

Uplizna® (Inebilizumab-Cdon) (for Ohio Only)

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[Instructions for Use](#)

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Related Policies
None

Application

This Medical Benefit Drug Policy only applies to the state of Ohio. Any requests for services that are stated as unproven or services for which there is a coverage or quantity limit will be evaluated for medical necessity using Ohio Administrative Code 5160-1-01.

Coverage Rationale

Uplizna (inebilizumab-cdon) is proven and medically necessary for the treatment of neuromyelitis optica spectrum disorder (NMOSD) when all of the following criteria are met:

- **Initial Therapy, all of the following:**
 - Diagnosis of neuromyelitis optica spectrum disorder (NMOSD) by a neurologist, confirming **all** of the following:
 - Past medical history of **one** of the following:
 - Optic neuritis
 - Acute myelitis
 - Area postrema syndrome: episode of otherwise unexplained hiccups or nausea and vomiting
 - Acute brainstem syndrome
 - Symptomatic narcolepsy or acute diencephalic clinical syndrome with NMOSD-typical diencephalic MRI lesions
 - Symptomatic cerebral syndrome with NMOSD-typical brain lesions
 - and**
 - Positive serologic test for anti-aquaporin-4 immunoglobulin G (AQP4-IgG)/NMO-IgG antibodies; **and**
 - Diagnosis of multiple sclerosis or other diagnoses have been ruled out
 - and**
 - **One** of the following:
 - History of failure of rituximab therapy; **or**
 - **Both** of the following:
 - History of intolerance or contraindication to rituximab; **and**
 - Physician attests that, in their clinical opinion, the same intolerance or severe adverse event would not be expected to occur with Uplizna
 - and**
 - Uplizna is initiated according to the U.S. Food and Drug Administration (FDA) labeled dosing for NMOSD; **and**
 - Prescribed by, or in consultation with, a neurologist; **and**
 - Patient is **not** receiving Uplizna in combination with **any** of the following for treatment of the same indication:

- Multiple sclerosis disease modifying therapies [e.g., dimethyl fumarate, fingolimod, Ocrevus (ocrelizumab), etc.]; **or**
- Complement inhibitors [e.g., eculizumab, PiaSky (crovalimab), Ultomiris (ravulizumab)]; **or**
- Anti-IL6 therapy (e.g., tocilizumab); **or**
- Anti-CD20 therapy (e.g., rituximab)

and

- Initial authorization will be for no more than 12 months
 - **Continuation of Therapy, all of the following:**
 - Documentation of positive clinical response; **and**
 - Uplizna is dosed according to the U.S. Food and Drug Administration (FDA) labeled dosing for NMOSD; **and**
 - Patient is **not** receiving Uplizna in combination with **any** of the following for treatment of the same indication:
 - Multiple sclerosis disease modifying therapies [e.g., dimethyl fumarate, fingolimod, Ocrevus (ocrelizumab), etc.]; **or**
 - Anti-IL6 therapy (e.g., tocilizumab); **or**
 - Complement inhibitors [e.g., eculizumab, PiaSky (crovalimab), Ultomiris (ravulizumab)]; **or**
 - Anti-CD20 therapy (e.g., rituximab)
- and**
- Reauthorization will be for no more than 12 months

Uplizna (inebilizumab-cdon) is proven and medically necessary for the treatment of Immunoglobulin G4-related disease (IgG4-RD) when all the following criteria are met:

- For **initial therapy, all of the following:**
 - Diagnosis of Immunoglobulin G4-related disease (IgG4-RD); **and**
 - Confirmation of IgG4-RD by a positive assessment using the [ACR/EULAR classification criteria](#), demonstrated by **all** of the following:
 - Involvement of at least 1 or more organ(s) in a manner consistent with IgG4-RD; **and**
 - Exclusion criteria is negative and consistent with an IgG4-RD diagnosis (e.g., clinical findings, serologic results, radiology assessments, pathology interpretations); **and**
 - Inclusion criteria is positive and signifies a diagnosis of IgG4-RD (e.g., clinical findings, serologic results, radiology assessments, pathology interpretations)

