COUPE HEALTH

PHARMACY UTILIZATION MANAGEMENT (UM) PROGRAM CRITERIA ACTIVITY

Provider Notification

Policies Effective: October 4, 2022 Notification Posted: August 19, 2022

CONTENTS	PAGE

Revisions are effective the first of the month following a 45-day notification and comment period.

UM PROGRAM CRITERIA REVISED			
Forteo (teriparatide)			
Program Type:	☒ Prior Authorization	☒ Quantity Limit	☒ Step Therapy
Forteo	1. Pricing updated based off of AWP (8-15-22) 2. Updated fail first criteria from 2 to 1 oral bisphosphonate if treatment failure, 2 if intolerance 3. Added Prolia trial requirement 4. Added max 24 month duration and updated initial duration from 6 to 12 months 5. Added requirement to use as monotherapy 6. Added "Y" to Medispan parameters		

Prior Authorization Approval Criteria

Forteo (teriparatide)

Generic name: teriparatide
Brand name: Forteo
Medispan GPI: 3004407000**** MONY
Medication class: Parathyroid Hormone Analog
FDA-approved uses: **Osteoporosis, postmenopausal, fracture risk reduction**
Primary or hypogonadal osteoporosis in men who are at high risk for fracture
Glucocorticoid-induced osteoporosis at high risk for fracture (men and women)

Usual dose range:

Osteoporosis, fracture risk reduction (male and female)	20 mcg subcutaneously once daily
Glucocorticoid-induced osteoporosis	20mcg subcutaneously once daily

Duration of Authorization:

Initial:	12 months
Ongoing:	Up to 1 year not to exceed 24 months of total cumulative treatment *Duration of teriparatide therapy should generally not exceed 2 years due to limited data with use beyond this; fracture reduction efficacy has been demonstrated over a period of 18 to 24 months.

Estimated Cost: $4759.93 per 600mcg/2.4mL pen (30 day supply) AWP

Criteria for use for Osteoporosis, postmenopausal, fracture risk reduction

- Submitted clinical documentation and prescription claims records must be consistent and non-contradictory to the treatment plan
- Grandfather criteria allowed
    - Please see policy and procedure "*14 – Grandfather Status Authorization*" for additional information.
- Patient is clinically diagnosed with postmenopausal osteoporosis with:
    - BMD T-score ≤ -3.5 based on BMD measurements from lumbar spine (at least two vertebral bodies), hip (femoral neck, total hip), or radius (one-third radius site)
      -OR-
        - BMD T-score between -3.5 and -2.5 (BMD T-score greater than -3.5 and less than or equal to -2.5) based on BMD measurements from lumbar spine (at least two vertebral bodies), hip (femoral neck, total hip), or radius (one-third radius site)
          -AND-
            - Patient must have documented history of one of the following resulting from minimal trauma:
                - Vertebral compression fracture
                - Fracture of the hip
                - Fracture of the distal radius
                - Fracture of the pelvis
                - Fracture of the proximal humerus

          -OR-
            - Patient has a FRAX 10-year fracture probability of ≥20% for major osteoporotic fracture or ≥3% for hip fracture

      -AND-
- Patient has clinical failure of ONE, or contraindication / intolerance to at least TWO oral or injectable bisphosphonates
    - Trial of injectable bisphosphonate is required in patients unable to take oral bisphosphonates due to a contraindication specific only to oral bisphosphonates (swallowing difficulties, esophageal motility disorders, inability to stand or sit upright for ≥30 minutes, increased risk of aspiration)
    - Failure is defined as a non-traumatic fracture while on bisphosphonate therapy, -OR- inadequate response as evidenced by worsening BMD after at least 1 year of therapy, -OR- intolerable side effects
- Patient has clinical failure, contraindication, or intolerance to treatment with Prolia
    - Failure is defined as a non-traumatic fracture while on Prolia therapy, -OR- inadequate response as evidenced by worsening BMD after at least 1 year of therapy, -OR- intolerable side effects

- Use of Forteo will not be used concurrently with other medications for osteoporosis, such as Tymlos (abaloparatide), Prolia (denosumab), bisphosphonates, calcitonin, teriparatide, etc.
- Treatment duration has not exceeded a total of 24 months of cumulative use of any parathyroid hormone analogs

Criteria for use for Primary or hypogonadal osteoporosis in men who are at high risk for fracture

- Submitted clinical documentation and prescription claims records must be consistent and non-contradictory to the treatment plan
- Grandfather criteria allowed
    - Please see policy and procedure "*14 – Grandfather Status Authorization*" for additional information.
- Patient is clinically diagnosed with primary or hypogonadal osteoporosis in men who are at high risk for fracture:
    - BMD T-score ≤ -3.5 based on BMD measurements from lumbar spine (at least two vertebral bodies), hip (femoral neck, total hip), or radius (one-third radius site)
      -OR-
        - BMD T-score between -3.5 and -2.5 (BMD T-score greater than -3.5 and less than or equal to -2.5) based on BMD measurements from lumbar spine (at least two vertebral bodies), hip (femoral neck, total hip), or radius (one-third radius site)
          -AND-
            - Patient must have documented history of one of the following resulting from minimal trauma:
                - Vertebral compression fracture
                - Fracture of the hip
                - Fracture of the distal radius
                - Fracture of the pelvis
                - Fracture of the proximal humerus

          -OR-
            - Patient has a FRAX 10-year fracture probability of ≥20% for major osteoporotic fracture or ≥3% for hip fracture

      -AND-
- Patient has clinical failure of ONE, or contraindication / intolerance to at least TWO oral or injectable bisphosphonates
    - Trial of injectable bisphosphonate is required in patients unable to take oral bisphosphonates due to a contraindication specific only to oral bisphosphonates (swallowing difficulties, esophageal motility disorders, inability to stand or sit upright for ≥30 minutes, increased risk of aspiration)
    - Failure is defined as a non-traumatic fracture while on bisphosphonate therapy, -OR- inadequate response as evidenced by worsening BMD after at least 1 year of therapy, -OR- intolerable side effects
- Patient has clinical failure, contraindication, or intolerance to treatment with Prolia
    - Failure is defined as a non-traumatic fracture while on Prolia therapy, -OR- inadequate response as evidenced by worsening BMD after at least 1 year of therapy, -OR- intolerable side effects
- Use of Forteo will not be used concurrently with other medications for osteoporosis, such as Tymlos (abaloparatide), Prolia (denosumab), bisphosphonates, calcitonin, teriparatide, etc.
- Treatment duration has not exceeded a total of 24 months of cumulative use of any parathyroid hormone analogs

Criteria for use for Glucocorticoid-induced osteoporosis at high risk for fracture

- Submitted clinical documentation and prescription claims records must be consistent and non-contradictory to the treatment plan
- Grandfather criteria allowed
    - Please see policy and procedure "*14 – Grandfather Status Authorization*" for additional information.
- Patient is clinically diagnosed with postmenopausal osteoporosis with:

