NEW YORK STATE | Department of Health

# Management of Physician/Practitioner-Administered Drugs (PADs)

## Drug Utilization Review (DUR) Board

July 14, 2022

# Overview

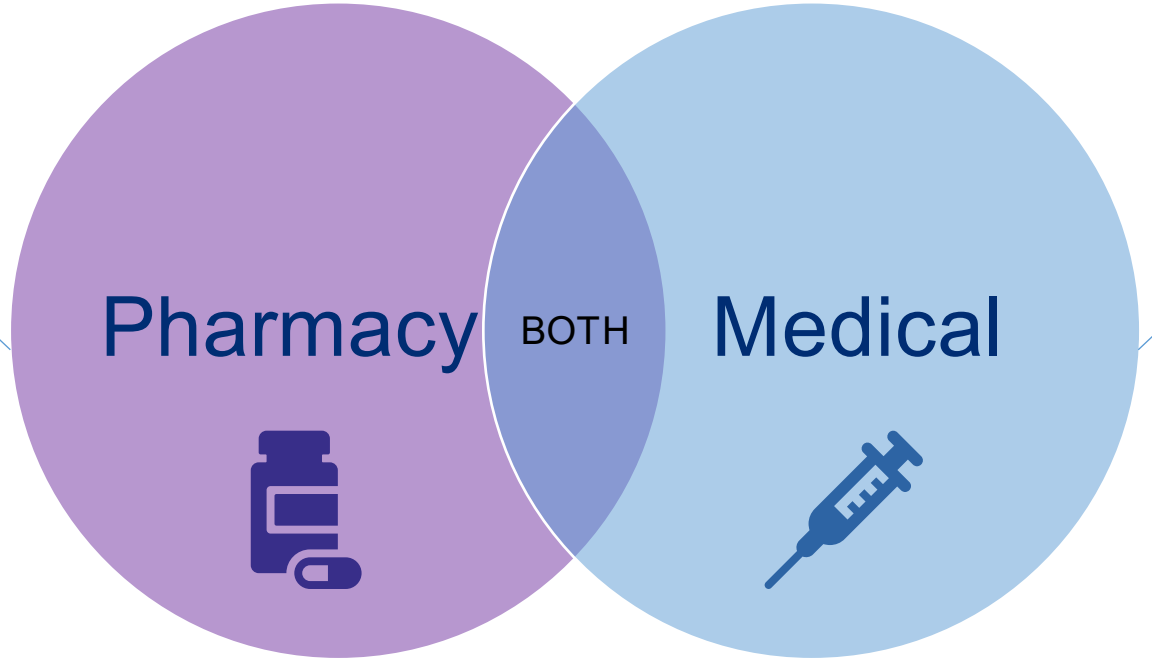
- Program Overview
- Current Process: Pharmacy Benefit
- Program Vision and Benefits
- Roadmap
- Summary and Resources
- Q&A

# Program Overview

# Establishing Parity and Uniform Clinical Standards for Coverage of Drugs

## 2022-23 Enacted Medicaid Budget

- Typically self-administered
- Billed and dispensed by a pharmacy




- Typically administered by a healthcare professional
- Billed by the provider

NEW YORK STATE | Department of Health

# Pharmacy vs. Medical Drug Claims

## Pharmacy Drug Claims:

- Prospective billing
- Electronic claim submission
- Automated clinical criteria
- Real-time claim response
- Quick reimbursement

## Medical Drug Claims:

- Retrospective billing
- Paper claim submission
- Manual claim review
- Offline claim response
- Potential delays in reimbursement

# Program Goals

- Ensure patient safety and clinically appropriate use of medications
- Create a standard process for developing and implementing coverage criteria across the pharmacy and medical benefits
- Modernize the way drug claims are submitted on the medical benefit
- Improve efficiency of the claims review process for drugs covered under the medical benefit

# Current Process: Pharmacy Benefit

# Clinical Criteria Development

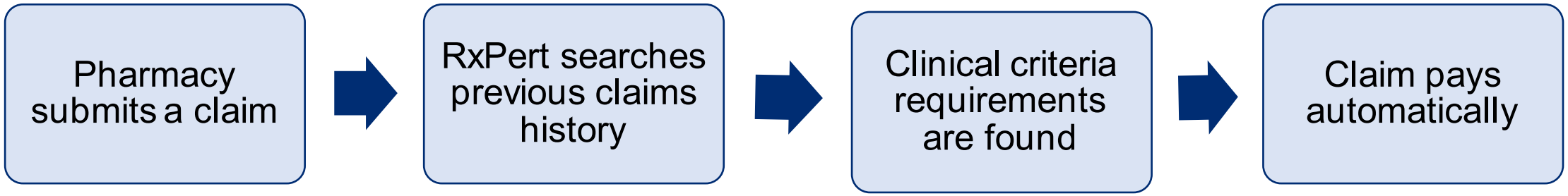
Drug/drug class identified for review

DUR Board makes clinical criteria recommendations

Clinical criteria are published and implemented

# RxPert by Kepro

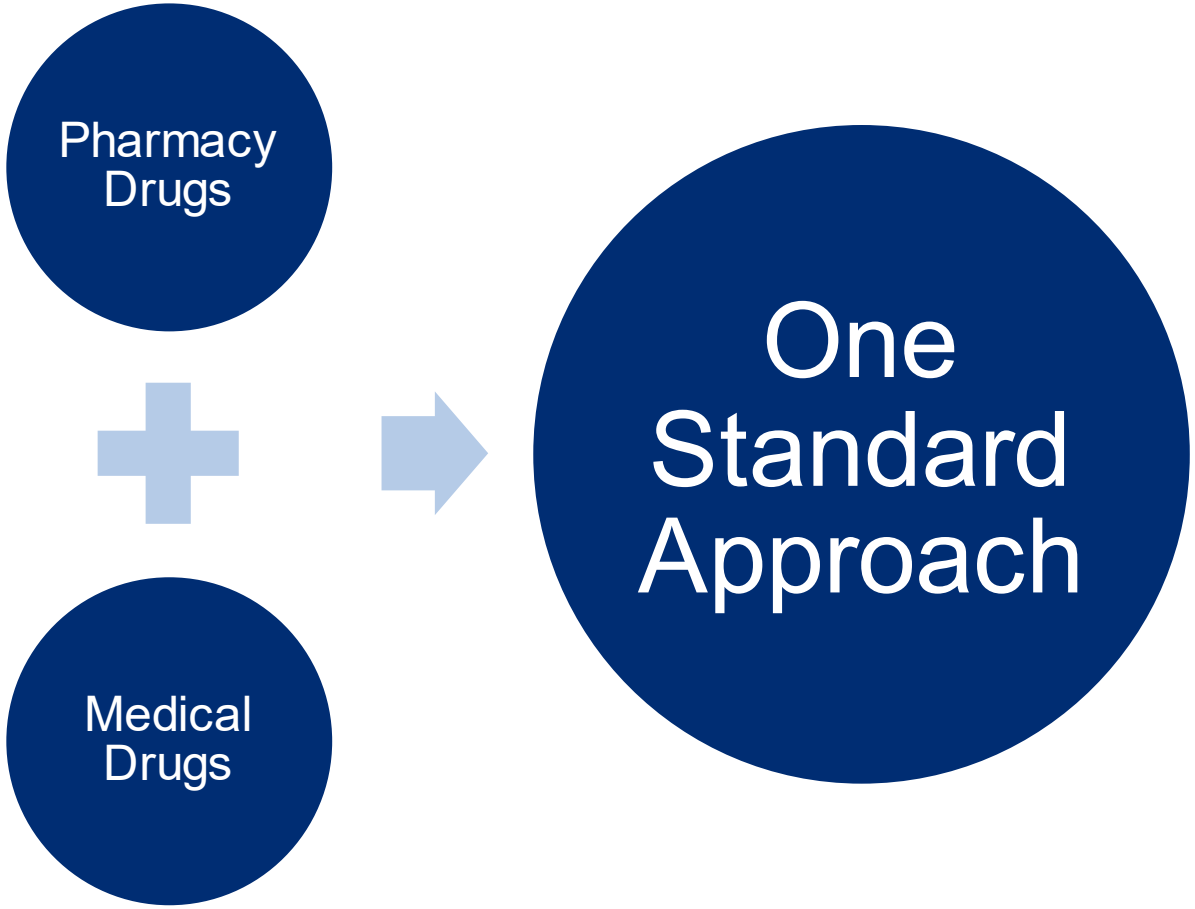
- Automated prior authorization (PA) adjudication system that looks back into a patient's claims history to determine if clinical criteria for a prescribed drug are met




