COUPE HEALTH

PHARMACY UTILIZATION MANAGEMENT (UM) PROGRAM CRITERIA ACTIVITY

Provider Notification

Policies Effective: 5/1/2023 Notification Posted: 3/10/2023

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

NEW UM PROGRAM CRITERIA			
Omnipod			
Program Type:	☒ Prior Authorization	☒ Quantity Limit	☒ Step Therapy

Prior Authorization Approval Criteria

Omnipod

Brand name: Omnipod
Medispan GPI: 9720103050**** MON
Medication class: Insulin pump (non-medical device)
FDA-approved uses: **Insulin dependent diabetes**

Usual dose range:
Diabetes Every 48 to 72 hours or after delivering 200 units of insulin.

Duration of Authorization:
Initial: 6 months
Ongoing: 12 months

Estimated Cost: $342.19 per 5 pods; $12,318.84 (for every 48 hour dosing) AWP

Criteria for use for Insulin Dependent Diabetes

- Submitted clinical documentation and prescription claims records must be consistent and non-contradictory to the treatment plan.
- Must be 2 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 either uncontrolled type I or type 2 diabetes mellitus.
    - Defined as an untreated A1c of greater than or equal to 7.0% (uncontrolled diabetes).
- Patient must have completed a comprehensive diabetic education program.
    - To include importance of nutrition including carbohydrate counting and meal planning, blood glucose monitoring, and reduction of risk of complications.
- For pump initiation: Patient must meet BOTH the following:
    - has previously been on a diabetic regimen requiring multiple daily insulin injections (of 3 or more injections) with frequent self-adjustments of insulin dose for at least 6 months prior to initiation of an insulin pump with documented adherence;
      -AND-
    - must have documented frequency of glucose self-testing (at least 4 per day on average) within the last two months prior to initiation of insulin pump.
- For patients on a pump prior to MedOne, patients must have documented frequency of glucose self-testing (at least 4 per day on average) within the last two months prior to enrollment/request.
- Patients must have at least ONE of the following:
    - documented history of recurring hypoglycemia or ketoacidosis, wide fluctuations of mealtime glucose, DKA, A1c greater than 7%, or DAWN phenomenon with fasting glucose levels often exceeding 200mg/dL

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. Submitted 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%.
    - Provider may apply a statement confirming access outside of the benefit or addressing correction in compliance for a 4-month authorization to reassess patients MPR

Contraindications:

- Patients who are unable to monitor glucose as recommended
- Patients who are unable to follow up with healthcare provider
- Patients who are taking hydroxyurea due to potential of false elevated glucose readings resulting in excess insulin administration
- Patients who are unable to follow Omnipod instructions or recognize Omnipod functioning alerts, alarms, and reminders
- Hypersensitivity to adhesive in Omnipods

Not approved if:

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

Special Considerations:

- Omnipods should not be used in high or low atmospheric pressures
    - Caution and frequent monitoring should be used when flying
- Omnipods should not be used in oxygen rich environments (greater than 25%oxygen)
- Monitor for skin irritation or infection
- Must require use of smartphone or Omnipod controller. Monitor for hardware defects, software glitches and pod failures
- Omnipod 5 system is designed to work with Dexcom G6.
- Only Rapid acting U-100 insulin should be used

References:

1. Omnipod safety. Insulet Corporation. 2023. https://www.omnipod.com/safety
2. American Diabetes Association. Standards of medical care in diabetes -2023. Diabetes Care. Dec 2022, Vol 46. https://doi.org/10.2337/dc23-S001

MedOne Clinical Review Subcommittee approval: Date: 1-23-23

Initial adoption: 1-23-23
Revised: 1-23-23
1. Updated with current AWP as of 1-23-23

Effective Date (most recent revisions): 5-1-23

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

UM PROGRAM CRITERIA REVISED		
Testosterone Injection		
Program Type:	☒ Prior Authorization ☒ Quantity Limit ☒ Step Therapy	
Testosterone Injection	1. Updated total testosterone range to 300 to 1000 ng/dL 2. References added to support increase in upper normal limit 3. Updated dosing for all indications 4. Added update to contraindications (h/o of prostate CA)	

Prior Authorization Approval Criteria

Testosterone Injection

Generic name:	Testosterone injection
Brand name:	Aveed; Depo-Testosterone; Testone CIK; Xyosted
Medispan GPI:	T cypionate - 231000301020** T enanthate - 2310003020D5** MONY T undecanoate - 231000308020**
Medication class:	Androgen
FDA-approved uses:	**Male primary hypogonadism (congenital or acquired)** **Male hypogonadotropic hypogonadism (congenital or acquired)** **Gender Dysphoria**

Usual dose range:

Testosterone cypionate – adult males	Initial: 75-100mg IM once weekly OR 150-200mg every 2 weeks	Maintenance: titrated to a total testosterone goal of 350 to 1000 ng/dL
Testosterone enanthate – adult males	Initial: 75-100mg IM once weekly OR 150-200mg every 2 weeks	Maintenance: titrated to a total testosterone goal of 350 to 1000 ng/dL
Testosterone undecanoate – adult males ***Ultra long acting***	Initial: 750 mg IM as single dose.	Maintenance: 750 mg IM 4 weeks after initial dose, then 750 mg IM every 10 weeks thereafter; titrated to a total testosterone goal of 350 to 1000 ng/dL
Testosterone cypionate – gender dysphoria	Initial: IM: 100 to 200 mg every 2 weeks **or** 50 to 100 mg every week SQ: 50 to 100 mg every week	Maintenance: 50-100 mg every week or 200mg every other week (titrated to a total testosterone goal of 350 to 1000 ng/dL)
Testosterone enanthate - gender dysphoria	Initial: IM: 100 to 200 mg every 2 weeks **or** 50 to 100 mg every week SQ: 50 to 100 mg every week	Maintenance: 50-100 mg every week or 200mg every other week (titrated to a total testosterone goal of 350 to 1000 ng/dL)
Testosterone cypionate – pediatric males	25 to 400 mg IM every 2 to 4 weeks.	
Testosterone enanthate – pediatric males	25 to 400 mg IM every 2 to 4 weeks.	