- BMD T-score ≤ -3.5 based on BMD measurements from lumbar spine (at least two vertebral bodies), hip (femoral neck, total hip), or radius (one-third radius site)
  -OR-
  - BMD T-score between -3.5 and -2.5 (BMD T-score greater than -3.5 and less than or equal to -2.5) based on BMD measurements from lumbar spine (at least two vertebral bodies), hip (femoral neck, total hip), or radius (one-third radius site)
    -AND-
    - Patient must have documented history of one of the following resulting from minimal trauma:
      - Vertebral compression fracture
      - Fracture of the hip
      - Fracture of the distal radius
      - Fracture of the pelvis
      - Fracture of the proximal humerus

    -OR-
    - Patient has a FRAX 10-year fracture probability of ≥20% for major osteoporotic fracture or ≥3% for hip fracture

  -AND-
- Patient has clinical failure of ONE, or contraindication / intolerance to at least TWO oral or injectable bisphosphonates
  - Trial of injectable bisphosphonate is required in patients unable to take oral bisphosphonates due to a contraindication specific only to oral bisphosphonates (swallowing difficulties, esophageal motility disorders, inability to stand or sit upright for ≥30 minutes, increased risk of aspiration)
  - Failure is defined as a non-traumatic fracture while on bisphosphonate therapy, -OR- inadequate response as evidenced by worsening BMD after at least 1 year of therapy, -OR- intolerable side effects
- Patient has clinical failure, contraindication, or intolerance to treatment with Prolia
  - Failure is defined as a non-traumatic fracture while on Prolia therapy, -OR- inadequate response as evidenced by worsening BMD after at least 1 year of therapy, -OR- intolerable side effects
- Use of Forteo will not be used concurrently with other medications for osteoporosis, such as Tymlos (abaloparatide), Prolia (denosumab), bisphosphonates, calcitonin, teriparatide, etc.
- Treatment duration has not exceeded a total of 24 months of cumulative use of any parathyroid hormone analogs

Criteria continuation of therapy

- Patient is tolerating and responding to medication and there continues to be a medical need for the medication.
- Updated chart notes or other clinical documentation confirming efficacy and tolerability of the requested treatment will be required for all renewal reviews. Summitted clinical documentation must be from an encounter after the start date of the current approval.
- Patient demonstrates adequate compliance as defined as an MPR >80%.
- Total duration of use is less than 24 months of therapy.

Contraindications:

- History of hypersensitivity to any of the product ingredients.

Not approved if:

- Patient does not meet any of the above criteria.
- Patient has a contraindication to treatment.
- Patient is premenopausal.

Special Considerations:

- Ensure adequate calcium and vitamin D intake; if dietary intake is inadequate, dietary supplementation is recommended. Patients should consume:
    - Calcium: 1,000 mg/day (males: 50 to 70 years of age) or 1,200 mg/day (females ≥51 years of age and males ≥71 years of age)
    - Vitamin D: 800 to 1,000 units/day (age ≥50 years) (NOF [Cosman 2014]). Recommended dietary allowance (RDA): 600 units/day (age ≤70 years) or 800 units/day (age ≥71 years)
- Serious worsening of previous stable cutaneous calcification or calciphylaxis has been reported; discontinue use if occurs. Patients with underlying autoimmune disease, kidney failure, or concomitantly taking warfarin or systemic corticosteroids are at increased risk.
- May cause orthostatic hypotension. Transient orthostatic hypotension usually occurs within 4 hours of dosing and within the first several doses; usually resolved without treatment within a few minutes to a few hours.
- In animal studies, teriparatide has been associated with an increase in osteosarcoma. Human cases have been reported in postmarketing; increased risk has not been seen in observational studies. Avoid use in patients with an increased risk of osteosarcoma (including Paget disease, bone metastases or a history of skeletal malignancies, prior external beam or implant radiation therapy involving the skeleton, hereditary disorders predisposing to osteosarcoma, or in patients with open epiphyses).

References:

1. Forteo (teriparatide) [prescribing information]. Indianapolis, IN: Lilly USA LLC; September 2021.
2. IOM (Institute of Medicine). Dietary Reference Intakes for Calcium and Vitamin D. The National Academies Press; 2011.
3. Rosen HN, Drezner MK. Overview of the management of osteoporosis in postmenopausal women. Post TW, ed. UpToDate. Waltham, MA: UpToDate Inc.
4. Eastell R, Rosen CJ, Black DM, Cheung AM, Murad MH, Shoback D. Pharmacological management of osteoporosis in postmenopausal women: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2019;104(5):1595-1622. doi:10.1210/jc.2019-00221[PubMed 30907953]

MedOne P&T Committee approval: Date: 12-1-2002

Initial adoption: 12-1-2002
Revised: 8-15-22

8-15-22
1. Pricing updated based off of AWP (8-15-22)
2. Updated fail first criteria from 2 to 1 oral bisphosphonate if treatment failure, 2 if intolerance
3. Added Prolia trial requirement
4. Added max 24 month duration and updated initial duration from 6 to 12 months
5. Added requirement to use as monotherapy
6. Added "Y" to Medispan parameters

Effective Date (most recent revisions): 10/4/2022

**Revisions are effective the first of the month following a 45 day notification and comment period.*

NEW UM PROGRAM CRITERIA			
Nayzilam (midazolam)			
Program Type:	☒ Prior Authorization	☒ Quantity Limit	☒ Step Therapy

Prior Authorization Approval Criteria

Nayzilam (midazolam)

Generic name:	Midazolam (intranasal)	
Brand name:	Nayzilam	
Medispan GPI:	72100060002010	MON
Medication class:	Antiseizure agent, benzodiazepine	
FDA-approved uses:	Seizures, acute intermittent	
Usual dose range:		
Nayzilam (adults, adolescents, and children ≥12 years of age)	Initial: 5mg (1 spray) as a single dose in 1 nostril; may repeat dose in 10 minutes in alternate nostril based on response and tolerability (can cause respiratory depression and excessive sedation	Max: 10mg (2 sprays) per single episode; treat no more than 1 episode every 3 days and no more than 5 episodes per month
Duration of Authorization:	12 months	
Estimated Cost:		
AWP (as of 8/16/22)	Nayzilam 5mg- $352.77 per unit **(2 unit per pack)** Estimated max annual cost of $8,466.48 if filled within quantity limits	

Criteria for use in acute intermittent seizures

- Submitted clinical documentation and prescription claims records must be consistent and non-contradictory to the treatment plan.
- Must be 12 years of age or older.
- Grandfather criteria allowed
    - Please see policy and procedure "*14 – Grandfather Status Authorization*" for additional information.
- Patient is clinically diagnosed with a seizure disorder and is experiencing stereotypic episodes of frequent seizure activity (i.e., seizure clusters, acute repetitive seizures) that are distinct from a patient's usual seizure pattern
- Must be prescribed by, or in consultation with a board certified neurologist or epileptologist
- Patient has failure, contraindication, or intolerance injectable midazolam for intranasal or buccal administration, or diazepam rectal gel.
    - In lieu of treatment contraindication or intolerance, prescriber may also submit clinical rationale to support the inability or impracticality of diazepam rectal gel use based on patient-specific factors (ie. body habitus, setting of predicted medication administration, etc)
- Patient is on a stable maintenance regimen of antiepileptic drugs
- Quantity limit of 2 units per 30 days
    - For requests of quantity limits greater than 2 units per 30 days, patients must be managed on seizure prevention medications with a treatment plan that includes optimized dosing and selection of prevention medications prior to approval of the increased quantity limit.