- If clinical criteria are not met, the prescriber has the option to adjust/change the prescribed therapy or contact the Magellan call center to request prior authorization

# Program Vision and Benefits

# Program Vision



# Program Benefits

- **Providers:**
  - Increased transparency into coverage criteria
  - Ability to secure authorization prior to drug administration
  - Decreased administrative burden- streamlined claim submission process
  - Expedited reimbursement
- **Patients:**
  - Improved safety checks will ensure medication use is appropriate and in line with current recommendations

# Roadmap

# Roadmap


Clinical criteria recommendations for PADs may not be fully implemented until go live date

# Summary and Resources

# Summary

- Uniform clinical standards for coverage of drugs will modernize the process for the review of drugs covered under the medical benefit
- Existing tools and processes in place on the pharmacy benefit will be leveraged
- Clinical criteria will be established for PADs and will be brought to the DUR Board for review when needed
- More information on timeline and details regarding implementation will be provided as they become available

# Resources

DOH Medicaid Update:
https://www.health.ny.gov/health_care/medicaid/program/update/main.htm

eMedNY LISTSERV:
https://www.emedny.org/Listserv/eMedNY_Email_Alert_System.aspx

FFS Practitioner Administered Drug Policies and Billing Guidance Website:
https://www.health.ny.gov/health_care/medicaid/program/practitioner_administered/ffs_practitioner_administer.htm

FFS Physician Manual:
https://www.emedny.org/ProviderManuals/Physician/index.aspx

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# Questions & Answers

# Antipsychotics, Injectable Therapeutic Class Review

NEW YORK MEDICAID
DRUG UTILIZATION REVIEW BOARD MEETING
JULY 14, 2022

Magellan Rx MANAGEMENT℠

# Antipsychotics, Injectable

## New Clinical Information

- New Drug Entity: Invega Hafyera™ (paliperidone palmitate)

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Antipsychotics, Injectable

# Invega Hafyera™ (paliperidone palmitate)

- **Indications:**
  - Atypical antipsychotic indicated for the treatment of schizophrenia in adults after they have been adequately treated with:
    1. A once-a-month paliperidone palmitate extended-release injectable suspension (e.g., INVEGA SUSTENNA) for at least four months or
    2. An every-three-month paliperidone palmitate extended-release injectable suspension (e.g., INVEGA TRINZA) for at least one three-month cycle

- **Dosage/Availability:**
  - Extended-release injectable suspension: 1,092 mg/3.5 mL or 1,560 mg/5 mL single dose prefilled syringes.
  - Administer INVEGA HAFYERA by gluteal injection once every 6 months by a healthcare professional. Do not administer by any other route.

Invega Hafyera [package insert]. Titusville, NJ; Janssen Pharmaceuticals, Inc.; August 2021.

# Invega Hafyera™ (paliperidone palmitate)cont.

- **Contraindications/Warnings:**
  - Known hypersensitivity to paliperidone, risperidone, or to any excipients in INVEGA HAFYERA
  - Cerebrovascular Adverse Reactions in Elderly Patients with Dementia-Related Psychosis
  - Neuroleptic Malignant Syndrome
  - QT Prolongation
  - Tardive Dyskinesia
  - Metabolic Changes
  - Orthostatic Hypotension and Syncope
  - Leukopenia, Neutropenia, and Agranulocytosis
  - Hyperprolactinemia
  - Potential for Cognitive and Motor Impairment
  - Seizures

Invega Hafyera [package insert]. Titusville, NJ; Janssen Pharmaceuticals, Inc.; August 2021.

# Invega Hafyera™ (paliperidone palmitate)cont.

- **Common Adverse Drug Reactions:**
  - Upper respiratory tract infection, injection site reaction, weight increase, headache, and parkinsonism

- **Drug Interactions:**
  - Strong CYP3A4/P-glycoprotein (P-gp) inducers: Avoid using strong CYP3A4 and/or P-gp inducers during a dosing interval for INVEGA HAFYERA
    - If administering a strong inducer is necessary, consider managing the patient using paliperidone extended-release tablets

- **Specific Populations:**
  - Pregnancy: May cause extrapyramidal and/or withdrawal symptoms in neonates with third trimester exposure
  - Renal Impairment: Not recommended

- **Clinical Comparative Studies (within class):**
  - Study demonstrated non-inferiority of Invega Hafyera to Invega Trinza

Invega Hafyera [package insert]. Titusville, NJ; Janssen Pharmaceuticals, Inc.; August 2021.

| Preferred Drugs | Non-Preferred Drugs | Prior Authorization/Coverage Parameters |
|---|---|---|
| **Antipsychotics - Injectable** | | |
| Abilify Maintena®<br>Aristada®<br>Aristada Initio®<br>fluphenazine decanoate<br>Haldol® decanoate<br>haloperidol decanoate<br>Invega Sustenna®<br>Invega Trinza®<br>Perseris™<br>Risperdal Consta®<br>Zyprexa Relprevv® | Invega Hafyera™ | |

# Antipsychotics, Second Generation Therapeutic Class Review

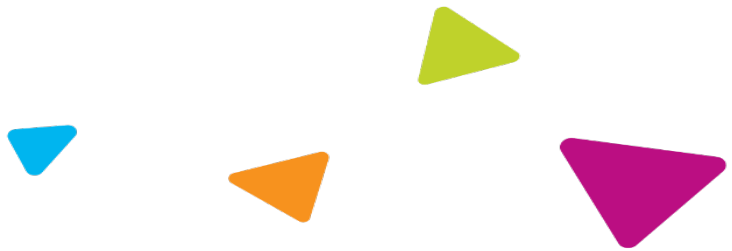
NEW YORK MEDICAID
DRUG UTILIZATION REVIEW BOARD MEETING
JULY 14, 2022

Magellan Rx MANAGEMENT℠

# Antipsychotics, Second Generation

## New Clinical Information

- New Drug Entity: Lybalvi® (olanzapine and samidorphan)
- New Indications: Caplyta® (lumateperone),
  Rexulti® (brexpiprazole)



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Antipsychotics, Second Generation

# Lybalvi® (olanzapine and samidorphan)

- **Indications:**
  - Combination of olanzapine, an atypical antipsychotic, and samidorphan, an opioid antagonist, indicated for the treatment of:
    1. Schizophrenia in adults
    2. Bipolar I disorder in adults
       - Acute treatment of manic or mixed episodes as monotherapy and as adjunct to lithium or valproate
       - Maintenance monotherapy treatment
- **Dosage/Availability:**
  - Tablets (olanzapine/samidorphan): 5 mg/10 mg, 10 mg/10 mg, 15 mg/10 mg and 20 mg/10 mg
  - Take once daily with or without food with recommended starting dose

Lybalvi [package insert]. Titusville, NJ; Janssen Pharmaceuticals, Inc.; August 2021.