and

 - **Both** of the following:
 - History of failure, contraindication, or intolerance to glucocorticoids; **and**
 - **One** of the following:
 - History of failure of rituximab therapy; **or**
 - **Both** of the following:
 - History of intolerance or contraindication to rituximab; **and**
 - Physician attests that, in their clinical opinion, the same intolerance or severe adverse event would not be expected to occur with Uplizna

and

 - Uplizna is initiated according to the U.S. FDA labeled dosing for IgG4-RD; **and**
 - Prescribed by, or in consultation with, a specialist with expertise in the treatment of IgG4-RD; **and**
 - Patient is **not** receiving Uplizna in combination with a disease modifying therapy for the treatment of IgG4-related disease (e.g., rituximab); **and**
 - Initial authorization will be for no more than 12 months
- For **continuation of therapy, all of the following:**
 - Documentation of positive clinical response; **and**
 - Uplizna is dosed according to the U.S. FDA labeled dosing for IgG4-RD; **and**
 - Prescribed by, or in consultation with, a specialist with expertise in the treatment of IgG4-RD; **and**
 - Patient is **not** receiving Uplizna in combination with a disease modifying therapy for the treatment of IgG4-related disease (e.g., rituximab); **and**
 - Reauthorization will be for no more than 12 months

Uplizna is proven and medically necessary for the treatment of generalized myasthenia gravis who are anti-acetylcholine receptor (AChR) antibody positive or antimuscle-specific tyrosine kinase (MuSK) antibody positive when all of the following criteria are met:

- For **initial therapy, all of the following:**
 - Submission of medical records (e.g., chart notes, laboratory values, etc.) confirming **all** of the following:
 - Patient has not failed a previous course of Uplizna therapy for the treatment of generalized myasthenia gravis; **and**

- Diagnosis of generalized myasthenia gravis (gMG); **and**
 - **One** of the following:
 - Positive serologic test for anti-AChR antibodies; **or**
 - Positive serologic test for anti-MuSK antibodies**and**
 - Patient has a Myasthenia Gravis Foundation of America (MGFA) Clinical Classification of class II, III, or IV at initiation of therapy; **and**
 - Patient has a Myasthenia Gravis Activities of Daily Living scale (MG-ADL) total score ≥ 5 at initiation of therapy
- and**
- **One** of the following:
 - If anti-acetylcholine receptor (AChR) antibody positive, **one** of the following:
 - History of failure of at least **two** immunosuppressive agents over the course of at least 12 months (e.g., azathioprine, corticosteroids, cyclosporine, methotrexate, mycophenolate, etc.); **or**
 - Patient has a history of failure of at least one immunosuppressive therapy and has required four or more courses of plasmapheresis/plasma exchanges and/or immune globulin over the course of at least 12 months without symptom control**or**
 - If anti-muscle-specific tyrosine kinase (MuSK) antibody positive:
 - History of failure of at least one immunosuppressive agent over the course of at least 12 months (e.g., azathioprine, corticosteroids, cyclosporine, methotrexate, mycophenolate, etc.)
- and**
- Patient is **not** receiving Uplizna in combination with any of the following for treatment of the same indication:
 - A complement inhibitor [e.g., eculizumab, Ultomiris (ravulizumab), Zilbrysq (zilucoplan)]; **and**
 - An FcRn blocker [e.g., Imaavy (nipocalimab), Rystiggo (rozanolixizumab), Vyvgart (efgartigimod alfa), Vyvgart Hytrulo (efgartigimod alfa and hyaluronidase)]; **and**
 - An immune globulin (e.g., Hizentra, Gammagard, Alyglo, etc.)
- and**
- Patient will be given Uplizna no sooner than two weeks after the first initial dose and every 6 months thereafter for subsequent infusions; **and**
 - Uplizna is dosed according to the US FDA labeled dosing for gMG; **and**
 - Prescribed by, or in consultation with, a neurologist; **and**
 - Initial authorization will be for no more than 12 months
- For continuation of therapy, **all** of the following:
 - Patient has previously been treated with Uplizna; **and**
 - Submission of medical records (e.g., chart notes, laboratory tests) demonstrating **all** of the following:
 - Improvement and/or maintenance of at least a 2 point improvement (reduction in score) in the MG-ADL score from pre-treatment baseline; **and**
 - Reduction in signs and symptoms of myasthenia gravis; **and**
 - Maintenance, reduction, or discontinuation of dose(s) of baseline immunosuppressive therapy (IST) prior to starting Uplizna (**Note:** Add on, dose escalation of IST, or additional rescue therapy from baseline to treat myasthenia gravis or exacerbation of symptoms while on Uplizna therapy will be considered as treatment failure.)
- and**
- Patient is **not** receiving Uplizna in combination with any of the following for treatment of the same indication:
 - A complement inhibitor [e.g., eculizumab, Ultomiris (ravulizumab), Zilbrysq (zilucoplan)]; **and**
 - An FcRn blocker [e.g., Imaavy (nipocalimab), Rystiggo (rozanolixizumab), Vyvgart (efgartigimod alfa), Vyvgart Hytrulo (efgartigimod alfa and hyaluronidase)]; **and**
 - An immune globulin (e.g., Hizentra, Gammagard, Alyglo, etc.)
- and**
- Patient is not being given Uplizna sooner than 6 months from the start of the previous treatment cycle; **and**
 - Uplizna is dosed according to the US FDA labeled dosing for gMG; **and**
 - Prescribed by, or in consultation with, a neurologist; **and**
 - Reauthorization will be for no more than 12 months