Criteria continuation of therapy

- Patient is tolerating and responding to medication and there continues to be a medical need for the medication.
- Updated chart notes or other clinical documentation confirming efficacy and tolerability of the requested treatment will be required for all renewal reviews. Summitted clinical documentation must be from an encounter after the start date of the current approval.

Contraindications:

- History of hypersensitivity to any of the product ingredients.
- History of acute narrow-angle glaucoma

Not approved if:

- Patient does not meet any of the above criteria.
- Patient has a contraindication to treatment.

Special Considerations:

- Concerns related to adverse effects:
    - Cardiorespiratory effects: Serious cardiorespiratory adverse events have occurred with midazolam administration, including cardiac arrest, permanent neurologic injury, and death. Risk of adverse events is increased in patients with abnormal airway anatomy, cyanotic congenital heart disease, sepsis, or severe pulmonary disease. In patients with a risk of respiratory depression, consider administering the first dose of intranasal midazolam under health care supervision; this may be performed in the absence of a seizure episode.
    - CNS depression: May cause CNS depression, which may impair physical or mental abilities; patients must be cautioned about performing tasks that require mental alertness (eg, operating machinery, driving). A minimum of one day should elapse after midazolam administration before attempting these tasks. Elapsed time to resume these tasks must be individualized, as pharmacologic effects are dependent on dose, route, duration of procedure, and presence of other medications.
    - Hypotension: May cause hypotension, particularly in pediatric patients or patients with hemodynamic instability. Hypotension may occur more frequently in patients who have received opioid analgesics.
    - Paradoxical reactions: Paradoxical reactions, including hyperactive or aggressive behavior, have been reported with benzodiazepines; risk may be increased in adolescent/pediatric patients, older adults, or patients with a history of alcohol use disorder or psychiatric/personality disorders (Mancuso 2004). Midazolam may cause involuntary movements (eg, tonic/clonic movements, tremor) and combativeness when used for sedation; may cause agitation when used for sedation or status epilepticus. Reactions may be due to improper dosing or administration; cerebral hypoxia should also be considered as a cause.
    - Suicidal ideation: Intranasal: Pooled analysis of trials involving various antiseizure medications (regardless of indication) showed an increased risk of suicidal thoughts/behavior (incidence rate: 0.43% treated patients compared to 0.24% of patients receiving placebo); risk observed as early as one week after initiation and continued through duration of trials (most trials ≤24 weeks). Monitor all patients for notable changes in behavior that might indicate suicidal thoughts or depression; notify health care provider immediately if symptoms occur.
- Disease-related concerns:
    - Cardiovascular disease: Use with caution in patients with heart failure. Adverse hemodynamic events have been reported in pediatric patients with cardiovascular instability; avoid rapid IV administration in these patients.
    - Glaucoma: Use with caution in patients with glaucoma; may increase intraocular pressure. May consider use in patients with open-angle glaucoma only if receiving appropriate therapy; consider evaluating ophthalmologic status after midazolam use.
    - Renal impairment: Use with caution in patients with renal impairment; half-life of midazolam and metabolites may be prolonged.
    - Respiratory disease: Reduce dose or avoid use in patients with respiratory disease, including chronic obstructive pulmonary disease or sleep apnea. Benzodiazepines may cause significant respiratory depression.

References:

5. Nayzilam (midazolam) [prescribing information]. Plymouth, MN: Proximagen, LLC; May 2019.
6. Brunton LL, Chabner BA, Knollmann BC, eds. *Goodman & Gilman's The Pharmacological Basis of Therapeutics*. 12th ed. New York, NY: McGraw-Hill Medical; 2011.
7. Glauser T, Shinnar S, Gloss D, Alldredge B, Arya R, Bainbridge J, Bare M, Bleck T, Dodson WE, Garrity L, Jagoda A, Lowenstein D, Pellock J, Riviello J, Sloan E, Treiman DM. Evidence-Based Guideline: Treatment of Convulsive Status Epilepticus in Children and Adults: Report of the Guideline Committee of the American Epilepsy Society. Epilepsy Curr. 2016 Jan-Feb;16(1):48-61. doi: 10.5698/1535-7597-16.1.48. PMID: 26900382; PMCID: PMC4749120.

MedOne P&T Committee approval: Date: 8-16-22

Initial adoption: 8-16-22
Revised: 8-16-22
8-16-22 1. Pricing updated based off of AWP (8-16-22)
Effective Date (most recent revisions): 10-4-22
**Revisions are effective the first of the month following a 45 day notification and comment period.*

UM PROGRAM CRITERIA REVISED			
Rinvoq (upadacitinib)			
Program Type:	☒ Prior Authorization	☒ Quantity Limit	☒ Step Therapy
Rinvoq	1. Added diagnosis of Ankylosing spondylitis and criteria for authorization 2. Added diagnosis of Ulcerative colitis and criteria for authorization 3. Pricing updated based off of AWP (8-11-22). 4. Added est UC cost for 45mg dose		

Prior Authorization Approval Criteria

Rinvoq (upadacitinib)

ProGeneric name: Upadacitinib
Brand name: Rinvoq
Medispan GPI: 6660307200**** MON
Medication class: Disease modifying, Janus Kinase Inhibitor
FDA-approved uses: **Ankylosing Spondylitis**
Atopic Dermatitis
Psoriatic Arthritis (PsA)
Rheumatoid Arthritis (RA)
Ulcerative Colitis

Usual dose range:
- **Ankylosing Spondylitis** 15mg once daily
- **Atopic Dermatitis** 15 to 30mg once daily
- **PsA** 15mg once daily
- **RA** 15mg once daily
- **Ulcerative Colitis** 45mg once daily for 8 weeks, 15 to 30mg once daily for maintenance dosing

Duration of Authorization:
- **Initial:** 4 months
- **Ongoing:** 12 months

Estimated Cost: $81,666/12 months (Rinvoq 15mg daily dosing) (AWP)
$12,703 per 28 day supply (Rinvoq 45mg daily dosing) (AWP)
$93,461 est cost 1 year UC including 45 mg loading dose

Criteria for use for Ankylosing Spondylitis (AS)

- Submitted clinical documentation and prescription claims records must be consistent and non-contradictory to the treatment plan.
- Grandfather criteria allowed
    - Please see policy and procedure "*14 – Grandfather Status Authorization*" for additional information.
- Patient is clinically diagnosed with active Ankylosing Spondylitis defined as a BASDAI score of at least 4.0 or a ASDAS score equivalent to moderate, high or very high disease activity.
- Must be 18 years of age or older.
- Must be prescribed by, or in consultation with a Rheumatologist
- Documentation of required baseline screening for viral infections (TB, HepB, HepC, HIV (high risk only)) completed within the last 3 months preceding request for treatment (new starts).
- Patient has failure, contraindication, or intolerance to at least one prescription strength formulary NSAID.
- -AND-
- Documentation of an adequate trial and failure/intolerance of at least one conventional systemic or non-biologic DMARD is encouraged but not required.

