue at week 12 was observed in patients treated with Rinvoq 15 mg compared to patients on placebo in combination with traditional DMARDs or methotrexate monotherapy.

Psoriatic Arthritis
The efficacy and safety of Rinvoq 15 mg once daily were assessed in two Phase 3 randomized, double-blind, multicenter, placebo-controlled studies in patients 18 years of age or older with moderately to severely active psoriatic arthritis. All patients had active psoriatic arthritis for at least 6 months based upon the Classification Criteria for Psoriatic Arthritis (CASPAR), at least 3 tender joints and at least 3 swollen joints, and active plaque psoriasis or history of plaque psoriasis. Although another dose has been studied, the recommended dose of Rinvoq is 15 mg once daily for psoriatic arthritis.

Study PsA-I was a 24-week trial in 1,705 patients with moderately to severely active psoriatic arthritis who had an inadequate response or intolerance to at least one non-biologic (i.e., traditional) DMARD. Patients received Rinvoq 15 mg or upadacitinib 30 mg once daily, adalimumab, or placebo, alone or in combination with background traditional DMARDs. At week 24, all patients randomized to placebo were switched to Rinvoq 15 mg or upadacitinib 30 mg once daily in a blinded manner. The primary endpoint was the proportion of patients who achieved an ACR20 response at week 12. The ACR20 response at week 12 was 71% in the Rinvoq 15 mg group vs. 36% in the placebo group.

Study PsA-II was a 24-week trial in 642 patients with moderately to severely active psoriatic arthritis who had an inadequate response or intolerance to at least one biologic DMARD. Patients received Rinvoq 15 mg or upadacitinib 30 mg once daily or placebo, alone or in combination with background traditional DMARDs. At week 24, all patients randomized to placebo were switched to Rinvoq 15 mg or upadacitinib 30 mg once daily in a blinded manner. The primary endpoint was the proportion of patients who achieved an ACR20 response at week 12. The ACR20 response at week 12 was 57% in the Rinvoq 15 mg group vs. 24% in the placebo group.

Atopic Dermatitis
The efficacy of Rinvoq 15 mg and 30 mg once daily, was assessed in three Phase 3 randomized, double-blind, multicenter trials (AD-1, AD-2, AD-3, respectively) in a total of 2,584 patients (12 years of age and older). Rinvoq was evaluated in 344 pediatric patients and 2,240 adult patients with moderate to severe atopic dermatitis (AD) not adequately controlled by topical medication(s).

Disease severity at baseline was defined by a validated Investigator's Global Assessment (vIGA-AD) score ≥ 3 in the overall assessment of atopic dermatitis on a severity scale of 0 to 4, an Eczema Area and Severity Index (EASI) score ≥ 16, a minimum body surface area (BSA) involvement of ≥ 10%, and weekly average Worst Pruritus Numerical Rating Scale (NRS) score ≥ 4. At baseline, 49% of patients had a vIGA-AD score of 3 (moderate atopic dermatitis), and 51% of patients had a vIGA-AD score of 4 (severe atopic dermatitis). The baseline mean EASI score was 29 and the baseline weekly average Worst Pruritus NRS score was 7. Approximately 52% of the patients had prior exposure to systemic atopic dermatitis treatment.

In all three trials, patients received Rinvoq once daily oral doses of 15 mg, 30 mg, or matching placebo for 16 weeks. In Trial AD-3, patients also received Rinvoq or placebo with concomitant topical corticosteroids (TCS) for 16 weeks. All three trials assessed the co-primary endpoints of the proportion of patients with a vIGA-AD score of 0 (clear) or 1 (almost clear) with at least a 2-point improvement and the proportion of patients with EASI-75 (improvement of at least 75% in EASI score from baseline) at week 16. Secondary endpoints included EASI-90 and EASI-100 at week 16, and the proportion of patients with reduction in itch (≥ 4-point improvement from baseline in the Worst Pruritus NRS) at weeks 1, 4, and 16. In Trials AD-1 and AD-2, the proportion of patients with reduction in pain (≥ 4- point improvement in the Atopic Dermatitis Symptom Scale [ADerm-SS] Skin Pain NRS) from baseline to week 16 was a secondary endpoint. All trials demonstrated statistically significant improvement in atopic dermatitis vs. placebo at week 16.

Ulcerative Colitis
In two identical induction trials (UC-1 and UC-2), patients were randomized 2:1 to receive either Rinvoq 45 mg once daily or placebo for 8 weeks. A total of 988 patients were analyzed across the two trials. These trials included adult patients with moderately to severely active ulcerative colitis who had an inadequate response, loss of response, or intolerance to oral aminosalicylates, corticosteroids, immunosuppressants, and/or biologic therapy. A total of 51% of patients had previously failed treatment with or were intolerant to at least one biologic therapy.