Antipsychotics, Second Generation

# Lybalvi® (olanzapine and samidorphan) cont.

- **Contraindications:**
  - Patients using opioids
  - Patients undergoing acute opioid withdrawal
- **Warnings and Precautions:**
  - Cerebrovascular Adverse Reactions in Elderly Patients with Dementia Related Psychosis
  - Precipitation of Opioid Withdrawal in Patients Who are Dependent on Opioids
  - Vulnerability to Life-Threatening Opioid Overdose
  - Neuroleptic Malignant Syndrome
  - Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS)
  - Metabolic Changes
  - Tardive Dyskinesia
  - Orthostatic Hypotension and Syncope
  - Leukopenia, Neutropenia, and Agranulocytosis
  - Seizures
  - Potential for Cognitive and Motor Impairment
  - Anticholinergic (Antimuscarinic) Effects
  - Hyperprolactinemia

Lybalvi [package insert]. Titusville, NJ; Janssen Pharmaceuticals, Inc.; August 2021.

# Lybalvi® (olanzapine and samidorphan) cont.

- **Black Box Warning:**
  - Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death
  - Lybalvi is not approved for the treatment of patients with dementia-related psychosis

- **Common Adverse Drug Reactions:**
  - Most common adverse reactions (incidence ≥5% and at least twice placebo):
    - Schizophrenia (LYBALVI): weight increase, somnolence, dry mouth, headache.
    - Bipolar I Disorder, Manic or Mixed Episodes (olanzapine): asthenia, dry mouth, constipation, increased appetite, somnolence, dizziness, tremor.
    - Bipolar I Disorder, Manic or Mixed Episodes, adjunct to Lithium or Valproate (olanzapine): dry mouth, dyspepsia, weight gain, increased appetite, dizziness, back pain, constipation, speech disorder, increased salivation, amnesia, paresthesia.



Lybalvi [package insert]. Titusville, NJ; Janssen Pharmaceuticals, Inc.; August 2021.

# Lybalvi® (olanzapine and samidorphan) cont.

- **Drug Interactions:**
  - Strong CYP3A4 Inducers: Not recommended.
  - Strong CYP1A2 Inhibitors: Consider dosage reduction of olanzapine component of LYBALVI.
  - CYP1A2 Inducer: Consider dosage increase of the olanzapine component of LYBALVI.
  - CNS Acting Drugs: May potentiate orthostatic hypotension.
  - Anticholinergic Drugs: Can increase risk for severe gastrointestinal adverse reactions.
  - Antihypertensive Agents: Monitor blood pressure.
  - Levodopa and Dopamine Agonists: Not recommended.

Lybalvi [package insert]. Titusville, NJ; Janssen Pharmaceuticals, Inc.; August 2021.

# Lybalvi® (olanzapine and samidorphan) cont.

- **Specific Populations:**
  - Pregnancy: May cause extrapyramidal and/or withdrawal symptoms in neonates with third trimester exposure.
  - Renal Impairment: Use is not recommended in patients with end-stage renal disease

- **Clinical Comparative Studies (within class):**
  - Evaluation of Weight Changes in Patient with Schizophrenia
    - Treatment with Lybalvi was associated with statistically significantly less weight gain than treatment with olanzapine, and with a smaller proportion of patients who gained ≥10% body weight

Lybalvi [package insert]. Titusville, NJ; Janssen Pharmaceuticals, Inc.; August 2021.

Antipsychotics, Second Generation

# Caplyta® (lumateperone)

- **New Indication:**
  - Depressive episodes associated with bipolar I or II disorder (bipolar depression) in adults, as monotherapy and as adjunctive therapy with lithium or valproate

- **New Strengths:**
  - 10.5 mg and 21 mg capsules
    - Moderate or severe hepatic impairment: Recommended dosage is 21 mg once daily
    - Strong CYP3A4 inhibitors: Recommended dosage is 10.5 mg once daily
    - Moderate CYP3A4 inhibitors: Recommended dosage is 21 mg once daily

Caplyta [package insert]. New York, NY; Intra-cellular Therapies, Inc.; April 2022.

Antipsychotics, Second Generation

# Rexulti®(brexpiprazole)

- **New Indication:**
  - FDA has expanded the indication to include treatment of schizophrenia in pediatric patients 13 to 17 years old; previously was only indicated for use in adults
  - Starting dose 0.5mg/day, recommended dose 2 to 4 mg/day, maximum dose 4 mg/day
  - Pediatric Patients (13 to 17 years of age): In the long-term, open-label study in pediatric patients with schizophrenia, 2.7% of pediatric patients with normal baseline fasting glucose experienced a shift from normal (<100 mg/dL) to high (≥126 mg/dL) while taking brexpiprazole

Rexulti [package insert]. Rockville, MD; Otsuka America Pharmaceutical Inc.; December 2021.

| Preferred Drugs | Non-Preferred Drugs | Prior Authorization/Coverage Parameters |
|---|---|---|
| **Antipsychotics – Second Generation** CC, ST | | |
| aripiprazole (tablet) DO<br>asenapine (gen Saphris®)<br>clozapine<br>Latuda® DO<br>olanzapine (tablet) DO<br>quetiapine F/Q/D<br>quetiapine ER F/Q/D, DO<br>risperidone<br>ziprasidone (capsules) | Abilify® (tablet) DO<br>Abilify MyCite®<br>aripiprazole (solution)<br>aripiprazole ODT<br>Caplyta™<br>clozapine ODT<br>Clozaril®<br>Fanapt®<br>Geodon®<br>Invega® DO, F/Q/D<br>Lybalvi™<br>Nuplazid®<br>olanzapine ODT DO<br>paliperidone ER F/Q/D, DO<br>Rexulti® DO<br>Risperdal®<br>Saphris®<br>Secuado® F/Q/D<br>Seroquel® F/Q/D<br>Seroquel XR® DO, F/Q/D<br>Versacloz®<br>Vraylar® DO<br>Zyprexa® DO<br>Zyprexa® Zydis | **DOSE OPTIMIZATION (DO)**<br>• See Dose Optimization Chart for affected drugs and strengths<br><br>**CLINICAL CRITERIA (CC)**<br>• Clinical editing will allow patients currently stabilized on a non-preferred agent to continue to receive that agent without PA<br>• Prior authorization is required when an oral SGA is utilized above the highest MDD according to FDA labeling.<br>• Prior authorization is required for patients less than 21 years of age when there is concurrent use of 2 or more different oral antipsychotics for greater than 90 days.<br>• Prior authorization is required for patients 21 years of age or older when 3 or more different oral second-generation antipsychotics are used for more than 180 days.<br>• Confirm diagnosis of FDA-approved or compendia-supported indication<br>• PA is required for initial prescription for beneficiaries younger than the drug-specific minimum age as indicated below: |

| | |
|---|---|
| aripiprazole (Abilify®) | 6 years |
| aripiprazole (Abilify MyCite®) | 18 years |
| asenapine (Saphris®) | 10 years |
| Asenapine (Secuado®) | 18 years |
| brexpiprazole (Rexulti®) | 13 years |
| cariprazine (Vraylar®) | 18 years |
| clozapine (Clozaril®, Versacloz®) | 12 years |
| iloperidone (Fanapt®) | 18 years |
| lumateperone (Caplyta™) | 18 years |
| lurasidone HCl (Latuda®) | 10 years |