Duration of Authorization:

Initial:	4 months
Ongoing:	12 months

Estimated Cost:

Criteria for use for adult male hypogonadism

- Submitted clinical documentation and prescription claims records must be consistent and non-contradictory to the treatment plan.
- Patient is clinically diagnosed with hypogonadism confirmed by medical record documentation including lab documentation of morning serum testosterone concentrations below normal range (less than 350ng/dL)
- Patient has persistent signs and symptoms of androgen deficiency (pre-treatment):
    - Low libido, decreased morning erections, loss of body hair, low bone mineral density, gynecomastia, small testes, fatigue, depression, anemia, reduced muscle strength, increased fat mass
- Other reasons for androgen deficiency have been ruled out (e.g. adrenal insufficiency, hypopituitarism)
- Requests for Aveed, Depo-Testosterone, Testone CIK, Xyosted; patient has failure, contraindication, or intolerance to generic testosterone cypionate -AND- one topical generic testosterone (gel or patch) product.

Criteria for use for gender dysphoria

- Request is for testosterone cypionate or testosterone enanthate only
- Submitted clinical documentation and prescription claims records must be consistent and non-contradictory to the treatment plan.
- Patient must be diagnosed with gender dysphoria, as defined by the current version of the Diagnostic and Statistical Manual of Mental Disorders (DSM)
- Requests for Depo-Testosterone, Testone CIK, Xyosted; patient has failure, contraindication, or intolerance to generic testosterone cypionate -AND- one topical generic testosterone (gel or patch) product.
- Patient is not taking any of the following
    - One of the following growth hormones, unless diagnosed with panhypopituitarism: Genotropin, Humatrope, Norditropin FlexPro, Nutropin AQ, Omnitrope, Saizen
    - Aromatase inhibitor (eg, Arimidex [anastrozole], Femara [letrozole], Aromasin [exemestane])

Criteria for use for pediatric males

- Request is for testosterone cypionate or testosterone enanthate only
- Submitted clinical documentation and prescription claims records must be consistent and non-contradictory to the treatment plan.
- Patient must be diagnosed with hypogonadism (primary) or hypogonadism (hypogonadotropic) (adolescent males)
- For patients diagnosed with delayed puberty, authorization will be for a limited duration (4 to 6 months)
- Requests for Depo-Testosterone, Testone CIK, Xyosted; patient has failure, contraindication, or intolerance to generic testosterone cypionate.

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%.
- Adult male - follow-up total serum testosterone level drawn within the past 4 months for patients new to testosterone therapy (i.e. on therapy for less than one year), or 12 months for patients continuing testosterone therapy (i.e. on therapy for one year or longer), is within or below the set therapeutic goal of 350 to 1000 ng/dL
- Gender Dysphoria - follow-up total serum testosterone level drawn within the past 4 months for patients new to testosterone therapy (i.e. on therapy for less than one year), or 12 months for patients continuing testosterone therapy (i.e. on therapy for one year or longer), is within or below the set therapeutic goal of 350 to 1000 ng/dL

Contraindications:

- History of hypersensitivity to any of the product ingredients.
- Patients with breast cancer (males)
- Patients with prostate cancer (known or suspected). Exception- s/p radical prostatectomy for cancer confined to the prostate and patient has been free of disease (undetectable PSA) for at least 2 years
- Pregnancy
- Patients who may become pregnant
- Patients with serious cardiac, hepatic, or renal disease (testosterone cypionate only)
- men with hypogonadal conditions that are not associated with structural or genetic etiologies (eg, age-related hypogonadism) (testosterone enanthate subcutaneous injection only).
- Documentation of allergenic cross-reactivity for androgens is limited. However, because of similarities in chemical structure and/or pharmacologic actions, the possibility of cross-sensitivity cannot be ruled out with certainty.

Not approved if:

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

Special Considerations:

- Subcutaneous testosterone enanthate can increase blood pressure (BP). Increased BP has been reported with other testosterone products as well. Check BP prior to initiation of therapy, at approximately 6 weeks and periodically thereafter. Some patients may require initiation or adjustment of antihypertensive therapy.
- Serious pulmonary oil microembolism (POME) reactions and anaphylaxis have been reported with testosterone undecanoate injection. Reactions include anaphylaxis, chest pain, urge to cough, dizziness, dyspnea, throat tightening, and syncope; may be life threatening. Reactions may occur after any injection during the course of therapy, including the first dose. Patients must be monitored for 30 minutes after injection. Due to the risk of serious POME reactions, Aveed is only available through the Aveed REMS Program. To minimize risk of adverse reactions, inject deeply into gluteal muscle. Rare reports of reactions involving urge to cough, coughing fits, and respiratory distress immediately after the intramuscular injection of testosterone enanthate (an oil-based depot preparation) have also been reported.
- May cause hypercalcemia in patients with prolonged immobilization or cancer.
- Prolonged use of high doses of androgens has been associated with serious hepatic effects (peliosis hepatis, hepatic neoplasms, cholestatic hepatitis, jaundice). Prolonged use of IM testosterone enanthate has been associated with multiple hepatic adenomas. Discontinue therapy if signs or symptoms of hepatic dysfunction such as jaundice develop.
- Use with caution in patients with diseases that may be exacerbated by fluid retention, including cardiac impairment; testosterone may cause fluid retention. Treatment of androgen deficiency syndromes is not recommended for patients with uncontrolled or poorly controlled heart failure.
- Long-term use (more than 10 years) of parenteral testosterone for male hypogonadism may increase the risk of breast cancer.
- May cause gynecomastia, which may persist in patients treated for hypogonadism.
- Venous thromboembolic events including deep vein thrombosis (DVT) and pulmonary embolism (PE) have been reported with testosterone products. Evaluate patients with symptoms of pain, edema, warmth, and erythema in the lower extremity for DVT and those with acute shortness of breath for PE. Discontinue testosterone if a venous thromboembolism is suspected. Use in hypogonadal men with thrombophilia is not recommended.
- May alter serum lipid profile; use caution with history of myocardial infarction or coronary artery disease.

