Clinical Policy: Rituximab (Rituxan), Rituximab-abbs (Truxima), Rituximab-Hyaluronidase (Rituxan Hycela)

Reference Number: CP.PHAR.260
Effective Date: 07.01.16
Last Review Date: 02.19
Line of Business: Medicaid, HIM*

Coding Implications
Revision Log

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

Description

Rituximab (Rituxan®) is a human monoclonal immunoglobulin G-1 (IgG1) kappa antibody directed against the CD20 antigen.

Rituximab-abbs (Truxima®) is a CD20-directed cytolytic antibody and biosimilar to Rituxan for the listed Truxima indications.

Rituximab and hyaluronidase (Rituxan Hycela™) is a combination of rituximab and human hyaluronidase that is used to increase the dispersion and absorption of the co-administered drugs when given subcutaneously.

**For Health Insurance Marketplace (HIM),* *if request is through the pharmacy benefit, Truxima and Rituxan Hycela are non-formulary and cannot be approved using these criteria; refer to the formulary exception policy, HIM.PA.103.*

FDA Approved Indication(s)

Indications		Rituxan	Truxima	Rituxan Hycela*
Oncology indications (adults)				
Low-grade and follicular B-cell NHL	Relapsed or refractory, low-grade *[Rituxan, Truxima]* or follicular *[Rituxan, Truxima, Rituxan Hycela]*, CD20-positive, B-cell NHL as a single agent.	X	X	X
	Previously untreated follicular, CD20-positive B-cell NHL in combination with first-line chemotherapy and, in patients achieving a complete or partial response to a rituximab product in combination with chemotherapy, as single-agent maintenance therapy.	X	X	X
	Non-progressing (including stable disease), low-grade *[Rituxan, Truxima]* or follicular *[Rituxan Hycela]*, CD20-positive B-cell NHL as a single agent after first-line CVP chemotherapy.	X	X	X

Indications		Rituxan	Truxima	Rituxan Hycela*
DLBCL *(a B-cell NHL)*	Previously untreated CD20-positive DLBCL in combination with CHOP or other anthracycline-based chemotherapy regimens.	X		X
CLL *(a B-cell NHL)*	Previously untreated and treated CD20-positive CLL in combination with FC chemotherapy.	X		X
Non-oncology indications (adults)				
RA	Moderately to severely active RA in combination with MTX in patients who have inadequate response to one or more TNF antagonist therapies.	X		
GPA, MPA	GPA and MPA in combination with glucocorticoids.	X		
PV	Moderate to severe PV.	X		

Abbreviations: CLL (chronic lymphocytic leukemia), DLBCL (diffuse large B-cell lymphoma), GPA (granulomatosis with polyangiitis; Wegener`s granulomatosis), MPA (microscopic polyangiitis), NHL (Non-Hodgkin's lymphoma), PV (pemphigus vulgaris), RA (rheumatoid arthritis).
**Rituxan Hycela limitations of use: 1) Initiate treatment with Rituxan Hycela only after patients have received at least one full dose of a rituximab product by intravenous infusion; 2) Rituxan Hycela is not indicated for the treatment of non-malignant conditions.*

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 Rituxan, Truxima and Rituxan Hycela are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria
A. Non-Hodgkin's Lymphoma *(includes CLL)* (must meet all)**:**
1. Diagnosis of any of the following non-Hodgkin's lymphoma (NHL) subtypes (a-m):
   a. Chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL)
   b. Follicular lymphoma (FL);
   c. Low- or high-grade B-cell lymphoma;
   d. MALT lymphoma (gastric or nongastric);
   e. Marginal zone lymphoma (nodal or splenic);
   f. Mantle cell lymphoma;
   g. Diffuse large B-cell lymphoma (DLBCL);
   h. Burkitt lymphoma;
   i. AIDS-related B-cell lymphomas;
   j. Post-transplant lymphoproliferative disorder;
   k. Castleman's disease;
   l. Hairy cell leukemia (Rituxan/Truxima only);
   m. Primary cutaneous B-cell lymphoma;
2. Prescribed by or in consultation with an oncologist or hematologist;

3. Age ≥ 18 years;
4. If request is for Rituxan Hycela, member has received at least one full dose of Rituxan or Truxima;
5. Request meets either of the following (a or b):
   a. Dose does not exceed (i or ii):
      i. Rituxan/Truxima: 500 mg/m^2 per IV infusion;
      ii. Rituxan Hycela: 1,600 mg/26,800 units SC;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration:
Medicaid – 6 months
HIM – 6 months for Rituxan *(Refer to HIM.PA.103 for Truxima and Rituxan Hycela)*