| | | |
|---|---|---|
| | | <table><tr><td>olanzapine (Zyprexa®)</td><td>10 years</td></tr><tr><td>paliperidone ER (Invega®)</td><td>12 years</td></tr><tr><td>pimavanserin (Nuplazid®)</td><td>18 years</td></tr><tr><td>quetiapine fum. (Seroquel®, Seroquel XR®)</td><td>10 years</td></tr><tr><td>risperidone (Risperdal®)</td><td>5 years</td></tr><tr><td>ziprasidone HCl (Geodon®)</td><td>10 years</td></tr></table><br>• Require confirmation of diagnosis that supports the concurrent use of a Second Generation Antipsychotic and a CNS Stimulant for patients < 18 years of age<br>**STEP THERAPY (ST)**<br>• For all Second Generation Antipsychotics used in the treatment of Major Depressive Disorder in the absence of other psychiatric comorbidities, trial with at least two different antidepressant agents is required<br><br>**FREQUENCY/QUANTITY/DURATION (F/Q/D)**<br>• **asenapine (Secuado®)** 7.6 mg/24 hours<br>• **lumateperone (Caplyta™)** 42 mg capsules: Maximum 1 unit/day<br>• **paliperidone ER (Invega®)** 1.5 mg, 3 mg, 9 mg tablets: Maximum 1 unit/day<br>• **paliperidone ER (Invega®)** 6 mg tablets: Maximum 2 units/day<br>• **quetiapine/quetiapine ER (Seroquel®/Seroquel XR®):** Minimum 100 mg/day; maximum 800 mg/day<br>• **quetiapine (Seroquel®):** Maximum 3 units per day, 90 units per 30 days<br>• **quetiapine ER (Seroquel XR®)** 150 mg, 200 mg: 1 unit/day, 30 units/30 days<br>**quetiapine ER (Seroquel XR®)** 50 mg, 300 mg, 400 mg: 2 units/day, 60 units/30 days |

# Immunomodulators, Systemic Therapeutic Class Review

NEW YORK MEDICAID
DRUG UTILIZATION REVIEW BOARD MEETING
JULY 14, 2022

Magellan Rx MANAGEMENT℠

# Immunomodulators, Systemic

## New Clinical Information

- New Drug Entity: Cibinqo™ (abrocitinib), Adbry™ (tralokinumab)
- New Indications
- New Practice Guidelines
- Key Label Revisions

Magellan Rx MANAGEMENT℠

Immunomodulators, Systemic

# Cibinqo (abrocitinib)

- **Indications and Usage:**
  - Janus kinase (JAK) inhibitor indicated for the treatment of adults with refractory, moderate-to-severe atopic dermatitis whose disease is not adequately controlled with other systemic drug products, including biologics, or when use of those therapies is inadvisable
  - Not recommended for use in combination with other JAK inhibitors, biologic immunomodulators, or with other immunosuppressants

- **Dosage/Availability:**
  - Tablets: 50 mg, 100 mg, and 200 mg
  - Recommended dosage is 100 mg orally once daily
  - 200 mg orally once daily is recommended for those patients who are not responding to 100 mg once daily
  - Moderate renal impairment: 50 mg once daily or 100 mg once daily for those patients who are not responding to 50 mg once daily
  - CYP2C19 poor metabolizer: 50 mg once daily or 100 mg once daily for those patients who are not responding to 50 mg once daily

Cibinqo [package insert]. New York, NY; Pfizer; January 2022.

Immunomodulators, Systemic

# Cibinqo (abrocitinib) cont.

- **Contraindications:**
  - Antiplatelet therapies except for low-dose aspirin (≤81 mg daily), during the first 3 months of treatment

- **Warnings:**
  - Laboratory Abnormalities: Laboratory monitoring is recommended due to potential changes in platelets, lymphocytes, and lipids.
  - Immunizations: Avoid use of live vaccines prior to, during, and immediately after treatment.

- **Black Box Warning:**
  - Serious infections, mortality, malignancy, major adverse cardiovascular events, and thrombosis

Cibinqo [package insert]. New York, NY; Pfizer; January 2022.

Immunomodulators, Systemic

# Cibinqo (abrocitinib) cont.

- **Common Adverse Drug Reactions:**
  - (≥1%) in subjects receiving 100 mg and 200 mg: nasopharyngitis, nausea, headache, herpes simplex, increased blood creatine phosphokinase, dizziness, urinary tract infection, fatigue, acne, vomiting, oropharyngeal pain, influenza, gastroenteritis
  - (≥1%) in subjects receiving either 100 mg or 200 mg: impetigo, hypertension, contact dermatitis, upper abdominal pain, abdominal discomfort, herpes zoster, and thrombocytopenia
- **Drug Interactions:**
  - Strong inhibitors of CYP2C19: 50 mg daily or 100 mg once daily
  - Moderate to strong inhibitors of both CYP2C19 and CYP2C9, or strong CYP2C19 or CYP2C9 inducers: Avoid concomitant use
  - P-gp substrate where small concentration changes may lead to serious or life-threatening toxicities: Monitor or titrate dosage of P-gp substrate
- **Specific Populations:**
  - Lactation: Breastfeeding not recommended.
  - Renal Impairment: Avoid use in patients with severe renal impairment or end-stage renal disease
  - Hepatic Impairment: Avoid use in patients with severe hepatic impairment.
- **Clinical Comparative Studies (within class):**
  - None available

Cibinqo [package insert]. New York, NY; Pfizer; January 2022.

Immunomodulators, Systemic

# Adbry (tralokinumab)

- **Indications and Usage:**
  - Interleukin-13 antagonist indicated for the treatment of moderate-to-severe atopic dermatitis in adult patients whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable
  - Can be used with or without topical corticosteroids

- **Dosing/Availability:**
  - SQ Injection: 150 mg/mL solution in a single-dose prefilled syringe with needle guard
  - Initial dose of 600 mg (four 150 mg injections), followed by 300 mg (two 150 mg injections) administered every other week
  - A dosage of 300 mg every 4 weeks may be considered for patients below 100 kg who achieve clear or almost clear skin after 16 weeks of treatment

Adbry [package insert]. Madison, NJ; LEO Pharma; January 2022.

Immunomodulators, Systemic

# Adbry (tralokinumab) cont.

- **Contraindications:**
  - Known hypersensitivity to tralokinumab-ldrm or any excipients

- **Warnings:**
  - Hypersensitivity
  - Conjunctivitis and Keratitis
  - Parasitic (Helminth) Infections
  - Risk of Infection with Live Vaccines

- **Common Adverse Drug Reactions (incidence ≥ 1%):**
  - Upper respiratory tract infections, conjunctivitis, injection site reactions, and eosinophilia

Adbry [package insert]. Madison, NJ; LEO Pharma; January 2022.

# Adbry (tralokinumab) cont.

- **Drug Interactions:**
  - Drug interactions have not been assessed

- **Specific Populations:**
  - Pregnancy: There are limited data in pregnant women to inform a drug-associated risk of adverse developmental outcomes. Human IgG antibodies are known to cross the placental barrier; therefore, Adbry may be transmitted from the mother to the developing fetus
  - Lactation: No data
  - Pediatrics: safety and effectiveness have not been established

- **Clinical Comparative Studies (within class):**
  - None available

Adbry [package insert]. Madison, NJ; LEO Pharma; January 2022.

Immunomodulators, Systemic

# New Indications

- **Dupixent® (dupilumab)**
  - Treatment of adult and pediatric patients aged 6 months and older with moderate-to-severe atopic dermatitis; previously indicated for atopic dermatitis patients ≥ 6 years old
  - Treatment of adult and pediatric patients aged 12 years and older, weighing at least 40 kg, with eosinophilic esophagitis
  - Expanded indication of add-on maintenance treatment of moderate-to-severe asthma in patients aged 6 years and older; previously 12 years and older

- **Olumiant (baricitinib)**
  - Treatment of COVID-19 in hospitalized adults requiring supplemental oxygen, noninvasive or invasive mechanical ventilation, or extracorporeal membrane oxygenation
  - The treatment of adult patients with severe alopecia areata

- **Nucala (mepolizumab)**
  - Add-on maintenance treatment of adult patients 18 years and older with chronic rhinosinusitis with nasal polyps

Please see most current individual prescribing information

Immunomodulators, Systemic

# New Indications – continued

- **Skyrizi® (risankizumab)**
  - Treatment of active psoriatic arthritis (PsA) in adults
  - Treatment of moderately to severely active Crohn's Disease

