MEDICAL NECESSITY GUIDELINE

DEPARTMENT: Pharmacy	DOCUMENT NAME: Biologic Drug Dose Escalation
PAGE: 1 of 6	REFERENCE NUMBER: GA.PMN.21
EFFECTIVE DATE: 9/2017	REPLACES DOCUMENT:
RETIRED:	REVIEWED:
PRODUCT TYPE: Medicaid/Ambetter	REVISED:

IMPORTANT REMINDER
This Clinical Policy has been developed by appropriately experienced and licensed health care professionals based on a thorough review and consideration of generally accepted standards of medical practice, peer- reviewed medical literature, government agency/program approval status, and other indicia of medical necessity.

The purpose of this Clinical Policy is to provide a guide to medical necessity. Benefit determinations should be based in all cases on the applicable contract provisions governing plan benefits ("Benefit Plan Contract») and applicable state and federal requirements, as well as applicable plan-level administrative policies and procedures. To the extent there are any conflicts between this Clinical Policy and the Benefit Plan Contract provisions, the Benefit Plan Contract provisions will control.

Clinical policies are intended to be reflective of current scientific research and clinical thinking. This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding results. 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.

Description: The intent of the criteria is to ensure that members follow selection elements established by Centene® medical policy for the use of dose frequency escalation as it relates to utilizing Biologic medications for autoimmune disorders.

Class of Medication: Biologic Monoclonal Antibodies to Tumor Necrosis Factor (TNF) and Integrin Antagonist

Policy Indication: Indicated for dose escalation of frequency after appropriate trail and failure of FDA dosing recommendations.

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DEPARTMENT: Pharmacy	DOCUMENT NAME: Biologic Drug Dose Escalation
PAGE: 2 of 6	REFERENCE NUMBER: GA.PMN.21
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Criteria for Approval:

Initiation of therapy for up to 6 months (must meet all):

A. Prescribed by a specialist for requested disease state;
B. Member meets existing individual drug clinical policy except for the requested dosing frequency;
C. Drug is Food and Drug Administration (FDA) approved for the requested use;
D. Member has tried and failed FDA approved maintenance dosing and one of the following;
    - Member does not have drug antibodies but has sub- therapeutic drug levels per table (See Table 1)
    - Member has developed antibodies to drug but not greater than recommendations in table (See Table 1)
    - If drug levels/antibody level testing is unavailable or not indicated, member must have signs and symptoms of severe disease (disease requiring hospitalization) or ongoing disease activity despite maintenance therapy while on FDA approved maintenance dosing
E. Symptoms are not due to active infection or other gastrointestinal (GI disorder);
F. Member is or will be using an applicable immunomodulator concurrently (i.e., methotrexate, hydrochloroquine, azathiopurine) unless contraindicated;
G. Dose escalation does not occur at frequency interval detriment of no more than every 2 weeks from previous requested frequency and no more frequent then what is listed in Table 1.

MEDICAL NECESSITY GUIDELINE

DEPARTMENT: Pharmacy	DOCUMENT NAME: Biologic Drug Dose Escalation
PAGE: 3 of 6	REFERENCE NUMBER: GA.PMN.21
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Continuation of therapy for up to 12 months (must meet all):

A. Prescribed by a specialist for requested disease state;
B. Member previously has meet criteria for initiation in individual drug policy and Biologic Drug Dose Escalation policy
C. Member has had a positive response to current therapy
D. Member is using an applicable immunomodulator concurrently (i.e., methrotrexate, hydroxychloroquine, azathiopurine) unless contraindicated;
E. Dose frequency is no more frequent that recommendations from table (See Table 1)

Background

Anti-TNF alpha blockers and Anti-Integrin Agents are common classes of biologics for inflammatory and autoimmune disorders. Despite these effective biologic medications, patients sometimes continue to demonstrate ongoing symptoms indicative of active inflammation or loss of response. After evaluation of infection and objective evidence of active inflammation is evident then determining whether symptoms are due to primary non-response versus secondary loss of response is indicated. Primary nonresponse refers to patients who do not respond adequately to the initial loading doses of a biologic agent. These patients usually have normal drug levels without antibodies present. When this is the case switching to a drug of different class or mechanism is recommended. Secondary loss of response refers to patients who had previously responded to a biologic agent but now has demonstrated evidence of ongoing disease activity despite continued therapy. Those patients found to have low drug levels are recommended to either increase the dose or decrease dosing interval and/or add an immunomodulator.

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DEPARTMENT: Pharmacy	DOCUMENT NAME: Biologic Drug Dose Escalation
PAGE: 4 of 6	REFERENCE NUMBER: GA.PMN.21
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References:

1. Roda G, Jharap B, Neeraj N, et al. Loss of Response to Ant-TNFs: Definitio, Epidemiology, and Managament. Clinical and Translational Gastroenterology (2016) 7, e135
2. Feuerstem J, Nguyen G, Kupfer S, et al. Therapeutic Drug Monitoring in Inflammatory Bowel Disease. Gastroeneterology 2017;1-8
3. De Vries H, Van Oijen M, Driessen R, et. al. Appropriate infliximab infusion dosage and monitoring: results of a panel meeting of rheumatologi.sts, dermatologists, and gastroenterologi.sts. Br J Clin Pharmacology.71:1:7-19
4. http://www.ouh.nhs.uk/ immunology/diagnostic-tests/tests- catalogue/infliximab-levels.aspx
5. https://www.healthcare.uiowa.edu/path_handbook/handbook/tes t342 4.html
6. Goel, Niti, and Sue Stephens. •certolizumab PegoL• mAbs 2.2 (2010): 137-147.
7. Curtis J, Chen L, Luijtens K, et. al. Dose Escalation of certolizumab from 200mg to 400m.g every other week provided no additional efficacy in rheumatoid arthritis:an analysis of individual patient level data. Arthritis Rheum. 2011 Aug; 63(8): 2203-2208.
8. Dalal S, Cohen R. What to Do When Biologic Agents Are Not working in Inflammatory Bowel Disease patients. Gastroenterol Hepatol (N Y). 2015 Oct;11(10):657-65.

MEDICAL NECESSITY GUIDELINE

DEPARTMENT: Pharmacy	DOCUMENT NAME: Biologic Drug Dose Escalation
PAGE: 5 of 6	REFERENCE NUMBER: GA.PMN.21
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Table 1			
	Normal Drug levels	Abnormal Antibody levels	Minimum Dosing Frequency
Jnfliximab (Remicade, Intlectra)	3-6mcg/ml (≥5mcg/ml suggested)	>10ng/ml	10mg/kg Q 4 weeks
Adalimumab (Humira, Amjevita)	≥5mcg/ml (≥7.5mcg/ml suggested)	>10ng/ml	40mg Qweek
Certolizumab Pegol (Cimzia)	unavailable (≥20mcg/ml studied)	unavailable	400mg Q 2 weeks
Golimumab (Simponi, Simponi Aria)	unavailable	unavailable	100mg Q 4 weeks
Natilizmnab (Tvsabri)	unavailable	unavailable	300mg Q 4 weeks
Vedolizumab (01nyvio)	2-60mcg/ml	35-500ng/ml	300mg Q 4 weeks

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Reviews, Revisions and Approvals	Date
New policy created and reviewed by GI Specialist	10/2017

POLICY AND PROCEDURE APPROVAL

Pharmacy & Therapeutics Committee:	Approval on file
Director, Pharmacy Operations:	Approval on file
Medical Director:	Approval on file