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by federal, state, or contractual requirements and

applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

HCPCS Code	Description
J1823	Injection, inebilizumab-cdon, 1 mg

Diagnosis Code	Description
D89.84	IgG4-related disease
G36.0	Neuromyelitis optica (Devic)
G70.00	Myasthenia gravis without (acute) exacerbation
G70.01	Myasthenia gravis with (acute) exacerbation

Background

Uplizna (inebilizumab-cdon) is a CD19-directed humanized afucosylated IgG1 monoclonal antibody. The exact mechanism of action by which inebilizumab exerts its therapeutic effects in neuromyelitis optica spectrum disorder (NMOSD), immunoglobulin G4 related disease (IgG4-RD), and generalized myasthenia gravis (gMG) is not known, but is presumed to involve binding to CD19, a cell surface antigen on pre-B and mature B lymphocytes. After cell surface binding to B lymphocytes, inebilizumab results in antibody-dependent cellular cytotoxicity.

Clinical Evidence

Proven

Neuromyelitis Optica Spectrum Disorder (NMOSD)

Inebilizumab-cdon is indicated for the treatment of NMOSD.

Cree et al., evaluated the efficacy and safety of inebilizumab in 230 patients with NMOSD over 44 months in a multicenter, double-blind, randomized placebo-controlled phase 2/3 study. One hundred seventy-four participants received inebilizumab and 56 participants received placebo. Eligible patients were adults (≥ 18 years old), an expanded disability status score (EDSS) of 8 or less, who required at least one rescue therapy treatment during the year prior to screening, or at least two attacks requiring rescue therapy in the 2 years before screening. Patients who were AQP4-IgG-seropositive and AQP4-IgG-seronegative were eligible; however, patients who were seronegative also needed to meet the criteria described by Wingerchuk and colleagues. The mean EDSS score was 4.0. The number of relapses in the two years prior to randomization was two or more in 83% of the patients. Participants were randomly allocated (3:1) to receive 300 mg intravenous inebilizumab or placebo on days 1 and 15, with a total dose of inebilizumab in the randomized controlled period of 600 mg. No further doses occurred after day 15 within the study period. All participants received oral corticosteroids to minimize the risk of an attack immediately following the first inebilizumab treatment. Primary endpoint was the time in days to the onset of an NMOSD attack, on or before day 197. Secondary endpoints included worsening of EDSS score from baseline, change from baseline in low-contrast visual acuity binocular score; cumulative total number of active MRI lesions, and number of NMOSD-related inpatient hospitalizations, longer than an overnight stay. The randomized controlled period was stopped prior to completion of enrollment, as there was a clear demonstration of efficacy: 12% of participants receiving inebilizumab had an attack, versus 39% of participants receiving placebo [RR 73%; HR 0.272 (95% CI 0.150-0.496); $p < 0.0001$]. In the anti-AQP4 antibody positive population, there was a 77.3% relative reduction (HR 0.227, $p < 0.0001$), whereas patients who were anti-AQP4 antibody negative had no evidence of benefit. 5 adverse events occurred in 72% of participants receiving inebilizumab and 73% of participants receiving placebo. Serious adverse events occurred in 5% of participants receiving inebilizumab and 9% of participants receiving placebo. The authors concluded that compared to placebo, inebilizumab reduced the risk of an NMOSD attack.⁶

Immunoglobulin G4-Related Disease (IgG4-RD)

Inebilizumab-cdon is indicated for the treatment of IgG4-RD in adult patients.