- **Otezla® (apremilast)**
  - Mild to moderate plaque psoriasis; previously moderate to severe

- **Cosentyx® (secukinumab)**
  - Expanded indication to include active juvenile PsA in pts ≥ 2 years of age; previously only indicated for adults with active PsA
  - Active enthesitis-related arthritis in pts ≥ 4 years of age
  - Expanded use for moderate to severe plaque psoriasis in patients who are candidates for systemic therapy or phototherapy to include patients ≥ 6 years; previously only approved for use in adults

- **Orencia® (abatacept)**
  - Prophylaxis of acute graft versus host disease (aGVHD) in combination with a calcineurin inhibitor and methotrexate, in adults and peds ≥2 yo undergoing hematopoietic stem cell transplantation

# New Indications – continued

- **Xeljanz® (tofacitinib)**
  - Treatment of adults with active ankylosing spondylitis who have had an inadequate response or intolerance to ≥ 1 TNF blocker

- **Rinvoq® (upadacitinib)**
  - Use in adults with active ankylosing spondylitis who have had an inadequate response or intolerance to one or more TNF blockers
  - Treatment of adult patients with moderately to severely active ulcerative colitis who have had an inadequate response or intolerance to 1 or more TNF blockers
  - Treatment of adults and pediatric patients ≥ 12 years old with refractory, moderate-to-severe atopic dermatitis
  - Treatment of adults with active psoriatic arthritis who had inadequate response or intolerance to ≥ 1 TNF blocker

# Practice Guidelines

- **American College of Rheumatology:**
  - For systemic juvenile idiopathic arthritis without macrophage activation syndrome, biologic disease-modifying antirheumatic drugs (DMARDs) are conditionally recommended as initial therapy, although there is no preferred agent, and these are strongly recommended over conventional DMARDs.

- **American Gastroenterological Association:**
  - Published guidelines for the management of moderate to severe luminal and fistulizing Crohn's disease in adult outpatients. They recommend anti-TNFα therapy over no treatment for induction and maintenance of remission.

https://www.rheumatology.org/Portals/0/Files/ACR-JIA%20Guideline-Oligo-TMJ-sJIA-EarlyView.pdf
https://www.gastrojournal.org/article/S0016-5085(21)00645-4/fulltext.

# Comparative Studies (within class)

- **Secukinumab (Cosentyx) versus Adalimumab (Humira) :**
  - EXCEED assessed the efficacy of secukinumab and adalimumab for the treatment of adults with active psoriatic arthritis
  - The primary endpoint analyzed superiority of secukinumab over adalimumab was not met
- **Ustekinumab (Stelara) versus Adalimumab (Humira)**
  - SEAVUE study evaluated the efficacy and safety of Stelara and adalimumab in adult patients with moderately to severely active Crohn's disease who were biologic-naïve
  - No statistically significant difference was found in clinical remission rates at week 52 (primary endpoint) between patients treated with Stelara and those treated with adalimumab

https://pubmed.ncbi.nlm.nih.gov/32386593/
https://pubmed.ncbi.nlm.nih.gov/35691323/

Immunomodulators, Systemic

# Key Label Revisions

- **Dupixent:**
  - Addition of angioedema and facial skin reactions, information on the conjunctivitis and keratitis adverse drug reaction from post marketing data
- **Orencia:**
  - Clinical considerations for live vaccines in infants exposed to Orencia
  - Addition of a Warning subsection for cytomegalovirus and Epstein-Barr virus reactivation in aGVHD
- **Olumiant:**
  - Boxed warning updates to include information about increased risks of serious heart-related events, cancer, blood clots, and death
- **Rinvoq:**
  - Boxed warning updates to include information about increased risks of serious heart-related events, cancer, blood clots, and death
  - RA revised to inadequate response or intolerance to ≥ 1 TNF blocker
- **Xeljanz / XR:**
  - Boxed warning updates to include information about increased risks of serious heart-related events, cancer, blood clots, and death
  - Rheumatoid arthritis, psoriatic arthritis, and polyarticular juvenile idiopathic arthritis revised to an inadequate response or intolerance to ≥ 1 TNF blocker

| Preferred Drugs | Non-Preferred Drugs | Prior Authorization/Coverage Parameters |
|---|---|---|
| **Immunomodulators – Systemic** CC, ST | | |
| Cosentyx®<br>Dupixent®<br>Enbrel®<br>Fasenra®<br>Humira®<br>Nucala®<br>Xolair® | Actemra® (subcutaneous)<br>Adbry™<br>Cibinqo™<br>Cimzia®<br>Ilumya®<br>Kevzara®<br>Kineret®<br>Olumiant®<br>Orencia® (subcutaneous)<br>Otezla®<br>Rinvoq™ ER<br>Siliq™<br>Simponi®<br>Skyrizi™<br>Stelara®<br>Taltz®<br>Tremfya®<br>Xeljanz®<br>Xeljanz® XR | **CLINICAL CRITERIA (CC)**<br>• Confirm diagnosis for FDA- or compendia-supported uses<br>**STEP THERAPY (ST)**<br>• Trial of a disease-modifying anti-rheumatic drug (DMARD) prior to treatment with an immunomodulator **for indications not specified below**<br>• Trial of a TNF inhibitor prior to treatment with a JAK inhibitor **for indications not specified below**<br>**INDICATION-SPECIFIC REQUIREMENTS:**<br>• Asthma: history and concurrent use of a corticosteroid<br>• Nasal polyps: history and concurrent use of an intranasal corticosteroid<br>• Atopic dermatitis: trial with a medium or high potency topical steroid AND one other topical prescription agent (other than a steroid), for a combined duration of at least 6 months prior |

# Systemic Immunomodulators for Atopic Dermatitis: Review of Preferred Drug List Clinical Criteria

## NYS Medicaid Drug Utilization Review Board
## July 14, 2022

NEW YORK STATE | Department of Health | Office of Health Insurance Programs
SUNY The State University of New York

# Systemic immunomodulators for atopic dermatitis

| Drug / Mechanism | FDA Indication for Atopic Dermatitis | Ages | Formulation / Usual Dosage |
|---|---|---|---|
| **Dupilumab (Dupixent®)**<br>IL-4 receptor alpha antagonist | **Moderate-to-severe atopic dermatitis not adequately controlled with topical prescription therapies** or when such therapies are not advised | ≥6 months | Single-dose syringes and pens for SUBQ injection<br>Adults: 600 mg initial dose, then 300 mg Q2W<br>Ages 6 months – 17 years: weight-based dosing |
| **Tralokinumab-ldrm (Adbry™)**<br>IL-13 antagonist | **Moderate-to-severe atopic dermatitis not adequately controlled with topical prescription therapies** or when such therapies are not advised | Adults | Single-dose syringes and pens for SUBQ injection<br>600 mg initial dose, then 300 mg Q2W |
| **Abrocitinib (Cibinqo™)**<br>JAK inhibitor | **Refractory, moderate-to-severe atopic dermatitis not adequately controlled with other systemic drug products**, including biologics, or when such therapies are not advised | Adults | Oral tablets<br>100 mg once daily<br>(may increase to 200 mg if response is inadequate) |
| **Upadacitinib (Rinvoq®)**<br>JAK inhibitor | **Refractory, moderate-to-severe atopic dermatitis not adequately controlled with other systemic drug products**, including biologics, or when such therapies are not advised | ≥12 years | Extended-release oral tablets<br>15 mg once daily<br>(may increase to 30 mg if response is inadequate) |

FDA=Food and Drug Administration; IL=interleukin; JAK=Janus kinase; Q2W=every other week; SC=subcutaneous

- The JAK inhibitors carry a boxed warning for serious infections, mortality, malignancy, major adverse cardiovascular events, and thrombosis

Adbry™ package insert. Madison, NY: LEO Pharma, Inc.; January 2022.
Cibinqo™ package insert. New York, NY: Pfizer, Inc.; February 2022.
Dupixent® package insert. Tarrytown, NY: Regeneron Pharmaceuticals; June 2022.
Rinvoq® package insert. North Chicago, IL: AbbVie Inc; April 2022.