- May increase the risk of prostate cancer. Withhold therapy pending urological evaluation in patients with palpable prostate nodule or induration, prostate-specific antigen (PSA) more than 4 ng/mL, or PSA more than 3 ng/mL in patients at high risk of prostate cancer.
- May potentiate sleep apnea in some patients especially those with risk factors (eg, obesity or chronic lung disease). Withhold initial treatment in patients with untreated obstructive sleep apnea.
- Androgens may worsen BPH; use in patients with severe lower urinary tract symptoms ([AUA]/IPSS greater than 19) is not recommended. Discontinue therapy if urethral obstruction develops in patients with BPH (use lower dose if restarted).
- Priapism or excessive sexual stimulation may occur; discontinue therapy if this occurs; if restarted, a lower dose should be used.
- May increase hematocrit requiring dose adjustment or discontinuation. Withhold initial treatment in patients with hematocrit greater than 48% or greater than 50% if living at higher altitudes. Discontinue therapy if hematocrit exceeds 54%; may reinitiate at lower dose.
- Testosterone therapy is indicated only for testosterone deficiency, NOT for impaired spermatogenesis. Testosterone therapy impairs spermatogenesis further by suppressing pituitary gonadotropin secretion.
- Use with caution in patients with depression; testosterone may increase risk of depression and suicidal ideation. Evaluate patients with new onset or worsening depression, anxiety, mood changes, or suicidal ideation or behavior.
- Some dosage forms may contain benzyl alcohol. Large amounts of benzyl alcohol (99 mg/kg/day or more) have been associated with a potentially fatal toxicity ("gasping syndrome") in neonates; the "gasping syndrome" consists of metabolic acidosis, respiratory distress, gasping respirations, CNS dysfunction (including convulsions, intracranial hemorrhage), hypotension, and cardiovascular collapse. Some data suggest that benzoate displaces bilirubin from protein-binding sites; avoid or use dosage forms containing benzyl alcohol with caution in neonates. See manufacturer's labeling.
- Available studies are inconclusive regarding the risk of developing major adverse cardiovascular events (MACE) such as nonfatal myocardial infarction (MI), stroke, or cardiovascular death following testosterone use. Some studies have suggested an increased risk of cardiovascular events among groups of men prescribed testosterone therapy, although the overall evidence does not demonstrate an increased or decreased cardiovascular risk. According to the FDA, prescribe testosterone therapy only for males with low testosterone levels caused by certain medical conditions (eg, disorders of the testicles, pituitary gland, or brain) and confirmed by laboratory tests. However, in a position statement issued by the American Association of Clinical Endocrinologists (AACE) and the American College of Endocrinology (ACE), they recommend that after a thorough diagnostic work-up, testosterone replacement should be guided by signs and symptoms and testosterone concentrations rather than the underlying cause. The Endocrine Society recommends avoiding testosterone therapy in men who have experienced an MI or stroke within the past 6 months. Evaluate patients for cardiovascular risk factors prior to initiating therapy and monitor closely during therapy for cardiovascular events.

References:

1. Depo-Testosterone (testosterone cypionate) [prescribing information]. New York, NY: Pfizer; August 2018.
2. Aveed (testosterone undecanoate) [prescribing information]. Malvern, PA: Endo Pharmaceuticals Inc; August 2021.
3. Testosterone. Lexi-Interact [database online]. Hudson, OH: Lexicomp Inc; 2015. http://online.lexi.com. Accessed April 20, 2015.
4. Testosterone. Lexi-Drugs [database online]. Hudson, OH: Lexicomp Inc; 2015. http://online.lexi.com. Accessed April 20, 2015.
5. Testosterone enanthate [prescribing information]. Eatontown, NJ: West-Ward Pharmaceuticals; November 2016.
6. Xyosted (testosterone) [prescribing information]. Ewing, NJ: Antares Pharma, Inc; September 2018.
7. . Bhasin S, Cunningham GR, Hayes FJ, et al. Testosterone therapy in men with androgen deficiency syndromes: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2010;95(6):2536-2559.[PubMed 20525905]
8. Medras M, Filus A, Jozkow P, Winowski J, Sicinska-Werner T. Breast cancer and long-term hormonal treatment of male hypogonadism. Breast Cancer Res Treat
9. Centers for Disease Control and Prevention (CDC). Neonatal deaths associated with use of benzyl alcohol—United States. MMWR Morb Mortal Wkly Rep. 1982;31(22):290-291. http://www.cdc.gov/mmwr/preview/mmwrhtml/00001109.htm.[PubMed 6810084]
10. American Academy of Pediatrics Committee on Drugs. "Inactive" ingredients in pharmaceutical products: update (subject review). Pediatrics. 1997;99(2):268-278.[PubMed 9024461]
11. Harmonized Reference Ranges for Circulating Testosterone Levels in Men of Four Cohort Studies in the United States and Europe, *The Journal of Clinical Endocrinology & Metabolism*, Volume 102, Issue 4, 1 April 2017, Pages 1161–1173
12. Le M, Flores D, May D, Gourley E, Nangia AK. Current Practices of Measuring and Reference Range Reporting of Free and Total Testosterone in the United States. J Urol. 2016 May;195(5):1556-1561.
13. Testosterone replacement therapy following radical prostatectomy. J Sex Med. 2009;6(4):1165. Epub 2009 Jan 22.