Disease severity was assessed on the modified Mayo score (mMS), a 3-component Mayo score (0-9) which consists of the following subscores (0 to 3 for each subscore): stool frequency (SFS), rectal bleeding (RBS), and findings on centrally read endoscopy score (ES). An ES of 2 was defined by marked erythema, lack of vascular pattern, any friability, and/or erosions, and a score of 3 was defined by spontaneous bleeding and ulceration. Enrolled patients had a mMS between 5 to 9 with an ES of 2 or 3; at baseline the median mMS was 7, with 61% of patients having a baseline mMS of 5 to 7 and 39% having a mMS of 8 to 9.

At baseline, 39% and 37% of patients received corticosteroids, 1% and 1% of patients received methotrexate, and 68% and 69% of patients received aminosalicylates in UC-1 and UC-2, respectively. Patient disease severity was moderate (mMS ≤ 7) in 61% and 60% of patients and severe (mMS > 7) in 39% and 40% of patients in UC-1 and UC-2, respectively.

The primary endpoint was clinical remission defined using the mMS at week 8. Secondary endpoints included clinical response, endoscopic improvement, and histologic endoscopic mucosal improvement. In UC-1, clinical remission was achieved in 26% of Rinvoq patients vs. 5% of placebo patients at week 8. In UC-2, clinical remission was achieved in 33% of Rinvoq patients vs. 4% of placebo patients at week 8.

In UC-3, a total of 451 patients who received Rinvoq 45 mg once daily in either UC-1, UC-2 or UC-4 and achieved clinical response were re-randomized to receive Rinvoq 15 mg, 30 mg or placebo once daily for up to 52 weeks. The primary endpoint was clinical remission defined using mMS at

week 52. Secondary endpoints included corticosteroid-free clinical remission, endoscopic improvement, and histologic endoscopic mucosal improvement. At week 52, 52% of the Rinvoq 30 mg patients, 42% of the Rinvoq 15 mg patients, and 12% of the placebo patients achieved clinical remission.

Ankylosing Spondylitis
The efficacy and safety of Rinvoq 15 mg once daily were assessed in two randomized, double-blind, multicenter, placebo-controlled trials in patients 18 years of age or older with active ankylosing spondylitis based upon the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) ≥ 4 and Patient's Assessment of Total Back Pain score ≥ 4. Trial AS-1 was a 14-week trial in 187 ankylosing spondylitis patients with an inadequate response to at least two nonsteroidal anti-inflammatory drugs (NSAIDs) or intolerance to or contraindication for NSAIDs and had no previous exposure to biologic DMARDs. Patients received Rinvoq 15 mg once daily or placebo. At week 14, all patients randomized to placebo were switched to Rinvoq 15 mg once daily. The primary endpoint was the proportion of patients achieving an Assessment of SpondyloArthritis International Society 40 (ASAS40) response at week 14. Trial AS-II was a 14-week trial in 420 ankylosing spondylitis patients with an inadequate response to 1 or 2 biologic DMARDs. Patients received Rinvoq 15 mg once daily or placebo. At week 14, all patients randomized to placebo were switched to Rinvoq 15 mg once daily. The primary endpoint was the proportion of patients achieving an ASAS40 response at week 14. In both trials, a significantly greater proportion of patients treated with Rinvoq 15 mg achieved an ASAS40 response compared to placebo at week 14 (50.5% in the Rinvoq group vs. 25.5% in the placebo group in Trial AS-1 and 44.5% in the Rinvoq group vs. 18.2% in the placebo group in Trial AS-2).

Non-Radiographic Axial Spondyloarthritis.
The efficacy and safety of Rinvoq 15 mg once daily were assessed in a randomized, double-blind, multicenter, placebo-controlled trial in patients 18 years of age or older with active non-radiographic axial spondyloarthritis. Trial nr-axSpA was a 52-week placebo-controlled trial in 314 patients with active non-radiographic axial spondyloarthritis with an inadequate response to at least two NSAIDs or intolerance to or contraindication for NSAIDs. Patients must have had objective signs of inflammation indicated by elevated C-reactive protein (defined as > upper limit of normal), and/or sacroiliitis on MRI, and no definitive radiographic evidence of structural damage on sacroiliac joints. Patients had active disease as defined by the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) ≥ 4, and a Patient's Assessment of Total Back Pain score ≥ 4 based on a 0 – 10 numerical rating scale (NRS) at the Screening and Baseline Visits. Patients received Rinvoq 15 mg once daily or placebo. The primary endpoint was the proportion of patients achieving an Assessment of SpondyloArthritis International Society 40 (ASAS40) response at week 14. A significantly greater proportion of patients treated with Rinvoq 15 mg achieved an ASAS40 response compared to placebo at week 14 (44.9% vs. 22.3%).