Criteria for use for Atopic Dermatitis

- Submitted clinical documentation and prescription claims records must be consistent and non-contradictory to the treatment plan.
- Grandfather criteria allowed
    - Please see policy and procedure "*14 – Grandfather Status Authorization*" for additional information.
- Patient is clinically diagnosed with Moderate to Severe Atopic Dermatitis consistent with any one of the following score tools: IGA, EASI, POEM, or SCORAD (results from the evaluation tool must be submitted with the clinical documentation).
    - IGA = 0 (clear), 1 (almost clear), 2 (mild), 3 (moderate), and 4 (severe)
    - EASI = 0 (clear), 0.1 – 1.0 (almost clear), 1.1 – 7.0 (mild), 7.1 – 21.0 (moderate), 21.1 – 50.0 (severe), 50.1 – 72.0 (very severe)
    - POEM = 0 – 2 (clear or almost clear), 3 – 7 (mild), 8 – 16 (moderate), 17 – 24 (severe), 25 – 28 (very severe)
    - SCORAD = <25 (mild), 25 to 50 (moderate), >50 (severe)
- Must be 12 years of age or older.
- Must be prescribed by, or in consultation with a board-certified dermatologist or an allergist/immunologist.
- Patient has atopic dermatitis involvement of ≥ 10% of BSA
- Patient has failure, contraindication, or intolerance to at least one high or super-high potency prescription topical corticosteroid for at least 30 consecutive days
- Patient has failure, contraindication, or intolerance to topical tacrolimus (generic Protopic) -OR- topical pimecrolimus (generic Elidel) for at least 30 consecutive days
- Patient has failure, contraindication, or intolerance to at least one generic traditional disease modifying therapies: oral corticosteroids, oral cyclosporine, oral azathioprine, oral methotrexate, oral mycophenolate mofetil
- Patient will not use in combination with other specialty medications for atopic dermatitis

Criteria for use for Psoriatic Arthritis (PsA)

- Submitted clinical documentation and prescription claims records must be consistent and non-contradictory to the treatment plan.
- Grandfather criteria allowed
    - Please see policy and procedure "*14 – Grandfather Status Authorization*" for additional information.
- Patient is clinically diagnosed with active Psoriatic Arthritis.
- Must be 18 years of age or older.
- Must be prescribed by, or in consultation with a Rheumatologist or Dermatologist.
- Must be used in combination with nonbiologic disease-modifying antirheumatic drugs.

- Documentation of required baseline screening for viral infections (TB, HepB, HepC, HIV (high risk only)) completed within the last 3 months preceding request for treatment (new starts).
    - HepC and HIV are not required for approval, and would be considered for high risk patients only
- Patient has failure, contraindication, or intolerance to at least one conventional systemic DMARD (acitretin, cyclosporine, leflunomide, methotrexate, sulfasalazine).

Criteria for use for Rheumatoid Arthritis (RA)

- Submitted clinical documentation and prescription claims records must be consistent and non-contradictory to the treatment plan.
- Grandfather criteria allowed
    - Please see policy and procedure "*14 – Grandfather Status Authorization*" for additional information.
- Patient is clinically diagnosed with active moderate to severe rheumatoid arthritis.
- Must be 18 years of age or older.
- Must be prescribed by, or in consultation with a Rheumatologist
- Documentation of required baseline screening for viral infections (TB, HepB, HepC, HIV (high risk only)) completed within the last 3 months preceding request for treatment (new starts).
- Patient has failure, contraindication, or intolerance to at least one conventional systemic DMARD (azathioprine, hydroxychloroquine, leflunomide, methotrexate, sulfasalazine).

Criteria for use for Ulcerative Colitis (UC)

- Submitted clinical documentation and prescription claims records must be consistent and non-contradictory to the treatment plan.
- Grandfather criteria allowed
    - Please see policy and procedure "*14 – Grandfather Status Authorization*" for additional information.
- Patient is clinically diagnosed with active moderate to severe ulcerative colitis.
- Must be 18 years of age or older.
- Must be prescribed by, or in consultation with a Gastroenterologist.
- Documentation of required baseline screening for viral infections (TB, HepB, HepC, HIV (high risk only)) completed within the last 3 months preceding request for treatment (new starts).
- Patient has failure, contraindication, or intolerance to systemic corticosteroids (prednisone, budesonide)
- -OR-
- Patient has failure, contraindication, or intolerance to at least one of the following:
    - Aminosalicylates (sulfasalazine, mesalamine)
    - Immunomodulators (azathioprine, 6-mercaptopurine)

Criteria continuation of therapy

- Patient is tolerating and responding to medication and there continues to be a medical need for the medication.
- Chart notes evaluating the safety and efficacy from within the prior 12 months are required for reauthorization.
- Patient demonstrates adequate compliance as defined as an MPR >80%.

Contraindications:

- History of hypersensitivity to any of the product ingredients.
- Patient has an active infection.

Not approved if:

- Patient does not meet any of the above criteria.
- Patient has a contraindication to treatment.
- Patient has a positive screening for viral infection and is not currently receiving appropriate management.

- Patient is currently using another specialty treatment for their condition.
- Quantity is limited to FDA approved dosing for the indication.