MedOne Clinical Review Subcommittee approval: Date: 1-1-17

Initial adoption:	1-1-17
Revised:	10-8-22
	2-8-23
10-8-22	2. Criteria updated to include Xyosted (testosterone enanthate)
2-8-2023	1. Updated total testosterone range to 300 to 1000 ng/dL
	2. References added to support increase in upper normal limit
	3. Updated dosing for all indications
	4. Added update to contraindications (h/o of prostate CA)
Effective Date (most recent revisions):	5-1-23

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

UM PROGRAM CRITERIA REVISED			
Copaxone (glatiramer)			
Program Type:	☒ Prior Authorization	☒ Quantity Limit	☒ Step Therapy
Copaxone (glatiramer)	1. Updated medication cost based on AWP for 2023 2. Updated generic vs brand criteria to align with other specialty MS medications on formulary 3. Updated continuation criteria to include MRI results every 24 months		

Prior Authorization Approval Criteria

Copaxone (glatiramer)

Generic name:	glatiramer	
Brand name:	Copaxone	
Medispan GPI:	6240003010**	MONY
Medication class:	Fumeric Acid Derivative	
FDA-approved uses:	**Multiple sclerosis; relapsing**	
Usual dose range:		
Adults	Initial: 120 mg orally twice daily for 7 days	Maintenance: 240 mg twice daily
Pediatric	Safety and efficacy not established in pediatric patients	
Duration of Authorization:		
Initial:	4 months	
Ongoing:	12 months	
Estimated Cost (AWP):	Brand- $90,980 per year Generic- $28,426 per year	

Criteria for Multiple Sclerosis (MS), relapsing

- Submitted clinical documentation and prescription claims records must be consistent and non-contradictory to the treatment plan.
- Grandfather criteria allowed, change from brand to generic formulations may be required
  - Please see policy and procedure "*14 – Grandfather Status Authorization*" for additional information.
- Must be 18 years of age or older.
- Must be prescribed after a consultation with a neurologist or a MS specialist.
- Documentation confirming that the patient has experienced a clinical episode and has MRI features consistent with relapsing forms of MS required for review.
  - McDonald diagnostic criteria preferred, but not required
- For brand Copaxone (new starts), patient must try/fail or have an intolerance to generic Copaxone (glatiramer or Glatopa) – AND – one other preferred generic MS medication (fingolimod or dimethyl fumerate)
- For brand Copaxone (currently stable), prescriber must submit clinical documentation confirming intolerance to the generic formulation.
  - Intolerance defined as hypersensitivity

Criteria continuation of therapy

- Submitted 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%.
- Patient is tolerating and responding to medication and there continues to be a medical need for the medication.
- Updated chart notes from an encounter within the last 12 months required for all annual reviews.
- Patient must be evaluated by neurology or a MS disease state specialist at least annually.
- Patient must have an updated MRI at least every 24 months.

Contraindications:

- Hypersensitivity to glatiramer acetate, mannitol, or any component of the formulation

Not approved if:

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

Special Considerations:

- DAW-1 (prescriber requests brand): see above information in first section.
- May or may not occur with the immediate postinjection reaction; described as a transient pain usually resolving in a few minutes; often unassociated with other symptoms. Episodes usually begin ≥1 month after initiation of treatment.
- Liver failure and hepatitis with jaundice (sometimes severe) have occurred from days to years after initiation of therapy; consider discontinuation of therapy if signs and symptoms occur.
- Although there has not been a systematic evaluation of glatiramer's potential to affect other immune functions, it may interfere with recognition of foreign antigens undermining the body's tumor surveillance and defense system against infection.
- In high-risk populations or in countries with high tuberculosis burden, screen for latent infections (eg, hepatitis, tuberculosis) prior to initiating therapy. For patients who screen positive for latent infections, consult infectious disease or other specialists (eg, liver specialists) regarding treatment options before initiating therapy.
- Postinjection systemic reactions may occur immediately (within seconds to minutes of injection; majority of reactions observed within 1 hour) and in a substantial percentage of patients (~16% [20 mg/mL] and ~2% [40 mg/mL] in studies); symptoms (anxiety, chest pain, constriction of the throat, dyspnea, flushing, palpitations, tachycardia, urticaria) are usually self-limited and transient. These symptoms generally occur several months after initiation of treatment.

References:

- Copaxone (glatiramer acetate) [prescribing information]. Parsippany, NJ: Teva Pharmaceuticals; April 2022.
- Farez MF, Correale J, Armstrong MJ, et al. Practice guideline update summary: vaccine-preventable infections and immunization in multiple sclerosis: report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. Neurology. 2019;93(13):584-594. doi:10.1212/WNL.0000000000008157[PubMed 31462584]

MedOne Clinical Review Subcommittee approval: Date: 1-1-17

Initial adoption:	1-1-17
Revised:	2-21-23
1-18-23	1. Updated medication cost based on AWP for 2023 2. Updated generic vs brand criteria to align with other specialty MS medications on formulary 3. Updated continuation criteria to include MRI results every 24 months
Effective Date (most recent revisions):	5-1-23

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

Please note:
This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions. Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy has been developed by licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by MedOne Pharmacy Benefits, or any of such health plan's affiliates, as applicable.

UM PROGRAM CRITERIA REVISED			
Dupixent (dupilumab)			
Program Type:	☒ Prior Authorization	☒ Quantity Limit	☒ Step Therapy
Dupixent (dupilumab)	1. Updated to include diagnosis of prurigo nodularis to include dosing and approval criteria for disease state.		

Prior Authorization Approval Criteria

Dupixent (dupilumab)

Generic name:	dupilumab
Brand name:	Dupixent
Medispan GPI:	9027302000**** MON
Medication class:	Monocolonal Antibodies (respiratory)
FDA-approved uses:	**Atopic dermatitis (AD) - moderate to severe, not adequately controlled with topical therapies or when those therapies are inadvisable** **Asthma – add-on maintenance treatment of adult and pediatric patients aged 6 years and older with moderate-to-severe asthma characterized by an eosinophilic phenotype or with oral corticosteroid dependent asthma.** **Eosinophilic esophagitis** **Rhinosinusitis (chronic) with nasal polyposis** **Prurigo Nodularis**

Usual dose range:

Adult – Atopic dermatitis	Initial: 600mg as a loading dose	Maintenance: 300mg once every other week
Pediatric (≥6 months of age) – Atopic dermatitis (5 to <15kg)	Loading dose not necessary in children under 6 years old	Maintenance: 200mg every 4 weeks