IgG4-RD is a fibroinflammatory condition that is brought about by an immune-mediated process. IgG4-RD is considered a variable condition that mirrors malignancies, infections, and other inflammatory disorders. It is a heterogeneous disease that can have unpredictable flares, tissue fibrosis, tumor-like masses, and affect single organs as well as span multiple organ systems. Involved organ systems most often include the lacrimal glands, major salivary glands (submandibular, parotid), thyroid gland, lungs, aorta, liver, bile ducts, pancreas, kidneys, retroperitoneal tissues, meninges, and lymph nodes. Unique to this disease, there are consistent histologic and immunologic findings within the affected organs that

include plasma cells and lymphocyte infiltration, fibrosis in a storiform pattern, luminal obliteration of venules, and disproportionate IgG class-switching to IgG4. IgG4-RD is therefore a discrete, unique multiorgan disease that is thought to be mediated through autoimmune mechanisms including aberrant CD19 B-cell activity. Prevalence is considered to be around 5 patients per 100,000. Hallmarks of the disease include an indolent phase and a period of time where flares occur. Often IgG4-RD progress undetected for months or years and the majority of patients have irreversible organ damage at the time of their initial diagnosis. Permanent damage can occur at any point in the course of the disease, but more frequent disease flares and incomplete disease control can increase the risk for permanent organ damage over time. The goal of the disease treatment is to reduce inflammation and stop any ongoing flare, as well as reducing the risk of future disease flares with maintenance therapy. The efficacy of inebilizumab for the treatment of IgG4-RD was established in a randomized, double-blind, placebo-controlled trial that enrolled 135 adult patients with a 52-week duration. Eligibility criteria was a newly diagnosed IgG4-RD requiring glucocorticoid treatment during screening, and a history of organ involvement at any time during the course of the disease. Other biologics or non-biologic immunosuppressive agents were prohibited during the blinded portion of the study. Enrolled individuals were randomized into a 1:1 ratio of those receiving placebo or inebilizumab. Glucocorticoids (GC) were tapered off once the trial period commenced and were only allowed for premedication of investigational treatment, treatment for a relapse, or in other conditions not related to IgG4-RD. The primary efficacy endpoint was the time to First Treated and Adjudication Committee (AC)-determined IgG4-RD flare within the 52-week RCP. The time to the First Treated and AC determined IgG4-RD flare was significantly longer in the inebilizumab group, compared with the placebo group (Figure 2). Inebilizumab reduced the risk of treated and AC-determined IgG4-RD flare by 87%, compared with placebo (hazard ratio: 0.13; $p < 0.0001$). A key secondary endpoint was the proportion of patients who were in complete remission at week 52 and had no AC-determined flares or steroid treatment for flares during the randomized clinical trial period (RCP). 40 out of 68 patients on UPLIZNA (58.8%) achieved steroid-free, flare-free complete remission vs. 15 out of 67 patients on placebo (22.4%) at week 52 [difference: 36.45% (95% CI: 21.0%, 51.9%); $p < 0.0001$]. Additionally, the mean (SD) total GC use for IgG4-RD control per patient other than the planned GC taper was lower in the inebilizumab-treated group compared with the placebo-treated group, with a mean (SD) of 118.25 (438.97) mg prednisone equivalent versus 1384.53 (1723.26) mg prednisone equivalent, respectively during the RCP. Forty-two (62.7%) placebo-treated patients and 7 (10.3%) Uplizna-treated patients received GC for IgG4-RD control other than the planned GC taper. The mean (SD) total GC use per patient for the 42 placebo-treated patients was 2202.76 (1709) mg prednisone equivalent and for the 7 Uplizna-treated patients was 1148.71 (878) mg prednisone equivalent.