Special Considerations:

- Hematologic toxicity, including lymphopenia, anemia, and neutropenia, may occur and is generally reversible and managed by treatment interruption. Do not initiate therapy in patients with an absolute lymphocyte count <500/mm3, ANC <1,000/mm3, or hemoglobin <8 g/dL. Monitor CBC at baseline and periodically thereafter.
- Patients receiving upadacitinib are at increased risk for serious infections, which may result in hospitalization and/or fatality. The most common serious infections reported included pneumonia and cellulitis. Reactivation of viral infections (eg, herpes zoster, hepatitis B) have been observed; the incidence of chronic viral hepatitis reactivation is unknown. If herpes zoster is reported, consider interrupting therapy until herpes zoster has resolved. Consultation with a hepatologist may be necessary if hepatitis B virus DNA is detected.
- Lymphoma and other malignancies have been reported in patients receiving upadacitinib. Consider risks versus benefits prior to use in patients with a known malignancy (other than successfully treated nonmelanoma skin cancers [NMSCs]) or when continuing upadacitinib in patients who develop a new malignancy. NMSCs have been reported.
- Tuberculosis (TB) (pulmonary or extrapulmonary) has been reported in patients receiving upadacitinib. Use with caution in patients who have resided or traveled in regions where TB is endemic. Consider anti-TB therapy if an adequate course of treatment cannot be confirmed in patients with a history of latent or active TB or for patients with risk factors despite negative skin test.
- Liver enzyme elevation has been observed. Monitor LFTs at baseline and periodically thereafter; interrupt therapy if LFTs increased and drug-induced liver injury is suspected.
- Use with caution in patients at increased risk for GI perforation (eg, history of diverticulitis, concomitant nonsteroidal anti-inflammatory drugs); perforations have been reported in clinical trials. Promptly evaluate new-onset abdominal symptoms in patients taking upadacitinib.
- Increased lipid parameters (eg, total, low-density lipoprotein [LDL], and high-density lipoprotein [HDL] cholesterol) have been observed. Mean LDL and HDL increased by ~15 mg/dL and ~8 mg/dL, respectively, 2 months after starting upadacitinib. Assess lipids 12 weeks after upadacitinib initiation and manage lipid abnormalities according to current clinical guidelines.
- Immunization status should be current before initiating therapy. Live vaccines should not be given concomitantly, or immediately prior to, upadacitinib; recommended interval between receipt of live vaccines and initiation of immunosuppressive agents such as upadacitinib should follow current vaccination clinical guidelines.
- There is an increased risk of cardiovascular related events (heart attack, stroke) cancer (lymphoma, lung cancer) thrombosis and death with use of JAK inhibitors. Consider risks and benefits with patients especially considering past or current smokers, patients with other CV risk factors and patients with malignancy or history of malignancy. FDA limits approval to patients who have tried/failed or cannot tolerate a tumor necrosis factor inhibitor (TNFi)

References:

2. Rinvoq (upadacitinib) [prescribing information]. North Chicago, IL: AbbVie Inc; January 2022.
3. US Department of Health and Human Services; Centers for Disease Control and Prevention; National Institute for Occupational Safety and Health. NIOSH list of antineoplastic and other hazardous drugs in healthcare settings 2016. https://www.cdc.gov/niosh/docs/2016-161/. Updated September 2016. Accessed September 17, 2019.

MedOne P&T Committee approval: Date: 1-1-17

Adopted:	1-1-17
Revised:	2-17-22
	3-9-22
	8-11-22
2-17-22	1. Grandfathering criteria requirements explained.
	2. Pricing updated based off of AWP (2-2-22).

	3. Updated the initial duration of authorization from 3 to 4 months. 4. Patients must have a moderate to severe clinical diagnosis 5. Added new start criteria for each diagnosis requiring documentation of baseline screening for viral infections to be completed within the last 3 months preceding request for treatment. 6. Included leflunomide as an option for failure, contraindication, or intolerance to at least one conventional systemic DMARD in the indications for PsA. 7. Included sulfasalazine as an option for failure, contraindication, or intolerance to at least one conventional systemic DMARD in the indications for RA. 8. New denial indication states a patient who has a positive screening for viral infection and is not currently receiving appropriate management or is using another specialty treatment will not be approved. 9. Added criteria for psoriatic arthritis and criteria for authorization 10. Added criteria for atopic dermatitis and criteria for authorization
3-9-22	1. Corrected minimum age to 12 years old for the indication of Atopic Dermatitis.
8-11-22	1. Added diagnosis of Ankylosing spondylitis and criteria for authorization 2. Added diagnosis of Ulcerative colitis and criteria for authorization 3. Pricing updated based off of AWP (8-11-22).
8-17-22	1. Added est UC cost for 45mg dose
Effective Date (most recent revisions):	10-4-22

**Revisions are effective the first of the month following a 45 day notification and comment period.*

UM PROGRAM CRITERIA REVISED			
Skyrizi (risankizumab)			
Program Type:	☒ Prior Authorization	☒ Quantity Limit	☒ Step Therapy
Skyrizi	1. Added Crohn's disease dosing 2. Added Crohn's disease indication and criteria for authorization 3. Updated estimated cost based on AWP for self-injection 4. Added reference to AGA Clinical Practice Guidelines for treatment of Crohn's disease 5. Added est cost for CD and PsO		

Prior Authorization Approval Criteria

Skyrizi (risankizumab)

Generic name: risankizumab
Brand name: Skyrizi
Medispan GPI: 9025057070**** MON
Medication class: Interleukin-23 Inhibitor; monoclonal antibody
FDA-approved uses: **Plaque Psoriasis (PsO)**
Psoriatic Arthritis (PsA)
Crohn's Disease (CD)

Usual dose range:

PsO Initial: 150mg at weeks 0 and 4 Maintenance: 150mg every 12 weeks

PsA	Initial: 150mg at weeks 0 and 4	Maintenance: 150mg every 12 weeks
CD	Initial: 600mg IV at weeks 0, 4, and 8	Maintenance: 360mg SQ at week 12 and every 8 weeks thereafter

Duration of Authorization:

Initial:	4 months
Ongoing:	12 months

Estimated Cost (AWP): $21,927 per 150mg injection
$21,927 per 360mg injection from on-body injector
$142,528 est cost per year CD
$109,637 est 1 year PsA, PsO
$95,019 est 2+ year PsA, PsO

Criteria for use for Plaque Psoriasis (PsO)

- Submitted clinical documentation and prescription claims records must be consistent and non-contradictory to the treatment plan.
- Grandfather criteria allowed
  - Please see policy and procedure "*14 – Grandfather Status Authorization*" for additional information.
- Patient is clinically diagnosed with chronic moderate to severe plaque psoriasis.
- Patient has minimum body surface area involvement of >10% OR involvement of <10% BSA with involvement in sensitive areas (hands, feet, face, genitals).
- Must be 18 years of age or older.
- Must be prescribed by, or in consultation with a Dermatologist.
- Documentation of required baseline screening for viral infections (TB, HepB, HepC, HIV (high risk only)) completed within the last 3 months preceding request for treatment (new starts).
- Documentation of an adequate trial/intolerance of phototherapy if eligible for phototherapy.
- Patient has failure, contraindication, or intolerance to at least one conventional systemic DMARD (acitretin, cyclosporine, methotrexate, sulfasalazine).