Pediatric (≥6 months of age) – Atopic dermatitis (15 to <30kg)	Initial: 600mg as a loading dose	Maintenance: 300mg once every 4 weeks
Pediatric (≥6 years of age) – Atopic dermatitis (30 to <60kg)	Initial: 400mg as a loading dose	Maintenance: 200mg once every other week
Pediatric (≥6 years of age) – Atopic dermatitis (≥60kg)	Initial: 600mg as a loading dose	Maintenance: 300mg once every other week
Adult – Asthma (oral corticosteroid dependent, or add-on maintenance of moderate-to-severe asthma characterized by an eosinophilic phenotype)	Initial: 400-600mg as a loading dose	Maintenance: 200mg or 300mg once every other week
Pediatric (≥6 years of age) – Asthma (oral corticosteroid dependent, or add-on maintenance of moderate-to-severe asthma characterized by an eosinophilic phenotype)	Initial: 400-600mg as a loading dose	Maintenance: 200mg or 300mg once every other week
Adult – Asthma (with comorbid moderate to severe atopic dermatitis)	Initial: 600mg as a loading dose	Maintenance: 300mg once every other week
Pediatric (≥6 years of age) – Asthma (with comorbid moderate to severe atopic dermatitis)	Initial: 600mg as a loading dose	Maintenance: 300mg once every other week
Adult – Rhinosinusitis (NP)	Initial: no loading dose	Maintenance: 300mg once every other week
Eosinophilic esophagitis	Initial: no loading dose	Maintenance: 3000mg once weekly
Prurigo Nodularis	Initial: 600 mg (two 300 mg injections) as a loading dose	Maintenance: 300mg once every other week

Duration of Authorization:

Initial:	3 months
Ongoing:	12 months

Criteria for use for Atopic Dermatitis in Adults

- Submitted clinical documentation and prescription claims records must be consistent and non-contradictory to the treatment plan.
- Patient is clinically diagnosed with Moderate to Severe Atopic Dermatitis consistent with an objective diagnostic evaluation tool to support the diagnosis and level of severity
- Patient must be 18 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 (for at least 30 consecutive days), contraindication, or intolerance to:
    - at least ONE of the following topical medication classes:
        - Topical corticosteroid (desonide, mometasone furoate, fluocinolone acetonide, fluocinonide)
        - Topical calcineurin inhibitor [Elidel (pimecrolimus), Protopic (tacrolimus)]
        - Eucrisa (crisaborole)

      -AND-
    - at least ONE generic preferred systemic agents:
        - 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 Atopic Dermatitis in Pediatric Patients

- Submitted clinical documentation and prescription claims records must be consistent and non-contradictory to the treatment plan.
- Patient is clinically diagnosed with Moderate to Severe Atopic Dermatitis consistent with an objective diagnostic evaluation tool to support the diagnosis and level of severity
- Must be >6 months to 17 years of age
- 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 (for at least 30 consecutive days), contraindication, or intolerance to:
    - at least ONE of the following topical medication classes:
        - Topical corticosteroid (desonide, mometasone furoate, fluocinolone acetonide, fluocinonide)
        - Topical calcineurin inhibitor [Elidel (pimecrolimus), Protopic (tacrolimus)]
        - Eucrisa (crisaborole)

      -AND-
    - at least ONE generic preferred systemic agents:
        - oral corticosteroids (infants)
        - oral mycophenolate mofetil (of note: oral mycophenolate has clinical data supporting its safety and efficacy in infants > 3 months of age for the treatment of atopic dermatitis, though this is not a current FDA approved indication for mycophenolate mofetil)

Criteria for use for Asthma – add-on maintenance treatment of adult and pediatric patients aged 6 years and older with moderate-to-severe asthma characterized by an eosinophilic phenotype or with oral corticosteroid dependent asthma.

- Submitted clinical documentation and prescription claims records must be consistent and non-contradictory to the treatment plan.
- Must be prescribed by, or in consultation with a board-certified pulmonologist, allergist, immunologist.
- Patient must be 6 years of age or older.
- Must have eosinophilic phenotype with eosinophil count greater than or equal to 150 cells/mcL (obtained within the past 6 weeks) -OR- has oral corticosteroid dependent asthma with at least 1 month of daily oral corticosteroid use within the last 3 months.
- Must have inadequate control of asthma symptoms after a minimum of 3 months of compliance use with ONE of the following (trial must have been completed within the last 6 months):
    - Inhaled corticosteroid and long-acting beta-agonist
    - Inhaled corticosteroid and long-acting muscarinic agonist
- Patient will not use in combination with other specialty/biologic medications for Asthma

- Patient must not be a current smoker

Criteria for use for Eosinophilic esophagitis

- Submitted clinical documentation and prescription claims records must be consistent and non-contradictory to the treatment plan.
- Must be prescribed by, or in consultation with a board-certified allergist, immunologist or gastroenterologist.
- Patient must be 12 years of age or older, weighing at least 40 kg
- Patient must have failure, intolerance, or contraindication to at least an 8 week trial of ONE generic proton pump inhibitor (PPI) (esomeprazole, lansoprazole, omeprazole, pantoprazole, rabeprazole) at the maximum tolerated FDA approved dose.
  -AND-
- Patient must have failure, intolerance, or contraindication to topical glucocorticoids (fluticasone using MDI without a spacer or budesonide administered as an oral slurry)

Criteria for use for Rhinosinusitis (chronic) with Nasal Polyposis

- Submitted clinical documentation and prescription claims records must be consistent and non-contradictory to the treatment plan
- Prescribed by or in collaboration with a board-certified allergist, immunologist, or otolaryngologist.
- Formal diagnosis as confirmed computed tomography (CT) or gross physical evidence.
- Presence of nasal polyps
- Patient has a history of prior nasal polyp removal surgery OR required systemic corticosteroid use within the last 6 months
- Patient has failure, contraindication, or intolerance to all preferred treatments
    - Nasal saline irrigations
    - Intranasal corticosteroids (fluticasone, mometasone, triamcinolone, etc.)
- Member will not use Dupixent® concomitantly with other specialty medications (e.g., Xolair, Nucala, etc.)