Crohn's Disease
In two induction trials, CD-1 and CD-2, patients were randomized 2:1 to receive Rinvoq 45 mg or placebo once daily for 12 weeks. Efficacy was assessed in a population of 857 patients (419 patients in CD-1 and 438 patients in CD-2) with moderately to severely active Crohn's disease, with baseline Crohn's Disease Activity Index (CDAI) score of at least 220 and centrally-reviewed Simple

Endoscopic Score for Crohn's Disease (SES-CD) of ≥ 6, or ≥ 4 for isolated ileal disease, excluding the narrowing component. In CD-1, all patients had inadequate response or were intolerant to treatment with one or more biological therapies (prior biologic failure). In CD-2, 45% (197/438) of patients had an inadequate response or were intolerant to treatment with one or more biological therapies (prior biologic failure). Enrolled patients in both studies were permitted to use stable doses of CD-related antibiotics, aminosalicylates, or methotrexate. Concomitant corticosteroids (up to 30 mg/day prednisone or equivalent) were permitted at enrollment; tapering was initiated at week 4.

The co-primary endpoints were the proportion of patients achieving clinical remission (by CDAI) at week 12, and the proportion of patients achieving endoscopic response (by SES-CD) at week 12. In CD-1, 36% of patients in the Rinvoq 45 mg group achieved clinical remission vs. 18% in the placebo group; 34% of patients in the Rinvoq 45 mg group achieved endoscopic response vs. 3% of patients in the placebo group. In CD-2, 46% of patients in the Rinvoq 45 mg group achieved clinical remission vs. 23% in the placebo group; 46% of patients in the Rinvoq 45 mg group achieved endoscopic response vs. 13% of patients in the placebo group.

The maintenance efficacy analysis for CD-3 evaluated 343 patients who responded to 12 weeks of Rinvoq 45 mg once daily induction treatment. Patients were re-randomized to receive a maintenance regimen of either Rinvoq 15 mg or 30 mg once daily or placebo for 52 weeks, representing a total of at least 64 weeks of therapy. The co-primary endpoints of clinical remission (by CDAI) and endoscopic response (by SES-CD) were assessed at week 52. In this study, 55% of patients in the Rinvoq 30 mg group, 42% of patients in the 15 mg group, and 14% of patients in the placebo group achieved clinical remission; 41% of patients in the Rinvoq 30 mg group, 28% of patients in the 15 mg group, and 7% of patients in the placebo group achieved endoscopic response.

Polyarticular Juvenile Idiopathic Arthritis
The efficacy of Rinvoq/Rinvoq LQ in pediatric patients with JIA with active polyarthritis is based on exposure-matched extrapolation of the established efficacy of Rinvoq in rheumatoid arthritis patients. Safety and efficacy of Rinvoq/Rinvoq LQ were also assessed in a multicenter, open-label, single-arm study in 83 children (2 to < 18 years of age) with JIA with active polyarthritis. The pJIA patient subtypes at study entry included rheumatoid factor negative polyarticular (68.7%), rheumatoid factor positive polyarticular (15.7%), extended oligoarticular (13.3%), and systemic JIA without systemic manifestations (2.4%). All patients received Rinvoq LQ or Rinvoq tablet dosages based on weight for up to 156 weeks. Patients treated with a stable dose of MTX were permitted to enter the study; changes in MTX dose were permitted during the study. Efficacy was assessed as supportive endpoints through Week 48. The efficacy was generally consistent with responses in patients with rheumatoid arthritis.

Giant Cell Arteritis
The efficacy and safety of Rinvoq 15 mg once daily were assessed in Trial GCA, a Phase 3 randomized, double-blind, multicenter, placebo-controlled study in patients 50 years of age and older with new-onset or relapsing giant cell arteritis. Trial GCA was a 52-week trial in which 428 patients were randomized in a 2:1:1 ratio and dosed once daily with Rinvoq 15 mg, upadacitinib 7.5 mg, or placebo. All patients received background corticosteroid therapy. The Rinvoq and upadacitinib-treated groups followed a pre-specified corticosteroid taper regimen with the aim to

reach 0 mg by 26 weeks, while the placebo-treated group followed a prespecified corticosteroid taper regimen with the aim to reach 0 mg by 52 weeks. The primary endpoint was the proportion of patients achieving sustained remission at Week 52 as defined by the absence of giant cell arteritis signs and symptoms from Week 12 through Week 52 and adherence to the protocol-defined corticosteroid taper regimen. A key secondary endpoint was the proportion of patients achieving sustained complete remission at Week 52 as defined by the absence of giant cell arteritis signs and symptoms from Week 12 through Week 52, normalization of erythrocyte sedimentation rate and hsCRP from Week 12 through Week 52, and adherence to the protocol-defined corticosteroid taper regimen. Sustained remission at Week 52 was achieved in 46.4% of patients in the Rinvoq group versus 29.0% in the placebo group. Sustained complete remission at Week 52 was achieved in 37.1% of patients in the Rinvoq group compared to 16.1% of patients in the placebo group.