Criteria for use for Psoriatic Arthritis (PsA)

- Submitted clinical documentation and prescription claims records must be consistent and non-contradictory to the treatment plan.
- Grandfather criteria allowed
  - Please see policy and procedure "*14 – Grandfather Status Authorization*" for additional information.
- Patient is clinically diagnosed with active Psoriatic Arthritis.
- Must be 18 years of age or older.
- Must be prescribed by, or in consultation with a Rheumatologist or Dermatologist.
- Documentation of required baseline screening for viral infections (TB, HepB, HepC, HIV (high risk only)) completed within the last 3 months preceding request for treatment (new starts).
- Patient has failure, contraindication, or intolerance to at least one conventional systemic DMARD (acitretin, cyclosporine, leflunomide, methotrexate, sulfasalazine).
- Risankizumab may be administered alone or in combination with non–biologic disease-modifying antirheumatic drugs.

Criteria for use for Crohn's Disease (CD)

- Submitted clinical documentation and prescription claims records must be consistent and non-contradictory to the treatment plan.
- Grandfather criteria allowed
    - Please see policy and procedure "*14 – Grandfather Status Authorization*" for additional information.
- Patient is clinically diagnosed with active moderate to severe Crohn's disease.
- Must be 18 years of age or older.
- Must be prescribed by, or in consultation with a Gastroenterologist.
- Documentation of required baseline screening for viral infections (TB, HepB, HepC, HIV (high risk only)) completed within the last 3 months preceding request for treatment (new starts).
- Patient has failure, contraindication, or intolerance to systemic corticosteroids (prednisone, budesonide)
- -OR-
- Patient has failure, contraindication, or intolerance to at least one of the following at maximally indicated doses:
    - Aminosalicylates (sulfasalazine, mesalamine)
    - Immunomodulators (azathioprine, 6-mercaptopurine, injectable methotrexate)

Criteria continuation of therapy

- Patient is tolerating and responding to medication and there continues to be a medical need for the medication.
- Chart notes evaluating the safety and efficacy from within the prior 12 months are required for reauthorization.
- Patient demonstrates adequate compliance as defined as an MPR >80%.

Contraindications:

- History of hypersensitivity to any of the product ingredients.

Not approved if:

- Patient does not meet any of the above criteria.
- Patient has a contraindication to treatment.
- Patient has a positive screening for viral infection and is not currently receiving appropriate management.
- Patient is currently using another specialty treatment for their condition.
- Patient is under the age of 18, safety and effectiveness have not been established.
- Quantity is limited to FDA approved dosing for the indication.

Special Considerations:

- Risankizumab may increase the risk of infections; upper respiratory tract and tinea infections have occurred more frequently. Consider the risks versus benefits prior to treatment initiation in patients with a history of chronic or recurrent infection; treatment should not be initiated in patients with clinically important active infections until it is resolved or treated. Monitor for infections; patients should seek medical attention for signs/symptoms of a clinically important infection (acute or chronic). If a serious infection develops or is unresponsive to appropriate therapy for the infection, monitor closely and discontinue risankizumab until the infection resolves.
- Patients should be evaluated for tuberculosis (TB) infection prior to initiating therapy. Do not administer to patients with an active TB infection. Treatment for latent TB should be administered prior to administering risankizumab. Consider anti-TB therapy prior to treatment initiation in patients with a history of latent or active TB in whom an adequate course of TB treatment cannon be confirmed. Monitor closely for signs/symptoms of active TB during and after risankizumab treatment.
- Patients should be brought up to date with all immunizations before initiating therapy. Live vaccines should not be given concurrently; there are no data available concerning secondary transmission of infection by live vaccines in patients receiving therapy.

- Formation of neutralizing anti-drug antibodies may occur with risankizumab and may be associated with loss of efficacy.
- In general, patients who may become pregnant should use effective contraception while using biologic therapy for the treatment of psoriasis.
- Patients using Skyrizi for Crohn's disease have and increased risk of drug induced hepatotoxity. LFTs will need to be monitored.

References:

7. Skyrizi (risankizumab-rzaa) [prescribing information]. North Chicago, IL: AbbVie Inc; April 2021.
8. Menter A, Strober BE, Kaplan DH, et al. Joint AAD-NPF guidelines of care for the management and treatment of psoriasis with biologics. J Am Acad Dermatol. 2019;80(4):1029-1072. doi:10.1016/j.jaad.2018.11.057[PubMed 30772098]
9. Smith CH, Yiu ZZN, Bale T, et al; British Association of Dermatologists' Clinical Standards Unit. British Association of Dermatologists guidelines for biologic therapy for psoriasis 2020: a rapid update. Br J Dermatol. 2020;183(4):628-637. doi:10.1111/bjd.19039[PubMed 32189327]
10. Yeung J, Gooderham MJ, Grewal P, et al. Management of plaque psoriasis with biologic therapies in women of child-bearing potential consensus paper. JCutan Med Surg. 2020;24(1 suppl):S3-S14. doi:10.1177/1203475420928376[PubMed 32500730]
11. Feuerstein JD, Ho EY, Shmidt E, et al. AGA Clinical Practice Guidelines on the Medical Management of Moderate to Severe Luminal and Perianal Fistulizing Crohn's Disease. Gastroenterology 2021;160:2496-2508. doi: 10.1053/j.gastro.2021.04.022. [PubMed **34051983]**

MedOne P&T Committee approval: Date: 1-1-17

Initial adoption:	1-1-17
Revised:	1-27-22
	2-11-22
	7-22-22
	8-22-22

1-27-22
1. Grandfathering criteria requirements explained.
2. Pricing updated based off of AWP (1-20-22).
3. Updated the initial duration of authorization from 3 to 4 months.
4. Added new start criteria for each diagnosis requiring documentation of baseline screening for viral infections to be completed within the last 3 months preceding request for treatment.
5. New denial indication states a patient who has a positive screening for viral infection and is not currently receiving appropriate management or is using another specialty treatment will not be approved.

2-11-22
1. Added indication of Psoriatic Arthritis and criteria for authorization

7-22-22
1. Added Crohn's disease dosing
2. Added Crohn's disease indication and criteria for authorization
3. Updated estimated cost based on AWP for self-injection
4. Added reference to AGA Clinical Practice Guidelines for treatment of Crohn's disease

8-22-22
1. Added est cost for CD and PsO

Effective Date (most recent revisions): 10-4-22

**Revisions are effective the first of the month following a 45 day notification and comment period.*

UM PROGRAM CRITERIA REVISED			
Tymlos (abaloparatide)			
Program Type:	☒ Prior Authorization	☒ Quantity Limit	☒ Step Therapy
Tymlos	1. Pricing updated based off of AWP (8-15-22) 2. Updated fail first criteria from 2 to 1 oral bisphosphonate if treatment failure, 2 if intolerance 3. Added Prolia trial requirement		

	4. Added max 24 month duration and updated initial duration from 6 to 12 months 5. Added requirement to use as monotherapy

Prior Authorization Approval Criteria

Tymlos (abaloparatide)

Generic name: abaloparatide
Brand name: Tymlos
Medispan GPI: 3004400500**** MON
Medication class: Parathyroid Hormone Analog
FDA-approved uses: **Osteoporosis, postmenopausal, fracture risk reduction**

Usual dose range:
Osteoporosis 80 mcg subcutaneously once daily

Duration of Authorization:
Initial: 12 months
Ongoing: Up to 1 year not to exceed 24 months of total cumulative treatment
*Duration of abaloparatide therapy should not exceed 2 years due to limited data with use beyond this; fracture reduction efficacy has been demonstrated over a period of 18 months.