# Current Clinical Criteria

## Atopic dermatitis drugs in systemic immunomodulators FFS PDL category

| Preferred | Non-preferred | Prior Authorization/Coverage Parameters |
|---|---|---|
| Dupixent® | Adbry™<br>Cibinqo™<br>Rinvoq® ER | Clinical criteria:<br>• Confirm diagnosis for FDA- or compendia-supported uses<br><br>Step therapy indication-specific requirements for atopic dermatitis:<br>• Trial with a medium or high potency topical steroid AND 1 other topical prescription agent (other than a steroid) for a combined duration of at least 6 months prior |

ER=extended-release; FDA=Food and Drug Administration; FFS=fee-for-service; PDL=Preferred Drug List
Source: NYS Medicaid FFS PDL; revised May 5, 2022. Available at: https://newyork.fhsc.com/downloads/providers/NYRx_PDP_PDL.pdf

- Clinical criteria and step therapy for Dupixent® (dupilumab) were implemented in 2017
- Adbry™ (tralokinumab-ldrm) was added after FDA approval for atopic dermatitis in 2021
- Cibinqo™ (abrocitinib) and Rinvoq® (upadacitinib) were added after FDA approval for atopic dermatitis in 2022

# Topical prescription agents (other than steroids) FDA approved for atopic dermatitis

- Crisaborole (Eucrisa®): phosphodiesterase-4 inhibitor indicated for mild-to-moderate atopic dermatitis in ages ≥3 months
- Pimecrolimus (Elidel®): calcineurin inhibitor indicated as 2nd line therapy for short-term, non-continuous treatment of mild-to-moderate atopic dermatitis in ages ≥2 years
- Ruxolitinib (Opzelura™): Janus kinase inhibitor indicated for short-term, non-continuous treatment of mild-to-moderate atopic dermatitis not adequately controlled with topical prescription therapies in patients ≥12 years
- Tacrolimus (Protopic®): calcineurin inhibitor indicated as 2nd line therapy for short-term, non-continuous treatment of moderate-to-severe atopic dermatitis in ages ≥2 years

Drugs that treat atopic dermatitis. In IBM Micromedex®. Armonk, NY: IBM Micromedex Corporation. www.micromedexsolutions.com. Accessed May 25, 2022.

# Clinical Guidance

- American Academy of Dermatology (AAD) guidelines:
  - New series of atopic dermatitis guidelines will supersede the 2014 guidelines
    - First update (published in January 2022) focuses on awareness of comorbidities associated with atopic dermatitis in adults and contains no updated guidance on treatments
  - 2014 guidelines recommended systemic immunomodulatory agents for patients with signs and symptoms not adequately controlled with optimized topical regimens and/or phototherapy
    - Data was insufficient to make firm recommendations on any agent
    - Published prior to FDA approval of the targeted therapies for atopic dermatitis

AAD atopic dermatitis clinical guideline. https://www.aad.org/member/clinical-quality/guidelines/atopic-dermatitis
Davis DMR et al. *J Am Acad Dermatol* 2022. https://doi.org/10.1016/j.jaad.2022.01.009
Sidbury R et al. *J Am Acad Dermatol* 2014. https://doi.org/10.1016/j.jaad.2014.03.030

# Clinical Guidance

- Expert perspectives on management of moderate-to-severe atopic dermatitis (2017):
  - Multidisciplinary consensus of US practitioners addressing current and emerging therapies
  - Defined treatment failure as any 1 of the following, despite appropriate dose, duration, and adherence to a therapeutic agent:
    - Inadequate clinical improvement
    - Failure to achieve stable long-term disease control
    - Presence of ongoing impairment
    - Unacceptable adverse events or intolerability
  - No generalizable time to demonstrate efficacy of topical treatments
    - Recommended regimen duration up to 4 weeks for active treatment and 2-3 times weekly to prevent recurrence; some patients and body sites may require >4 weeks of treatment
  - Role of emerging biologics:
    - Dupilumab recommended as a first-line systemic treatment in adults with moderate-to-severe atopic dermatitis who are uncontrolled with topical therapies
    - Safety and efficacy of future biologics or small molecules need to be evaluated to determine place in therapy

US=United States

Boguniewicz M et al. *J Allery Clin Immunol Pract* 2017. https://doi.org/10.1016/j.jaip.2017.08.005

# Clinical Guidance

- "Atopic Dermatitis Yardstick": practical recommendations for an evolving therapeutic landscape (American College of Allergy, Asthma, & Immunology [ACAAI], 2018)
- Step care management:

| | Non-Lesional | Mild | Moderate | Severe |
|---|---|---|---|---|
| Maintenance | Basic management:<br>1. Skin care<br>2. Trigger avoidance | Basic management:<br>1. Skin care<br>2. Antiseptic measures<br>3. Trigger avoidance | Basic management + topical anti-inflammatory medication:<br>• Maintenance TCS (low- to medium-potency)<br>• ***OR*** Maintenance TCI<br>• ***OR*** Crisaborole | Basic management + referral to specialist<br>• Phototherapy<br>• Dupilumab<br>• Systemic immunosuppressants*<br>Consider acute treatment for some patients:<br>• Wet wrap therapy<br>• Short-term hospitalization |
| Acute | Low- to medium-potency TCS on inflamed skin [consider TCI, crisaborole] | | Medium- to high-potency TCS on inflamed skin [consider TCI, crisaborole] | |

TCI=topical calcineurin inhibitor; TCS=topical corticosteroid; *systemic immunosuppressants include: cyclosporine, methotrexate, mycophenolate mofetil, azathioprine (none of which are FDA-approved for atopic dermatitis), corticosteroids (not recommended for long-term maintenance)

- Use shared decision-making for treatment decisions
- Before stepping up, reassess adherence, potential comorbidities; confirm that increased symptom level is due to AD
- When stepping up (mild to moderate or moderate to severe): 3-month therapeutic trial with reassessment at 4-8 weeks

Boguniewicz M et al. *Ann Allergy Asthma Immunol* 2018. https://doi.org/10.1016/j.anai.2017.10.039

# Clinical Guidance

- Living systematic review and network meta-analysis of systemic immunomodulatory treatments for atopic dermatitis (updated in March 2022)
  - Total of 60 trials with 16,579 patients, most in adults receiving up to 16 weeks of therapy, most vs placebo; insufficient data to conduct analysis in children
  - Results for 5 targeted therapies 8 to 16 weeks in adults:

| Drug regimens vs dupilumab 600 mg, then 300 mg Q2W | Comparison of reductions in EASI scores* |
|---|---|
| Abrocitinib 200 mg once daily | MD 2.2 (95% CrI, 0.2-4.0) |
| Abrocitinib 100 mg once daily | MD −2.1 (95% CrI, −4.1 to −0.3) |
| Upadacitinib 30 mg once daily | MD 2.7 (95% CrI, 0.6-4.7) |
| Upadacitinib 15 mg once daily | MD 0.2 (95% CrI, −1.9 to 2.2) |
| Tralokinumab 600 mg, then 300 mg Q2W | MD −3.5 (95% CrI, −5.8 to −1.3) |
| Baricitinib 4 mg once daily | MD −3.2 (95% CrI, −5.7 to −0.8) |
| Baricitinib 2 mg once daily | MD −5.2 (95% CrI, −7.5 to −2.9) |

*All results with high certainty of evidence CrI=credible interval; EASI=Eczema Area & Severity Index; MD=mean difference; Q2W=every other week

  - Pattern of results was similar for Dermatology Life Quality Index and Peak Pruritis Numeric Rating Scale.
  - Authors concluded abrocitinib, baricitinib, upadacitinib, and tralokinumab were associated with comparable improvements in index scores compared to dupilumab for moderate-to-severe atopic dermatitis.