Generalized Myasthenia Gravis (gMG)

Inebilizumab-cdon is indicated for the treatment generalized myasthenia gravis (gMG) in adult patients who are anti-acetylcholine receptor (AChR) or anti-muscle specific tyrosine kinase (MuSK) antibody positive.

In a randomized, double-blind, multicenter, placebo-controlled trial, inebilizumab demonstrated efficacy in gMG in adult patients who are anti-acetylcholine receptor (AChR) or anti-muscle specific tyrosine kinase (MuSK) antibody positive. The treatment period was 52 weeks for the anti-AChR antibody positive population and 26 weeks for the anti-MuSK antibody positive population and involved a total of 238 patients randomized in a 1:1 ratio to receive inebilizumab or placebo. 190 individuals (80%) were anti-AChR antibody positive and 48 individuals (20%) were anti-MuSK antibody positive. The primary efficacy endpoint was the change from baseline in the Myasthenia Gravis-Activities of Daily Living (MG-ADL) with a baseline score between 6 and 10 (with > 50% of this score attributed to non-ocular items) or an MG-ADL score ≥ 11 . Subjects also had Myasthenia Gravis Foundation of America (MGFA) Clinical Classification Class II to IV and a quantitative Myasthenia Gravis (QMG) score of ≥ 11 . The QMG score is a 13-item categorical grading system that assesses muscle weakness. Each item is assessed on a 4-point scale where a score of 0 represents no weakness and a score of 3 represents severe weakness. A total possible score ranges from 0 to 39, where higher scores indicate more severe impairment. The secondary endpoint was the change from baseline in the QMG score at week 26 in the overall population. A statistically significant difference favoring inebilizumab was observed in the mean change from baseline in MG-ADL total score (-4.2 points in the UPLIZNA-treated group compared to -2.2 points for placebo, difference of -1.9, 95% CI: -2.9, -1.0; p -value < 0.0001). In the secondary endpoint, a statistically significant difference favoring inebilizumab was observed in the mean change from baseline in QMG total score in the overall population (-4.8 points in the inebilizumab-treated group compared to -2.3 for placebo, difference -2.5, 95% CI: -3.8, -1.2; p -value = 0.0002). The primary endpoint was significant in the individual subpopulations for those who were anti-AChR antibody positive and anti-MuSK antibody positive. The secondary endpoint of QMG score was significantly different in the individual subpopulation for those who were anti-AChR antibody positive but did not meet statistical significance in the anti-MuSK antibody positive subpopulation.

U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

Uplizna is a CD19-directed cytolytic antibody indicated for the treatment of neuromyelitis optica spectrum disorder (NMOSD) in adult patients who are anti-aquaporin-4 (AQP4) antibody positive, for the treatment of Immunoglobulin G4-related disease (IgG4-RD) in adult patients, and generalized myasthenia gravis (gMG) in adult patients who are anti-acetylcholine receptor (AChR) or anti-muscle specific tyrosine kinase (MuSK) antibody positive.

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Policy History/Revision Information

Date	Summary of Changes
04/01/2026	<p>Coverage Rationale</p> <p>Neuromyelitis Optica Spectrum Disorder (NMOSD)</p> <ul style="list-style-type: none"> ● Revised coverage criteria; removed criterion requiring one of the following: <ul style="list-style-type: none"> ○ History of one or more relapses that required rescue therapy during the previous 12 months prior to initiating Uplizna ○ History of two or more relapses that required rescue therapy during the previous 24 months prior to initiating Uplizna <p>Generalized Myasthenia Gravis (gMG)</p> <ul style="list-style-type: none"> ● Added language to indicate Uplizna is proven and medically necessary for the treatment of gMG in patients who are anti-acetylcholine receptor (AChR) antibody positive or antimuscle-specific tyrosine kinase (MuSK) antibody positive when all of the following criteria are met: <p>Initial Therapy</p> <ul style="list-style-type: none"> ○ Submission of medical records (e.g., chart notes, laboratory values, etc.) confirming all of the following: <ul style="list-style-type: none"> ▪ Patient has not failed a previous course of Uplizna therapy for the treatment of generalized myasthenia gravis ▪ Diagnosis of gMG ▪ One of the following: <ul style="list-style-type: none"> – Positive serologic test for anti-AChR antibodies – Positive serologic test for anti-MuSK antibodies ▪ Patient has a Myasthenia Gravis Foundation of America (MGFA) Clinical Classification of class II, III, or IV at initiation of therapy ▪ Patient has a Myasthenia Gravis Activities of Daily Living scale (MG-ADL) total score ≥ 5 at initiation of therapy ○ One of the following: <ul style="list-style-type: none"> ▪ If anti-acetylcholine receptor (AChR) antibody positive, one of the following:

Date	Summary of Changes
	<ul style="list-style-type: none"> – History of failure of at least two immunosuppressive agents over the course of at least 12 months (e.g., azathioprine, corticosteroids, cyclosporine, methotrexate, mycophenolate, etc.) – Patient has a history of failure of at least one immunosuppressive therapy and has required four or more courses of plasmapheresis/plasma exchanges and/or immune globulin over the course of at least 12 months without symptom control <ul style="list-style-type: none"> ▪ If anti-muscle-specific tyrosine kinase (MuSK) antibody positive, history of failure of at least one immunosuppressive agent over the course of at least 12 months (e.g., azathioprine, corticosteroids, cyclosporine, methotrexate, mycophenolate, etc.) ○ Patient is not receiving Uplizna in combination with any of the following for treatment of the same indication: <ul style="list-style-type: none"> ▪ A complement inhibitor [e.g., eculizumab, Ultomiris (ravulizumab), Zilbrysq (zilucoplan)] ▪ An FcRn blocker [e.g., Imaavy (nipocalimab), Rystiggo (rozanolixizumab), Vyvgart (efgartigimod alfa), Vyvgart Hytrulo (efgartigimod alfa and hyaluronidase)] ▪ An immune globulin (e.g., Hizentra, Gammagard, Alyglo, etc.) ○ Patient will be given Uplizna no sooner than two weeks after the first initial dose and every 6 months thereafter for subsequent infusions ○ Uplizna is dosed according to the U.S. FDA labeled dosing for gMG ○ Prescribed by, or in consultation with, a neurologist ○ Initial authorization will be for no more than 12 months <p>Continuation of Therapy</p> <ul style="list-style-type: none"> ○ Patient has previously been treated with Uplizna ○ Submission of medical records (e.g., chart notes, laboratory tests) demonstrating all of the following: <ul style="list-style-type: none"> ▪ Improvement and/or maintenance of at least a 2 point improvement (reduction in score) in the MG-ADL score from pre-treatment baseline ▪ Reduction in signs and symptoms of myasthenia gravis ▪ Maintenance, reduction, or discontinuation of dose(s) of baseline immunosuppressive therapy (IST) prior to starting Uplizna (note: add on, dose escalation of IST, or additional rescue therapy from baseline to treat myasthenia gravis or exacerbation of symptoms while on Uplizna therapy will be considered as treatment failure) ○ Patient is not receiving Uplizna in combination with any of the following for treatment of the same indication: <ul style="list-style-type: none"> ▪ A complement inhibitor [e.g., eculizumab, Ultomiris (ravulizumab), Zilbrysq (zilucoplan)] ▪ An FcRn blocker [e.g., Imaavy (nipocalimab), Rystiggo (rozanolixizumab), Vyvgart (efgartigimod alfa), Vyvgart Hytrulo (efgartigimod alfa and hyaluronidase)] ▪ An immune globulin (e.g., Hizentra, Gammagard, Alyglo, etc.) ○ Patient is not being given Uplizna sooner than 6 months from the start of the previous treatment cycle ○ Uplizna is dosed according to the U.S. FDA labeled dosing for gMG ○ Prescribed by, or in consultation with, a neurologist ○ Reauthorization will be for no more than 12 months <p>Applicable Codes</p> <ul style="list-style-type: none"> ● Added ICD-10 diagnosis codes G70.00 and G70.01 <p>Supporting Information</p> <ul style="list-style-type: none"> ● Updated <i>Background</i>, <i>Clinical Evidence</i>, <i>FDA</i>, and <i>References</i> sections to reflect the most current information ● Archived previous policy version CSOH2025D0091.D

Instructions for Use

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