Criteria for use for Prurigo Nodularis

- Submitted clinical documentation and prescription claims records must be consistent and non-contradictory to the treatment plan.
- Patient is clinically diagnosed with Prurigo Nodularis with widespread or recalcitrant with at least a 7 on the WI-NRS itch scale (0-10), and at least 20 lesions throughout the body.
- Patient must be 18 years of age or older.
- Must be prescribed by, or in consultation with a board-certified dermatologist or an allergist/immunologist.
- Patient has widespread or recalcitrant disease
- Patient has failure (for at least 30 consecutive days), contraindication, or intolerance to:
    - at least ONE of the following treatments:
        - Topical corticosteroid ((desonide, mometasone furoate, fluocinolone acetonide, fluocinonide)) for at LEAST a 2 week trial
        - Intralesional corticosteroid (betamethasone, methylprednisolone, dexamethasone)
        - Phototherapy (narrowband ultraviolet B (NBUVB) phototherapy)

      -AND-
    - at least ONE generic preferred systemic agents:
        - oral corticosteroids
        - oral cyclosporine
- Patient will not use in combination with other specialty medications for Prurigo Nodularis

Criteria continuation of therapy

- The patient has responded to Dupixent therapy as determined by the prescribing physician (e.g., marked improvements erythema, induration/papulation/edema, excoriations, and lichenification; reduced pruritus;

decreased requirement for other topical or systemic therapies; reduced body surface area (BSA) affected with atopic dermatitis; or other responses observed)

- For eosinophilic Asthma: must be an improvement in the patients baseline FEV1.
- For Rhinosinusitis (chronic): patient has continued use of intranasal corticosteroids and use of Dupixent is add-on maintenance therapy, not mono-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 the requirements of all the inclusion criteria listed above
- Patient is also taking another interleukin antagonist
- Not approved for relief of acute bronchospasm or status asthmaticus.
- Not approved if taking another monoclonal antibody for the treatment of asthma.

Special Considerations:

- Avoid the use of live vaccines in patients treated with dupilumab.
- Gradually taper systemic, topical, or inhaled corticosteroid therapy; do not discontinue corticosteroids abruptly following initiation of dupilumab therapy.
- If a dose is missed, administer within 7 days from the missed dose and then resume the original schedule. If the missed dose is not administered within 7 days, wait until the next dose on the original schedule.
- Conjunctivitis and keratitis have been reported; report new onset or worsening eye symptoms to health care provider.
- In rare cases, patients may present with serious systemic eosinophilia, sometimes presenting with clinical features of eosinophilic pneumonia or vasculitis consistent with eosinophilic granulomatosis with polyangiitis, a condition which is often treated with systemic corticosteroid therapy. Monitor for eosinophilia, vasculitic rash, worsening pulmonary symptoms, cardiac complications, and/or neuropathy; especially upon reduction of oral corticosteroids. A causal association between dupilumab and these underlying conditions has not been established.
- Discontinuation or adjustment of asthma medications in patients treated for atopic dermatitis or rhinosinusitis with comorbid asthma should not be done without consulting health care provider.
- It is unknown if administration of dupilumab will influence a patient's response against parasitic infections; patients with known helminth infections were not studied. Therefore, patients with preexisting helminth infections should undergo treatment of the infection prior to initiation of dupilumab therapy. Patients who become infected during treatment and do not respond to anti-helminth therapy should discontinue dupilumab until the infection resolves.
- For Prurigo Nodularis severity is defined from the PRIME and PRIME2 studies.

References:

14. Dupixent (dupilumab) [prescribing information]. Tarrytown, NY: Regeneron Pharmaceuticals; October 2022.
15. Eichenfield LF, Tom WL, Berger TG, Krol A, Paller AS, Schwarzenberger K, et al. Guidelines of care for the management of atopic dermatitis: section 2. Management and treatment of atopic dermatitis with topical therapies. J Am Acad Dermatol. 2014 Jul; 71(1):116-32
16. Simpson EL, Bieber T, Guttman-Yassky E, et al. Two phase 3 trials of dupilumab versus placebo in atopic dermatitis. N Engl J Med. 2016;375(24):2335-2348.
17. Schneider L, Tilles S, Lio P, et al. Atopic dermatitis: a practice parameter update 2012. J Allergy Clin Immunol. 2013;131:295-299.
18. Weston W., Howe W. Treatment of atopic dermatitis (eczema). Up to Date. Accessed August 4, 2018.

MedOne P&T Committee approval: Date: 3-18-2017

Adopted:	3-18-2017
Revised:	10-8-2021 2-17-22 10-14-2022 11-11-2022

Updates:

10-8-21	3. Added appropriate dose ranges for both adult and pediatric for each specific diagnosis 4. Specified, drug must be prescribed by a board-certified dermatologist 5. Adjusted age restriction from 18 to 6 or older for Atopic Dermatitis 6. Explicitly defined the range of scores that would fall under each category using a specific evaluation tool 7. Introduced specific criteria of not allowing the use of Atopic Dermatitis as well as Asthma in combination with other specialty treatments 8. Updated requirement of obtaining an eosinophilic phenotype with eosinophil count greater then or equal to 150 cells within 6 weeks rather then 12 months. 9. Defined continuation of therapy can occur for Rhinosinusitis if patient continues the use of intranasal corticosteroid as well as using Dupixent as an add-on maintenance therapy method.
2-17-22	1. Updated fail first criteria in setting of AD to topical tacrolimus (generic Protopic) -OR- topical pimecrolimus (generic Elidel), previously was -AND- 2. Updated diagnostic criteria requirement for atopic dermatitis 3. Updated age for asthma to > 6 years of age, was >12 years of age
10-14-2022	1. Formatting updates 2. Removed discrepancy in “not approved if” section indication lack of coverage for certain indication 3. Added clarification language around use of mycophenolate in pediatric patients for the treatment of atopic dermatitis
11-11-2022	1. Updated to include diagnosis of prurigo nodularis to include dosing and approval criteria for disease state.