Drucker AM et al. *JAMA Dermatol* 2022. https://doi.org/10.1001/jamadermatol.2022.0455

# Comparator State Medicaid Programs

- Preferred drug list criteria for 9 comparator state programs were reviewed
  - California, Colorado, Florida, Illinois, Massachusetts, Michigan, Pennsylvania, Texas, Washington
- Dupixent® is a preferred drug for atopic dermatitis in 4/9 states
- Dupixent® and other systemic immunomodulators for atopic dermatitis require prior authorization in 9/9 states
- Prior authorization criteria include some or all of the following:
  - FDA-indicated age and diagnosis, documented disease severity, consultation with a specialist, failure with a trial of 1 or more topical and/or systemic agents

California Department of Health Care Services. Medi-Cal Formulary. Available at https://medi-calrx.dhcs.ca.gov/home/cdl/. Accessed May 31, 2022; Colorado Department of Health Care Policy and Financing. Health First Colorado Pharmacy Benefit. PDL effective July 1, 2022. Available at https://hcpf.colorado.gov/medicaid-pharmacy-benefits. Accessed May 31, 2022; Florida Agency for Health Care Administration. Florida Medicaid Drug Criteria. Available at https://ahca.myflorida.com/medicaid/prescribed_drug/drug_criteria.shtml. Accessed May 31, 2022; Illinois Department of Healthcare and Family Services. Medicaid Preferred Drug List. Available at https://www2.illinois.gov/hfs/MedicalProviders/Pharmacy/preferred/Pages/default.aspx. Accessed May 31, 2022; Commonwealth of Massachusetts MassHealth Drug Utilization Review Program. Available at https://mhdl.pharmacy.services.conduent.com/MHDL/. Accessed June 1, 2022; Michigan Department of Health and Human Services. Medicaid Health Plan Pharmacy Benefit. Available at https://www.michigan.gov/mdhhs/0,5885,7-339-71547_4860-380454--,00.html. Accessed June 1, 2022; Pennsylvania Department of Human Services. Statewide Preferred Drug List. Available at https://papdl.com/preferred-drug-list. Accessed June 1, 2022; Texas Medicaid & Healthcare Partnership. Formulary search. Available at https://www.txvendordrug.com/formulary/prior-authorization/preferred-drugs. Accessed June1, 2022; Washington State Health Care Authority. Apple Health Preferred Drug List (5/20/22 – 6/2/22). Available at https://www.hca.wa.gov/billers-providers-partners/programs-and-services/apple-health-preferred-drug-list-pdl. Accessed June 1, 2022.

# Summary

- Clinical guidance for treatment of atopic dermatitis is evolving as evidence for targeted systemic therapies is accumulating
- Four systemic immunomodulators have been FDA approved for treatment of moderate-to-severe atopic dermatitis:
  - Biologics: Dupixent® (dupilumab) in 2017 and Adbry™ (tralokinumab-ldrm) in 2021
  - JAK inhibitors: Cibinqo™ (abrocitinib) and Rinvoq® (upadacitinib) in 2022
- Dupilumab and tralokinumab are FDA indicated when topical therapies are inadequate
- Abrocitinib and upadacitinib are FDA indicated when other systemic drugs, including biologics, are inadequate

# Summary

- In 2017 dupilumab was defined by expert consensus as a first-line systemic treatment for patients with moderate-to-severe atopic dermatitis that is uncontrolled with topical therapies
- Per the “Atopic Dermatitis Yardstick” published by ACAAI in 2018:
  - Stepping up to maintenance treatment with dupilumab is recommended for patients who are symptomatic despite an aggressive course of topical prescription therapy (TCS, TCI, or crisaborole) for ≥3 weeks and following basic management for skin care, antiseptic treatment, and avoidance of triggers; a 3-month therapeutic trial and referral to a specialist are recommended
- Current FFS clinical criteria for all 4 systemic agents require confirmed diagnosis for FDA-approved or compendia-supported use and step therapy with a trial of a medium- or high-potency topical steroid AND 1 other topical prescription agent (other than a steroid) for a combined duration of at least 6 months prior

# Recommendation

- Consider prior authorization for systemic immunomodulators for atopic dermatitis with clinical criteria including:
  - FDA-approved or compendia-supported diagnosis and age, documented disease severity, and consultation with a specialist
  - Modification of the indication-specific step therapy requirements as follows:
    - Trial with a topical prescription agent for a duration of at least 3 months prior to initiating a biologic systemic immunomodulator
    - Trial with a topical prescription agent AND a trial with another systemic agent for a combined duration of at least 6 months prior to initiating a systemic JAK inhibitor

# Glucagon Agents Therapeutic Class Review

NEW YORK MEDICAID
DRUG UTILIZATION REVIEW BOARD MEETING
JULY 14, 2022

Magellan Rx MANAGEMENT℠

Glucagon Agents

# Overview

- Hypoglycemia is classified as level 1 (glucose < 70 mg/dL and ≥ 54 mg/dL), level 2 (glucose < 54 mg/dL), or level 3 (severe event: altered mental and/or physical status requiring assistance to treat).

- Hypoglycemia can be reversed through administration of rapid-acting glucose or glucagon. For patients unable or not willing to consume carbohydrates by mouth, use of glucagon is indicated for treating hypoglycemia.

American Diabetes Association. Glycemic Targets: Standards of Medical Care in Diabetes -2022. Diabetes Care. 2022; 45 (Supplement 1): S83-S96. Available at: https://diabetesjournals.org/care/article/45/Supplement_1/S83/138927/6-Glycemic-Targets-Standards-of-Medical-Care-in. Accessed February 7, 2022. DOI: 10.2337/dc22-S006.

Magellan Rx MANAGEMENT℠

Glucagon Agents

# Mechanism of Action

- **Glucagon, Gvoke (glucagon), Zegalogue (dasiglucagon), Baqsimi (glucagon)**
  - Glucagon increases blood glucose concentration by activating hepatic glucagon receptors, thereby stimulating glycogen breakdown and release of glucose from the liver. Hepatic stores of glycogen are necessary for glucagon to produce an antihypoglycemic effect.

Gvoke [package insert]. Chicago, IL; Xeris; August 2021.
Baqsimi [package insert]. Indianapolis, IN; Eli Lilly; October 2020.
Zegalogue [package insert]. Durham, NC; Zealand; April 2021
Glucagon for Injection [package insert]. September 2019

Glucagon Agents

# Indications and Usage

| Drug | Indications |
|---|---|
| Glucagon, Glucagon Emergency Kit | Treatment of severe hypoglycemia in pediatric and adult patients with diabetes<br>Indicated as a diagnostic aid for use during radiologic examinations to temporarily inhibit movement of the gastrointestinal tract in adult patients |
| Gvoke (glucagon) | Treatment of severe hypoglycemia in pediatric and adult patients with diabetes ages 2 years and above |
| Zegalogue (dasiglucagon) | Treatment of severe hypoglycemia in pediatric and adult patients with diabetes aged 6 years and above |
| Baqsimi (glucagon) | Treatment of severe hypoglycemia in adult and pediatric patients with diabetes ages 4 years and above |

Gvoke [package insert]. Chicago, IL; Xeris; August 2021.
Baqsimi [package insert]. Indianapolis, IN; Eli Lilly; October 2020.
Zegalogue [package insert]. Durham, NC; Zealand; April 2021
Glucagon for Injection [package insert]. September 2019