B. Rheumatoid Arthritis (must meet all)**:**
1. Diagnosis of RA;
2. Request is for Rituxan/Truxima;
3. Prescribed by or in consultation with a rheumatologist;
4. Age ≥ 18 years;
5. Member meets one of the following (a or b):
   a. Failure of a ≥ 3 consecutive month trial of MTX at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
   b. If intolerance or contraindication to MTX (*see Appendix D*), failure of a ≥ 3 consecutive month trial of at least ONE conventional disease-modifying antirheumatic drug [DMARD] (e.g., sulfasalazine, leflunomide, hydroxychloroquine) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
6. Failure of etanercept *(Enbrel® is preferred)* AND adalimumab *(Humira® is preferred)*, each used for ≥ 3 consecutive months, unless contraindicated or clinically significant adverse effects are experienced;
   **Prior authorization is required for etanercept and adalimumab*
7. Rituxan/Truxima will be administered in combination with MTX unless contraindicated or clinically significant adverse effects are experienced;
8. Dose does not exceed two-1,000 mg IV infusions separated by 2 weeks followed by two-1,000 mg IV infusions every 16 weeks.

Approval duration:
Medicaid – 6 months
HIM – 6 months for Rituxan *(Refer to HIM.PA.103 for Truxima)*

C. Granulomatosis with Polyangiitis (Wegener's Granulomatosis) and Microscopic Polyangiitis (must meet all)**:**
1. Diagnosis of GPA or MPA;
2. Request is for Rituxan/Truxima;
3. Prescribed by or in consultation with a rheumatologist;
4. Age ≥ 18 years;
5. Rituxan/Truxima will be administered in combination with glucocorticoid therapy;

6. Dose does not exceed (a or b):
   a. Induction: 375 mg/m^2 weekly for 4 weeks;
   b. Follow up treatment: two-500 mg infusions separated by 2 weeks, then 500 mg every 6 months.

Approval duration:
Medicaid – 6 months
HIM – 6 months for Rituxan *(Refer to HIM.PA.103 for Truxima)*

D. Pemphigus Vulgaris and Pemphigus Foliaceus (must meet all)**:**
1. Diagnosis of PV or pemphigus foliaceus (PF);
2. Request is for Rituxan/Truxima;
3. Prescribed by or in consultation with a dermatologist;
4. Age ≥ 18 years;
5. Dose does not exceed (a or b):
   a. Initial: two-1,000 mg infusions separated by 2 weeks;
   b. Maintenance: 500 mg every 6 months (starting 12 months after initial dose).

Approval duration:
Medicaid – 6 months
HIM – 6 months for Rituxan *(Refer to HIM.PA.103 for Truxima)*

E. NCCN Compendium Indications (off-label) (must meet all)**:**
1. Diagnosis of any of the following:
   a. Primary CNS lymphoma;
   b. Leptomeningeal metastases from lymphoma;
   c. Nodular lymphocyte-predominant Hodgkin lymphoma;
   d. Acute lymphoblastic leukemia;
   e. Waldenström's macroglobulinemia/lymphoplasmacytic lymphoma;
   f. Immune checkpoint inhibitor-related toxicities;
2. Request is for Rituxan/Truxima;
3. Prescribed by or in consultation with an oncologist or hematologist;
4. Age ≥ 18 years;
5. Dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration:
Medicaid – 6 months
HIM – 6 months for Rituxan *(Refer to HIM.PA.103 for Truxima)*

F. Other diagnoses/indications
1. Members with any of the following diagnoses may be covered if the off-label criteria policy is met:
   a. Myasthenia gravis;
   b. Nephrotic syndrome;
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): HIM.PHAR.21 for health insurance marketplace and CP.PMN.53 for Medicaid.