Effective Date (most recent revisions): 5-1-2023

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

Please note:

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions. Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy has been developed by licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards

of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by MedOne Pharmacy Benefits, or any of such health plan's affiliates, as applicable.

UM PROGRAM CRITERIA REVISED			
Tecfidera (dimethyl fumerate)			
Program Type:	☒ Prior Authorization	☒ Quantity Limit	☒ Step Therapy
Tecfidera (dimethyl fumerate)	1. Updated medication cost based on AWP for 2023 2. Updated generic vs brand criteria to align with other specialty MS medications on formulary 3. Updated continuation criteria to include MRI results every 24 months		

Prior Authorization Approval Criteria

Tecfidera (dimethyl fumerate)

Generic name:	dimethyl fumerate	
Brand name:	Tecfidera	
Medispan GPI:	6240552500****	MONY
Medication class:	Fumeric Acid Derivative	
FDA-approved uses:	**Multiple sclerosis; relapsing**	
Usual dose range:		
Adults	Initial: 120 mg orally twice daily for 7 days	Maintenance: 240 mg twice daily
Pediatric	Safety and efficacy not established in pediatric patients	
Duration of Authorization:		
Initial:	4 months	
Ongoing:	12 months	
Estimated Cost (AWP):	Brand- $130,676 per year Generic- $4043 per year	

Criteria for Multiple Sclerosis (MS), relapsing

- Submitted clinical documentation and prescription claims records must be consistent and non-contradictory to the treatment plan.
- Grandfather criteria allowed, change from brand to generic formulations may be required
    - Please see policy and procedure "*14 – Grandfather Status Authorization*" for additional information.
- Must be 18 years of age or older.
- Must be prescribed after a consultation with a neurologist or a MS specialist.
- Documentation confirming that the patient has experienced a clinical episode and has MRI features consistent with relapsing forms of MS required for review.
    - McDonald diagnostic criteria preferred, but not required

- For brand Tecfidera (new starts), patient must try/fail or have an intolerance generic Tecfidera (dimethyl fumerate) – AND – one other preferred generic MS medication (fingolimod or glatiramer)
- For brand Tecfidera (currently stable), prescriber must submit clinical documentation confirming intolerance to the generic formulation.
    - Intolerance defined as hypersensitivity

Criteria continuation of therapy

- Submitted 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%.
- Patient is tolerating and responding to medication and there continues to be a medical need for the medication.
- Updated chart notes from an encounter within the last 12 months required for all annual reviews.
- Patient must be evaluated by neurology or a MS disease state specialist at least annually.
- Patient must have an updated MRI at least every 24 months.

Contraindications:

- Hypersensitivity to dimethyl fumarate or to any component of the product

Not approved if:

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

Special Considerations:

- DAW-1 (prescriber requests brand): see above information in first section.
- May cause rash, pruritus, or erythema. There are case reports of contact dermatitis resulting from dimethyl fumarate exposure after use as a fungicide and desiccant in the shipping of furniture.
- Commonly causes mild to moderate flushing (eg, warmth, redness, itching, burning sensation); flushing generally appears soon after initiation, and improves or resolves with subsequent dosing. Administration with food may decrease flushing incidence. Administration of aspirin (nonenteric coated ≤325 mg) 30 minutes prior to dimethyl fumarate or a temporary dose reduction may also reduce the incidence and severity of flushing.
- GI events (eg, nausea, vomiting, diarrhea, abdominal pain, dyspepsia) commonly occur with use; GI events generally occur in the first month of use and decrease thereafter. To improve tolerability, administer with food or temporarily reduce the dosage
- Clinically significant post marketing cases of hepatic injury have been reported, with an onset ranging from a few days to several months after treatment initiation. Signs/symptoms of hepatic injury, including transaminase elevations >5 times the upper ULN and total bilirubin elevations >2 times ULN have been observed. Some cases have required hospitalization; however, none of the cases were fatal or resulted in liver failure or transplant. Liver function test abnormalities resolved upon discontinuation. Drug-induced hepatocellular injury resulting in new-onset transaminase elevations combined with increased bilirubin levels is an important predictor of serious hepatic injury that may lead to acute hepatic failure, liver transplant, or death in some patients. Transaminase elevations (usually <3 times ULN) were observed in clinical trials, generally occurring in the first 6 months of treatment. Transaminase elevations ≥3 times ULN occurred rarely. Monitor liver function tests prior to treatment initiation and during treatment. Discontinue treatment if dimethyl fumarate-induced hepatic injury is suspected.
- Serious cases of herpes zoster (eg, disseminated, ophthalmicus, meningoencephalitis, meningomyelitis) have been reported; may develop any time during treatment. Other serious opportunistic infections have occurred, including viral (eg, Cytomegalovirus, herpes simplex, West Nile), fungal (eg, Aspergillus, Candida), and bacterial (eg, Listeria monocytogenes, Mycobacterium tuberculosis, Nocardia), in patients with and without lymphopenia. Consider temporary interruption of therapy until infection has resolved. In high-risk populations or in countries with high tuberculosis burden, screen for latent infections (eg, hepatitis, tuberculosis) prior to

initiating therapy. For patients who screen positive for latent infections, consult infectious disease or other specialists (eg, liver specialists) regarding treatment options before initiating therapy

References:

- Tecfidera (dimethyl fumarate) [prescribing information]. Cambridge, MA: Biogen Inc; September 2022.
- Bruze M and Zimerson E, "Dimethyl Fumarate," Dermatitis, 2011, 22(1):3-7.[PubMed 21291637]
- Farez MF, Correale J, Armstrong MJ, et al. Practice guideline update summary: vaccine-preventable infections and immunization in multiple sclerosis: report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. Neurology. 2019;93(13):584-594. doi:10.1212/WNL.0000000000008157[PubMed 31462584]
- Giménez-Arnau A, "Dimethyl Fumarate: A Human Health Hazard," Dermatitis, 2011, 22(1):47-9.[PubMed 21291643]
- Ropper AH, "The 'Poison Chair' Treatment for Multiple Sclerosis," N Engl J Med, 2012, 367(12):1149-50.[PubMed 22992079]