Estimated Cost: $2747.21 per 3120mcg/1.56mL pen (30 day supply) AWP

Criteria for use for Osteoporosis

- Submitted clinical documentation and prescription claims records must be consistent and non-contradictory to the treatment plan
- Grandfather criteria allowed
  - Please see policy and procedure "*14 – Grandfather Status Authorization*" for additional information.
- Patient is clinically diagnosed with postmenopausal osteoporosis with:
  - BMD T-score ≤ -3.5 based on BMD measurements from lumbar spine (at least two vertebral bodies), hip (femoral neck, total hip), or radius (one-third radius site)
    -OR-
    - BMD T-score between -3.5 and -2.5 (BMD T-score greater than -3.5 and less than or equal to -2.5) based on BMD measurements from lumbar spine (at least two vertebral bodies), hip (femoral neck, total hip), or radius (one-third radius site)
      -AND-
      - Patient must have documented history of one of the following resulting from minimal trauma:
        - Vertebral compression fracture
        - Fracture of the hip
        - Fracture of the distal radius
        - Fracture of the pelvis
        - Fracture of the proximal humerus

    -OR-
    - Patient has a FRAX 10-year fracture probability of ≥20% for major osteoporotic fracture or ≥3% for hip fracture

-AND-

- Patient has clinical failure of ONE, or contraindication / intolerance to at least TWO oral or injectable bisphosphonates
    - Trial of injectable bisphosphonate is required in patients unable to take oral bisphosphonates due to a contraindication specific only to oral bisphosphonates (swallowing difficulties, esophageal motility disorders, inability to stand or sit upright for ≥30 minutes, increased risk of aspiration)
    - Failure is defined as a non-traumatic fracture while on bisphosphonate therapy, -OR- inadequate response as evidenced by worsening BMD after at least 1 year of therapy, -OR- intolerable side effects
- Patient has clinical failure, contraindication, or intolerance to treatment with Prolia
    - Failure is defined as a non-traumatic fracture while on Prolia therapy, -OR- inadequate response as evidenced by worsening BMD after at least 1 year of therapy, -OR- intolerable side effects
- Use of Tymlos will not be used concurrently with other medications for osteoporosis, such as Prolia (denosumab), bisphosphonates, calcitonin, teriparatide, etc.
- Treatment duration has not exceeded a total of 24 months of cumulative use of any parathyroid hormone analogs

Criteria continuation of therapy

- Patient is tolerating and responding to medication and there continues to be a medical need for the medication.
- Updated chart notes or other clinical documentation confirming efficacy and tolerability of the requested treatment will be required for all renewal reviews. Summitted clinical documentation must be from an encounter after the start date of the current approval.
- Patient demonstrates adequate compliance as defined as an MPR >80%.
- Total duration of use is less than 24 months of therapy.

Contraindications:

- History of hypersensitivity to any of the product ingredients.

Not approved if:

- Patient does not meet any of the above criteria.
- Patient has a contraindication to treatment.
- Patient is premenopausal.

Special Considerations:

- Ensure adequate calcium and vitamin D intake; if dietary intake is inadequate, dietary supplementation is recommended. Patients should consume:
    - Calcium: 1,000 mg/day (males: 50 to 70 years of age) or 1,200 mg/day (females ≥51 years of age and males ≥71 years of age)
    - Vitamin D: 800 to 1,000 units/day (age ≥50 years) (NOF [Cosman 2014]). Recommended dietary allowance (RDA): 600 units/day (age ≤70 years) or 800 units/day (age ≥71 years)
- May cause or exacerbate hypercalcemia; use is not recommended in patients with preexisting hypercalcemia or with an underlying hypercalcemic disorder (eg, primary hyperparathyroidism).
- May cause orthostatic hypotension. Transient orthostatic hypotension usually occurs within 4 hours of dosing.
- In animal studies, abaloparatide has been associated with an increase in osteosarcoma; risk was dependent on both dose and duration. Avoid use in patients with an increased risk of osteosarcoma (including Paget disease, bone metastases or skeletal malignancies, hereditary disorders predisposing to osteosarcoma, prior external beam or implant radiation therapy involving the skeleton, or in patients with open epiphyses).

References:

12. Tymlos (abaloparatide) [prescribing information]. Boston, MA: Radius Health Inc; December 2021.

13. IOM (Institute of Medicine). Dietary Reference Intakes for Calcium and Vitamin D. The National Academies Press; 2011.
14. Rosen HN, Drezner MK. Overview of the management of osteoporosis in postmenopausal women. Post TW, ed. UpToDate. Waltham, MA: UpToDate Inc.
15. Eastell R, Rosen CJ, Black DM, Cheung AM, Murad MH, Shoback D. Pharmacological management of osteoporosis in postmenopausal women: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2019;104(5):1595-1622. doi:10.1210/jc.2019-00221[PubMed 30907953]

MedOne P&T Committee approval: Date: 5-1-17

Initial adoption: 5-1-17
Revised: 8-15-22
8-15-22
1. Pricing updated based off of AWP (8-15-22)
2. Updated fail first criteria from 2 to 1 oral bisphosphonate if treatment failure, 2 if intolerance
3. Added Prolia trial requirement
4. Added max 24 month duration and updated initial duration from 6 to 12 months
5. Added requirement to use as monotherapy

Effective Date (most recent revisions): 10/4/2022

**Revisions are effective the first of the month following a 45 day notification and comment period.*

NEW UM PROGRAM CRITERIA			
Valtoco (diazepam)			
Program Type:	☒ Prior Authorization	☒ Quantity Limit	☒ Step Therapy

Prior Authorization Approval Criteria

Valtoco (diazepam)

Generic name: Diazepam (intranasal)
Brand name: Valtoco
Medispan GPI: 7210003000**** MON
Medication class: Antiseizure agent, benzodiazepine
FDA-approved uses: Seizures, acute intermittent

Usual dose range:

Valtoco (adults, adolescents, and children ≥6 years of age)

Recommended Intranasal Valtoco Dosage for Adults			
Weight	**Dose (rounded from 0.2mg/kg)**	**Number of nasal spray devices**	**Number of sprays**
28 to 50 kg	10mg	One 10 mg device	One spray in one nostril
51 to 75 kg	15mg	Two 7.5 mg devices	One spray in each nostril
76 kg and up	20mg	Two 10 mg devices	One spray in each nostril

Recommended Intranasal Valtoco Dosage for Children ≥12 years of age and Adolescents			
Weight	**Dose**	**Quantity and type of nasal device**	**Number of sprays**
14 to <28 kg	5mg	One 5 mg device	1 spray in 1 nostril