II. Continued Approval

A. All Indications in Section I (must meet all)**:**

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Documentation supports that member is currently receiving Rituxan, Truxima or Rituxan Hycela for a covered oncology indication and has received this medication for at least 30 days;
2. Meets one of the following (a or b):
   a. Member is responding positively to therapy;
   b. If PV or PF, member has experienced relapse;
3. If request is for a dose increase, request meets either of the following (a or b):
   a. New dose does not exceed the following:
      i. NHL:
         a) Rituxan/Truxima: 500 mg/m^2 per IV infusion;
         b) Rituxan Hycela: 1,600 mg/26,800 units SC;
      ii. RA (Rituxan/Truxima): two-1,000 mg IV infusions every 16 weeks;
      iii. GPA/MPA (Rituxan/Truxima):
         a) Induction: 375 mg/m^2 IV weekly for up to 4 weeks total;
         b) Follow-up treatment: two-500 mg IV infusions separated by two weeks, then 500 mg IV every 6 months;
      iv. PV or PF (Rituxan/Truxima) (a or b):
         a) Maintenance: 500 mg IV every 6 months (starting 12 months after initial dose);
         b) Relapse: 1,000 mg IV once then 500 mg IV 16 weeks later, then 500 mg IV every 6 months;
   b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration:
Medicaid – 12 months
HIM – 12 months for Rituxan *(Refer to HIM.PA.103 for Truxima and Rituxan Hycela)*

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. Members with any of the following diagnoses may be covered if the off-label criteria policy is met:
   a. Myasthenia gravis;
   b. Nephrotic syndrome;
3. 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): HIM.PHAR.21 for health insurance marketplace and 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 policies – HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

CHOP: cyclophosphamide, doxorubicin, vincristine, prednisone
CLL: chronic lymphocytic leukemia
CVP: cyclophosphamide, vincristine, prednisone
DLBCL: diffuse large B-cell lymphoma
DMARD: disease-modifying antirheumatic drug
FC: fludarabine and cyclophosphamide
FDA: Food and Drug Administration
FL: follicular lymphoma
GPA: granulomatosis with polyangiitis (Wegener's granulomatosis)
MALT: mucosa-associated lymphoid tissue
MPA: microscopic polyangiitis
MTX: methotrexate
NHL: Non-Hodgkin's lymphoma
PF: pemphigus foliaceus
PV: pemphigus vulgaris
RA: rheumatoid arthritis
SLL: small lymphocytic lymphoma

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 and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
RA		
azathioprine (Azasan®, Imuran®)	1 mg/kg/day PO QD or divided BID	2.5 mg/kg/day
Cuprimine® (d-penicillamine) *Off-label*	Initial dose: 125 or 250 mg PO QD Maintenance dose: 500 – 750 mg/day PO QD	1,500 mg/day
cyclosporine (Sandimmune®, Neoral®)	2.5 – 4 mg/kg/day PO divided BID	4 mg/kg/day
hydroxychloroquine (Plaquenil®) *Off-label*	Initial dose: 400 – 600 mg/day PO QD Maintenance dose: 200 – 400 mg/day PO QD	5 mg/kg/day
leflunomide (Arava®)	100 mg PO QD for 3 days, then 20 mg PO QD	20 mg/day
methotrexate (Rheumatrex®)	7.5 mg/week PO, SC, or IM or 2.5 mg PO Q12 hr for 3 doses/week	30 mg/week
Ridaura® (auranofin)	6 mg PO QD or 3 mg PO BID	9 mg/day
sulfasalazine (Azulfidine®)	2 g/day PO in divided doses	3 gm/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Enbrel (etanercept)	25 mg SC twice weekly or 50 mg SC once weekly	50 mg/week
Humira (adalimumab)	40 mg SC every other week (may increase to once weekly)	40 mg/week
GPA, MPA		
glucocorticoids	Varies	Varies

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.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): none reported
- Boxed warning(s):
  - Fatal infusion reactions (Rituxan, Truxima)
  - Severe mucocutaneous reactions, hepatitis B virus reactivation, progressive multifocal leukoencephalopathy (Rituxan, Truxima, Rituxan Hycela).

Appendix D: General Information

- Definition of MTX or Disease-Modifying Antirheumatic Drug (DMARD) failure
  - 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.
  - 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 RA therapy may include, but are not limited to:
  - Reduction in joint pain/swelling/tenderness
  - Improvement in ESR/CRP levels
  - Improvements in activities of daily living

V. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
Rituxan, Truxima	Low-grade and follicular B-cell NHL	375 mg/m^2 IV infusion according to the following schedules: • Relapsed or refractory, low-grade or follicular, CD20+, B-cell NHL o Once weekly for 4 or 8 doses o Retreatment: once weekly for 4 doses • Previously untreated, follicular, CD20+, B-cell NHL: o Administer on Day 1 of each cycle of chemotherapy for up to 8 doses; o If complete or partial response, initiate Rituxan/Truxima maintenance treatment as a single-agent every 8 weeks for 12 doses to start 8 weeks following completion of a rituximab product in combination with chemotherapy. • Non-progressing, low-grade, CD20+, B-cell NHL, after first-line CVP chemotherapy: o Following completion of 6-8 cycles of CVP chemotherapy, administer once weekly for 4 doses at 6-month intervals to a maximum of 16 doses.	375 mg/m^2 IV infusion
Rituxan	Low-grade and follicular B-cell NHL	• Rituxan in combination with Zevalin for low-grade or follicular B-cell NHL: o 250 mg/m^2 IV within 4 hrs prior to administration of Indium-111-(In-111-) Zevalin and Yttrium-90-(Y-90) Zevalin. o Administer rituximab and In-111-Zevalin 7–9 days prior to rituximab and Y-90-Zevalin. o Refer to the Zevalin package insert for full prescribing information regarding the Zevalin therapeutic regimen.	375 mg/m^2 IV infusion

Drug Name	Indication	Dosing Regimen	Maximum Dose
Rituxan Hycela	Follicular B-cell NHL	1,400 mg rituximab and 23,400 units hyaluronidase SC according to the following schedules: ***First dose must be with IV Rituxan/Truxima if indicated with an asterisk (*).*** • Relapsed or refractory FL: o Once weekly for 3 or 7 weeks (i.e., 4 or 8 weeks in total)* o Retreatment: once weekly for 3 weeks (i.e., 4 weeks in total)* • Previously untreated FL: o Administer on Day 1 of Cycles 2–8 of chemotherapy (every 21 days), for up to 7 cycles (i.e., up to 8 cycles in total)* o If complete/partial response, initiate Rituxan Hycela maintenance treatment as a single-agent every 8 weeks for 12 doses to start 8 weeks following completion of Rituxan Hycela in combination with chemotherapy • Non-progressing FL after first-line CVP chemotherapy: o Following completion of 6–8 cycles of CVP chemotherapy, administer once weekly for 3 weeks (i.e., 4 weeks in total) at 6 month intervals to a maximum of 16 doses*	1,400 mg/23,400 units SC per injection
Rituxan	DLBCL *(a B-cell NHL)*	375 mg/m^2 IV infusion on Day 1 of each cycle of chemotherapy for up to 8 doses total.	375 mg/m^2 IV infusion
Rituxan Hycela	DLBCL *(a B-cell NHL)*	***First dose must be with IV Rituxan*** • 1,400 mg rituximab and 23,400 units hyaluronidase SC on Day 1 of Cycles 2–8 of CHOP chemotherapy for up to 7 cycles (i.e., up to 6–8 cycles in total)	1,400 mg/23,400 units SC per injection
Rituxan	CLL *(a B-cell NHL)*	375 mg/m^2 IV infusion on the day prior to initiation of FC chemotherapy, then 500 mg/m^2 on Day 1 of cycles 2-6 (every 28 days).	500 mg/m^2 per day
Rituxan Hycela	CLL *(a B-cell NHL)*	***First dose must be with IV Rituxan*** • 1,600 mg/26,800 units on Day 1 of Cycles 2–6 (every 28 days) for a total of 5 cycles (i.e., 6 cycles in total)	1,600 mg/26,800 units SC per injection
Rituxan	RA	Two 1000 mg IV infusions separated by 2 weeks (i.e., day 1 and day 15), followed by two-1000	1000 mg per week

Drug Name	Indication	Dosing Regimen	Maximum Dose
		mg IV infusions every 16 weeks. Rituxan is given in combination with MTX.	
Rituxan	GPA/MPA	Induction: • 375 mg/m^2 IV once weekly for 4 weeks in combination with glucocorticoids Follow-up treatment if disease control with induction treatment: • Two 500 mg IV infusions separated by 2 weeks, followed by 500 mg IV every 6 months thereafter based on clinical evaluation. Follow up treatment should be initiated: o Within 24 weeks after the last Rituxan induction infusion or based on clinical evaluation, but no sooner than 16 weeks after the last Rituxan induction infusion. o Within the 4 week period following achievement of disease control if induction was achieved with other immunosuppressants.	Induction: 375 mg/m^2 per week Follow-up treatment: 500 mg/dose (see regimen for dosing frequency)
Rituxan	PV	Initial and maintenance therapy: • Two 1000 mg IV infusions separated by 2 weeks with a tapering course of glucocorticoids, then 500 mg IV at month 12 and every 6 months thereafter or based on clinical evaluation Relapse: • 1000 mg IV once. Subsequent infusions may be administered no sooner than 16 weeks following the previous infusion.	Initial/relapse: 1000 mg/dose Maintenance: 500 mg/6 months