References

1. Rinvoq [package insert]. Abbvie. North Chicago, Illinois. Updated October 2025.

Policy History

Original Effective Date: 12/11/2019
Current Effective Date: 07/01/2026

12/05/2019	Medical Policy Committee review
12/11/2019	Medical Policy Implementation Committee approval. New policy.
12/03/2020	Medical Policy Committee review
12/09/2020	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
12/02/2021	Medical Policy Committee review
12/08/2021	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
01/06/2022	Medical Policy Committee review
01/12/2022	Medical Policy Implementation Committee approval. Added a requirement for the trial and failure of Humira or Enbrel in rheumatoid arthritis. Added a new FDA approved indication, psoriatic arthritis, along with subsequent patient selection criteria. Updated background information to reflect the FDA label changes. Switched traditional DMARD usage to a not medically necessary denial due to label changes.
03/03/2022	Medical Policy Committee review
03/09/2022	Medical Policy Implementation Committee approval. Added criteria and updated policy for a new FDA approved indication: atopic dermatitis. Clarified that other TNF failures can count in lieu of a trial and failure of Humira or Enbrel, where applicable.
05/05/2022	Medical Policy Committee review
05/11/2022	Medical Policy Implementation Committee approval. Updated policy with a new FDA approved indication: moderately to severely active ulcerative colitis. Changed trial of systemic therapy for atopic dermatitis from 4 months to 3 months.
06/02/2022	Medical Policy Committee review

06/08/2022 Medical Policy Implementation Committee approval. Updated policy with a new FDA approved indication: active ankylosing spondylitis.
12/01/2022 Medical Policy Committee review
12/14/2022 Medical Policy Implementation Committee approval. Added a new FDA approved indication for active non-radiographic axial spondyloarthritis. Updated relevant sections of the policy with this new indication.
07/06/2023 Medical Policy Committee review
07/12/2023 Medical Policy Implementation Committee approval. Added a new FDA approved indication for moderately to severely active Crohn's disease. Updated relevant sections of the policy with this new indication.
03/07/2024 Medical Policy Committee review
03/13/2024 Medical Policy Implementation Committee approval. Removed requirement for trial and failure of topical therapies, updated list of systemic therapy to include tralokinumab-ldrm (Adbry).
08/01/2024 Medical Policy Committee review
08/14/2024 Medical Policy Implementation Committee approval. Changed title from "upadacitinib (Rinvoq)" to "upadacitinib (Rinvoq™®, Rinvoq LQ®)" to reflect new dosage form. Added Rinvoq LQ and new indication, polyarticular juvenile idiopathic arthritis to policy. Updated psoriatic arthritis indication to reflect expanded age approval to pediatric patients 2 years of age and older.
09/04/2025 Medical Policy Committee review
09/10/2025 Medical Policy Implementation Committee approval. Added new indication, giant cell arteritis, to policy with criteria. Added continuation criteria to each indication.
04/02/2026 Medical Policy Committee review
04/10/2026 Medical Policy Implementation Committee review.
04/16/2026 Medical Quality Management Committee approval. Added a requirement in the atopic dermatitis criteria for trial and failure of a topical corticosteroid or topical calcineurin inhibitor. Revised ulcerative colitis and Crohn's disease criteria to align with the FDA label, specifying trial and failure of a TNF inhibitor (not limited to adalimumab) and requiring a conventional agent only when TNF inhibitor therapy is clinically inadvisable.

Next Scheduled Review Date: 04/2027

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or

B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.

NOTICE: If an authorization for an ongoing course of treatment has been provided to a member and the member changes from one health plan to another health plan (e.g., a member moves from carrier A to Louisiana Blue), Louisiana Blue may honor the previous health plan's authorization for the same service under the same type of in-network benefit for a 90-day transition period.

Documentation of the authorization for the ongoing course of treatment from the previous health plan must be provided to us by the member or their provider and the services provided for the course of treatment must otherwise be a covered service under the Louisiana Blue health plan. This provision does not apply to medications covered under the plan's pharmacy benefit.