MedOne Clinical Review Subcommittee approval: Date: 1-1-17

Initial adoption:	1-1-17
Revised:	2-21-23
1-18-23	1. Updated medication cost based on AWP for 2023 2. Updated generic vs brand criteria to align with other specialty MS medications on formulary 3. Updated continuation criteria to include MRI results every 24 months
Effective Date (most recent revisions):	5-1-23

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

UM PROGRAM CRITERIA REVISED			
Vumerity (diroximel fumerate)			
Program Type:	☒ Prior Authorization	☒ Quantity Limit	☒ Step Therapy
Vumerity (diroximel fumerate)	1. Updated medication cost based on AWP for 2023 2. Updated generic vs brand criteria to align with other specialty MS medications on formulary 3. Updated continuation criteria to include MRI results every 24 months		

Prior Authorization Approval Criteria

Vumerity (diroximel fumerate)

Generic name:	diroximel fumerate	
Brand name:	Vumerity	
Medispan GPI:	6240553000****	MON
Medication class:	Fumeric Acid Derivative	
FDA-approved uses:	**Multiple sclerosis; relapsing**	

Usual dose range:

Adults	Initial: 231 mg orally twice daily for 7 days	Maintenance: 462 mg (as two 231-mg capsules) twice daily
Pediatric	Safety and efficacy not established in pediatric patients	

Duration of Authorization:

Initial:	4 months
Ongoing:	12 months

Estimated Cost (AWP): Brand- $117,677 per year

Criteria for Multiple Sclerosis (MS), relapsing

- Submitted clinical documentation and prescription claims records must be consistent and non-contradictory to the treatment plan.
- Grandfather criteria allowed, change from brand to generic formulations may be required
    - Please see policy and procedure "*14 – Grandfather Status Authorization*" for additional information.
- Must be 18 years of age or older.
- Must be prescribed after a consultation with a neurologist or a MS specialist.
- Documentation confirming that the patient has experienced a clinical episode and has MRI features consistent with relapsing forms of MS required for review.
    - McDonald diagnostic criteria preferred, but not required
- For brand Vumerity (new starts), patient must try/fail or have an intolerance TWO generic preferred medications dimethyl fumarate (generic Tecfidera), glatiramer or Glatopa (generic Copaxone), fingolimod (generic Gilenya)

Criteria continuation of therapy

- Submitted 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%.
- Patient is tolerating and responding to medication and there continues to be a medical need for the medication.
- Updated chart notes from an encounter within the last 12 months required for all annual reviews.
- Patient must be evaluated by neurology or a MS disease state specialist at least annually.
- Patient must have an updated MRI at least every 24 months.

Contraindications:

- Hypersensitivity to diroximel fumarate, dimethyl fumarate (shares the same active metabolite), or any component of this product; reactions may include anaphylaxis or angioedema.
- Concomitant use of dimethyl fumarate.

Not approved if:

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

Special Considerations:

- Dimethyl fumarate, which has the same active metabolite as diroximel fumarate, commonly causes mild to moderate flushing (eg, warmth, redness, itching, burning sensation); flushing generally appears soon after initiation, and improves or resolves with subsequent dosing. Administration with food may decrease flushing incidence. Administration of aspirin (nonenteric coated ≤325 mg) 30 minutes prior to diroximel fumarate may also reduce the incidence or severity of flushing.
- GI events (eg, diarrhea, nausea, upper abdominal pain, vomiting, constipation) commonly occur with dimethyl fumarate, which has the same active metabolite as diroximel fumarate. GI events generally occur in the first month of use and decrease thereafter.
- Clinically significant postmarketing cases of hepatic injury have been reported with dimethyl fumarate, which has the same active metabolite as diroximel fumarate. Onset has ranged from a few days to several months after treatment initiation. Signs/symptoms of hepatic injury, including transaminase elevations >5 times ULN and total bilirubin elevations >2 times ULN have been observed with dimethyl fumarate. Some cases have required hospitalization; however, none of the cases were fatal or resulted in liver failure or transplant. LFT abnormalities resolved upon discontinuation. Drug-induced hepatocellular injury resulting in new-onset transaminase elevations combined with increased bilirubin levels is an important predictor of serious hepatic injury that may lead to acute hepatic failure, liver transplant, or death in some patients. Transaminase elevations (usually <3 times ULN) were observed in dimethyl fumarate clinical trials, generally occurring in the first 6 months of treatment. Transaminase elevations ≥3 times ULN occurred rarely. Monitor LFTs; discontinue treatment if diroximel fumarate–induced hepatic injury is suspected.
- Anaphylaxis and angioedema may occur after the first dose or at any time during treatment. Discontinue therapy if signs and symptoms of anaphylaxis or angioedema occur.
- Serious cases of herpes zoster (eg, disseminated, ophthalmicus, meningoencephalitis, meningomyelitis) have been reported with dimethyl fumarate, which has the same active metabolite as diroximel fumarate; may develop any time during treatment. Other serious opportunistic infections have occurred with dimethyl fumarate, including viral (eg, Cytomegalovirus, herpes simplex, West Nile), fungal (eg, Aspergillus, Candida), and bacterial (eg, Listeria monocytogenes, Mycobacterium tuberculosis, Nocardia), in patients with and without lymphopenia. Consider temporary interruption of therapy until infection has resolved. In high-risk populations or in countries with high tuberculosis burden, screen for latent infections (eg, hepatitis, tuberculosis) prior to initiating therapy. For patients who screen positive for latent infections, consult infectious disease or other specialists (eg, liver specialists) regarding treatment options before initiating therapy

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MedOne Clinical Review Subcommittee approval: Date: 1-1-17

Initial adoption: 1-1-17
Revised: 2-21-23

1-18-23	1. Updated medication cost based on AWP for 2023 2. Updated generic vs brand criteria to align with other specialty MS medications on formulary 3. Updated continuation criteria to include MRI results every 24 months
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