VI. Product Availability

Drug Name	Availability
Rituximab (Rituxan)	Single-dose vials for IV injection: 100 mg/10 mL, 500 mg/50 mL
Rituximab-abbs (Truxima)	Single-dose vials for IV injection: 100 mg/10 mL, 500 mg/50 mL
Rituximab-hyaluronidase (Rituxan Hycela)	Single-dose vials for SC injection: 1,400 mg/23,400 units, 1,600 mg/26,800 units

VII. References

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Coding Implications
Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J9310	Injection, rituximab, 100 mg
C9467	Injection, rituximab and hyaluronidase, 10 mg

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy split from CP.PHAR.86.Arthritis Treatments. All Indications: Criteria related to HBV, malignant disease, concomitant use with other biologics, and concurrent administration of live vaccines removed from contraindications. Added dosing. Changed contraindication/discontinuation reason from “active infection, including localized infection” to “active, serious infection.” RA: changed age requirement to 18; added requirement for trial and failure of PDL Enbrel and Humira, unless contraindicated; if the former are contraindicated, to require trial of methotrexate; if the former is contraindicated, added sulfasalazine as an alternative.	06.16	07.16

Reviews, Revisions, and Approvals	Date	P&T Approval Date
In addition to RA, all other FDA-approved indications are added as well as NCCN compendia uses. Re-auth: combined into All Indications; added dosing and reasons to discontinue. Approval durations are 3 and 6 months for oncology and 6 and 12 months for all other indications.		
Added ICD-10 code table	10.16	
CP.PHAR.148.Rituximab Oncology Hematology policy is incorporated into the present policy (criteria, codes). NHL: The FDA CLL labeled indication is added under NHL. Nodal marginal zone lymphoma is added under NCCN uses. Maximum dose is added. Safety information is removed. Duration is increased to 6 months. RA: modified the RA diagnostic criteria from requiring one or more of the following: ≥ 5 inflamed joints, elevation in the erythrocyte sedimentation rate (ESR) and/or serum C-reactive protein (CRP) concentration; positive rheumatoid factor and/or anticyclic citrullinated peptide (CCP) antibodies (present in most patients), evidence of inflammation on plain radiography of the hands, wrists, or feet, such as osteopenia and/or periarticular swelling to the ACR diagnostic criteria. Safety information is removed. Autoimmune hemolytic anemia (from policy 148): Warm and cold agglutinin disease are combined into one criteria set and edited to reflect rituximab as first-line for cold agglutinin disease and post glucocorticoids for warm agglutinin disease. ICD-10 CM code table updated per NCCN compendia: added C79.32, D36.0, Z85.71, Z85.72, Z85.79	07.17	07.17
2Q 2018 annual review: added HIM line of business; summarized NCCN and FDA approved uses for improved clarity for Non-Hodgkin's Lymphoma; added specialist involvement in care into one criteria set; removed diagnosis requirement for ACR criteria in RA; revised conventional DMARD requirement in RA to require at least one conventional DMARD (e.g., sulfasalazine, leflunomide, hydroxychloroquine); off-label criteria added for additional NCCN-recommended diagnoses; removed off-label criteria for autoimmune hemolytic anemia and immune thrombocytopenia, will instead defer to off-label policy; approval durations updated; references reviewed and updated.	02.27.18	05.18
Criteria added for new indication for Rituxan: pemphigus vulgaris; myasthenia gravis and nephrotic syndrome diagnoses added to policy as covered diagnoses if off-label criteria is met; references reviewed and updated.	07.31.18	11.18

Reviews, Revisions, and Approvals	Date	P&T Approval Date
1Q 2019 annual review: Rituxan biosimilar Truxima is added and applied to all policy criteria applicable to Rituxan; NHL criteria is edited to include all FDA approved or NCCN recommended NHL subtypes; additional NCCN recommended uses other than NHL are added section I.E. (NCCN compendium uses); hematologist added for all oncology indications; GPA/MPA dosing updated to delineate induction versus follow-up treatment and approval duration is edited from 4 weeks total to 6/12 months; PF off-label criteria is added; references reviewed and updated.	01.15.19	02.19

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.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

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.

For Health Insurance Marketplace members, when applicable, this policy applies only when the prescribed agent is on your health plan approved formulary. Request for non-formulary drugs must be reviewed using the formulary exception policy.