28 to <51 kg	10mg	One 10 mg device	1 spray in 1 nostril
51 to <76 kg	15mg	Two 7.5 mg devices	2 sprays delivered as 1 spray in each nostril
≥76 kg	20mg	Two 10 mg devices	2 sprays delivered as 1 spray in each nostril

Recommended Intranasal Valtoco Dosage for Children 6 to 11 years of age			
Weight	**Dose**	**Quantity and type of nasal device**	**Number of sprays**
10 to <19 kg	5mg	One 5 mg device	1 spray in 1 nostril
19 to <38 kg	10mg	One 10 mg device	1 spray in 1 nostril
38 to <56 kg	15mg	Two 7.5 mg devices	2 sprays delivered as 1 spray in each nostril
56 to 74 kg	20mg	Two 10 mg devices	2 sprays delivered as 1 spray in each nostril

Duration of Authorization: 12 months

Estimated Cost:

AWP (as of 8/16/22) Valtoco 5/10/15/20mg spray- $373.97 per unit **(2 units per pack)**
Estimated max annual cost of $8,975.28 when filled within quantity limits

Criteria for use in acute intermittent seizures

- Submitted clinical documentation and prescription claims records must be consistent and non-contradictory to the treatment plan.
- Must be 6 years of age or older.
- Grandfather criteria allowed
    - Please see policy and procedure "14 – Grandfather Status Authorization" for additional information.
- Patient is clinically diagnosed with a seizure disorder and is experiencing stereotypic episodes of frequent seizure activity (i.e., seizure clusters, acute repetitive seizures) that are distinct from a patient's usual seizure pattern
- Must be prescribed by, or in consultation with a board certified neurologist or epileptologist
- Patient has failure, contraindication, or intolerance injectable midazolam for intranasal or buccal administration, or diazepam rectal gel.
    - In lieu of treatment contraindication or intolerance, prescriber may also submit clinical rationale to support the inability or impracticality of diazepam rectal gel use based on patient-specific factors (ie. body habitus, setting of predicted medication administration, etc)
- Patient is on a stable maintenance regimen of antiepileptic drugs
- Quantity limit of 2 units per 30 days
    - For requests of quantity limits greater than 2 units per 30 days, patients must be managed on seizure prevention medications with a treatment plan that includes optimized dosing and selection of prevention medications prior to approval of the increased quantity limit.

Criteria continuation of therapy

- Patient is tolerating and responding to medication and there continues to be a medical need for the medication.

- Updated chart notes or other clinical documentation confirming efficacy and tolerability of the requested treatment will be required for all renewal reviews. Summitted clinical documentation must be from an encounter after the start date of the current approval.

Contraindications:

- History of hypersensitivity to any of the product ingredients.
- History of acute narrow-angle glaucoma

Not approved if:

- Patient does not meet any of the above criteria.
- Patient has a contraindication to treatment.

Special Considerations:

- Concerns related to adverse effects:
    - Cardiorespiratory effects: Serious cardiorespiratory adverse events have occurred with midazolam administration, including cardiac arrest, permanent neurologic injury, and death. Risk of adverse events is increased in patients with abnormal airway anatomy, cyanotic congenital heart disease, sepsis, or severe pulmonary disease. In patients with a risk of respiratory depression, consider administering the first dose of intranasal midazolam under health care supervision; this may be performed in the absence of a seizure episode.
    - CNS depression: May cause CNS depression, which may impair physical or mental abilities; patients must be cautioned about performing tasks that require mental alertness (eg, operating machinery, driving). A minimum of one day should elapse after midazolam administration before attempting these tasks. Elapsed time to resume these tasks must be individualized, as pharmacologic effects are dependent on dose, route, duration of procedure, and presence of other medications.
    - Hypotension: May cause hypotension, particularly in pediatric patients or patients with hemodynamic instability. Hypotension may occur more frequently in patients who have received opioid analgesics.
    - Paradoxical reactions: Paradoxical reactions, including hyperactive or aggressive behavior, have been reported with benzodiazepines; risk may be increased in adolescent/pediatric patients, older adults, or patients with a history of alcohol use disorder or psychiatric/personality disorders (Mancuso 2004). Midazolam may cause involuntary movements (eg, tonic/clonic movements, tremor) and combativeness when used for sedation; may cause agitation when used for sedation or status epilepticus. Reactions may be due to improper dosing or administration; cerebral hypoxia should also be considered as a cause.
    - Suicidal ideation: Intranasal: Pooled analysis of trials involving various antiseizure medications (regardless of indication) showed an increased risk of suicidal thoughts/behavior (incidence rate: 0.43% treated patients compared to 0.24% of patients receiving placebo); risk observed as early as one week after initiation and continued through duration of trials (most trials ≤24 weeks). Monitor all patients for notable changes in behavior that might indicate suicidal thoughts or depression; notify health care provider immediately if symptoms occur.
- Disease-related concerns:
    - Cardiovascular disease: Use with caution in patients with heart failure. Adverse hemodynamic events have been reported in pediatric patients with cardiovascular instability; avoid rapid IV administration in these patients.
    - Glaucoma: Use with caution in patients with glaucoma; may increase intraocular pressure. May consider use in patients with open-angle glaucoma only if receiving appropriate therapy; consider evaluating ophthalmologic status after midazolam use.
    - Renal impairment: Use with caution in patients with renal impairment; half-life of midazolam and metabolites may be prolonged.
    - Respiratory disease: Reduce dose or avoid use in patients with respiratory disease, including chronic obstructive pulmonary disease or sleep apnea. Benzodiazepines may cause significant respiratory depression.

References:

8. Valtoco (diazepam intranasal) [prescribing information]. San Diego, CA: Neurelis Inc; February 2021.
9. Brunton LL, Chabner BA, Knollmann BC, eds. *Goodman & Gilman's The Pharmacological Basis of Therapeutics*. 12th ed. New York, NY: McGraw-Hill Medical; 2011.
10. Glauser T, Shinnar S, Gloss D, Alldredge B, Arya R, Bainbridge J, Bare M, Bleck T, Dodson WE, Garrity L, Jagoda A, Lowenstein D, Pellock J, Riviello J, Sloan E, Treiman DM. Evidence-Based Guideline: Treatment of Convulsive Status Epilepticus in Children and Adults: Report of the Guideline Committee of the American Epilepsy Society. Epilepsy Curr. 2016 Jan-Feb;16(1):48-61. doi: 10.5698/1535-7597-16.1.48. PMID: 26900382; PMCID: PMC4749120.

MedOne P&T Committee approval: Date: 8-16-22

Initial adoption: 8-16-22
Revised: 8-16-22
8-16-22 11. Pricing updated based off of AWP (8-16-22)
Effective Date (most recent revisions): 10-4-22

**Revisions are effective the first of the month following a 45 day notification and comment period.*