Glucagon Agents

# Dosage/Availability/Formulation

| Drug | Availability/Formulation |
|---|---|
| Glucagon, Glucagon Emergency Kit | Injection Powder for Solution: 1 mg |
| Gvoke (glucagon) | Gvoke Kit: Subcutaneous Solution 1 mg/0.2 mL<br>Gvoke HypoPen 1 Pack: Subcutaneous Solution 1 mg/0.2 mL, 0.5 mg/0.1 mL<br>Gvoke HypoPen 2 Pack: Subcutaneous Solution 0.5 mg/0.1 mL, 1 mg/0.2 mL<br>Gvoke PFS 1 Pack: Subcutaneous Solution 1 mg/ 0.2 mL, 0.5 mg/0.1 mL<br>Gvoke PFS 2 Pack: Subcutaneous Solution 1 mg/0.2 mL, 0.5 mg/0.1 mL |
| Zegalogue (dasiglucagon) | Autoinjector and Prefilled Syringe: 0.6 mg/0.6 mL |
| Baqsimi (glucagon) | Nasal Powder: 3 mg/1 actuation |

Glucagon Agents

# Contraindications/Warnings

- **Glucagon Class Contraindications:**
  - Pheochromocytoma, insulinoma, known hypersensitivity to glucagon or to any of the excipients

- **Glucagon Class Warnings:**
  - Administration may stimulate catecholamine release in patients with pheochromocytoma
  - Patients with insulinoma may experience a lack of efficacy due to exaggerated insulin release after administration
  - Hypersensitivity and allergic reactions have been reported including generalized rash, hypotension, and anaphylactic shock with breathing difficulties
  - Lack of efficacy in patients with decreased hepatic glycogen; these patients should be treated with glucose

- **Specific Drugs:**
  - Gvoke: Post marketing reports of Necrolytic Migratory Erythema (NME)

Gvoke [package insert]. Chicago, IL; Xeris; August 2021.
Baqsimi [package insert]. Indianapolis, IN; Eli Lilly; October 2020.
Zegalogue [package insert]. Durham, NC; Zealand; April 2021
Glucagon for Injection [package insert]. September 2019

# Glucagon Agents

- **Common Adverse Drug Reactions:**
  - Injectables: Nausea, vomiting, headache, and injection site reaction
  - Nasal: Nausea, vomiting, headache, upper respiratory tract irritation (e.g., rhinorrhea, nasal discomfort, nasal congestion, cough, epistaxis), watery eyes, redness of eyes, itchy nose, itchy throat, itchy eyes, sneezing
- **Drug Interactions:**
  - Patients taking beta-blockers may experience a transient increase in blood pressure and pulse
  - Patients taking indomethacin may not experience an increase in blood sugar after glucagon administration and could potentially experience hypoglycemia
  - Concomitant use with warfarin may increase the anticoagulant effect of the drug
- **Specific Populations:**
  - Pregnancy: Limited data with use have not found a drug-associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes.
  - Pediatrics: Safety and efficacy established for Gvoke 2 years and above, Zegalogue 6 years and above, Baqsimi 4 years and above, Glucagon infants and above

Gvoke [package insert]. Chicago, IL; Xeris; August 2021.
Baqsimi [package insert]. Indianapolis, IN; Eli Lilly; October 2020.
Zegalogue [package insert]. Durham, NC; Zealand; April 2021
Glucagon for Injection [package insert]. September 2019

Glucagon Agents

# Comparative Studies (within class)

- **Baqsimi vs intramuscular glucagon (IMG):**
  - Three studies used primary outcome measures in increase in BG ≥ 70 mg/dL or an increase of ≥ 20 mg/dL from glucose nadir within 30 minutes after receiving glucagon
  - All studies demonstrated non-inferiority of Baqsimi to IMG in reversing insulin-induced hypoglycemia

- **Gvoke vs glucagon emergency kit (GEK):**
  - Treatment success was defined as an increase in plasma glucose > 70 mg/dL or a relative increase of ≥ 20 mg/dL at 30 minutes after glucagon administration
  - Results were non-inferior with a similar tolerability profile

Safety and Efficacy of G-Pen Compared to Lilly Glucagon for Hypoglycemia Rescue in Adult Type 1 Diabetics. Available at: https://clinicaltrials.gov/ct2/show/NCT02656069?term=NCT02656069&draw=2&rank=1.
Rickels MR, Ruedy JR, Foster NC, et al. Intranasal glucagon for treatment of insulin-induced hypoglycemia in adults with type 1 diabetes: a randomized crossover noninferiority study. Diabetes Care. 2016; 39(2): 264-270. DOI: 10.2337/dc15-1498.

Glucagon Agents

# Place in Therapy

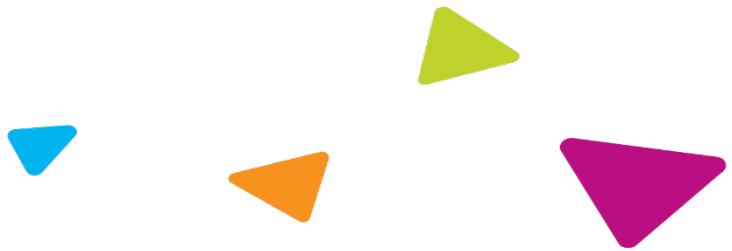
- The American Diabetes Association (ADA) guidelines acknowledge that intranasal glucagon and ready-to-inject glucagon preparations for subcutaneous injection are available in addition to traditional glucagon injection powder requiring reconstitution. No specific glucagon product is identified as being preferred.

- The ADA 2022 Standards of Medical Care in Diabetes recommends glucagon should be prescribed for all individuals who are at an increased risk for level 2 hypoglycemia (blood glucose < 54 mg/dL) or level 3 hypoglycemia, accessible as needed.

American Diabetes Association. Glycemic Targets: Standards of Medical Care in Diabetes -2022. Diabetes Care. 2022; 45 (Supplement 1): S83-S96. Available at: https://diabetesjournals.org/care/article/45/Supplement_1/S83/138927/6-Glycemic-Targets-Standards-of-Medical-Care-in. Accessed February 7, 2022. DOI: 10.2337/dc22-S006.

New York State Medicaid Drug Utilization Review Board Meeting – July 14, 2022
Preferred Drug Program – Drug Class Review

| Preferred Drugs | Non-Preferred Drugs | Prior Authorization/Coverage Parameters |
|---|---|---|
| **Glucagon Agents *new class to add to the PDL after the JUL 2022 DURB mtg** | | |
| | | |



Magellan Rx MANAGEMENT℠

# Aduhelm® (aducanumab-avwa [BBIIB037])

July 14, 2022
DURB Meeting

NEW YORK STATE | Department of Health | Office of Health Insurance Programs
SUNY The State University of New York

# Purpose

- The aim of the DURB review is to provide recommendations for the management of aducanumab in the Medicaid program.

- Aduhelm® (aducanumab-avwa or aducanumab) was approved by the Food and Drug Administration (FDA) on June 7, 2021.

# Background

- FDA approved for the treatment of Alzheimer's disease.
- Treatment should be initiated in patients with mild cognitive impairment (MCI) or mild dementia stage of Alzheimer's disease.
- Approved under the FDA accelerated approval process based on the surrogate endpoint of reducing amyloid-beta (Aβ) plaques in people with MCI or mild dementia stage of Alzheimer's disease.
- A recombinant human immunoglobulin G1 (IgG1) monoclonal antibody designed to promote the clearance of amyloid aggregates and insoluble forms of Aβ in the brain.
- Aβ plaques in the brain are a pathophysiological feature of Alzheimer's disease.

Aduhelm® [Package Insert]. Cambridge, MA; Biogen and Eisai. April 2022.

# Background

| | |
|---|---|
| Recommended Doses | IV Infusions should be administered every 4 weeks.<br>• Dose 1 and 2: 1 mg/kg<br>• Dose 3 and 4: 3 mg/kg<br>• Dose 5 and 6: 6 mg/kg<br>• Maintenance dose (Infusion 7 and beyond): 10 mg/kg |
| Monitoring | The drug can cause amyloid-related imaging abnormalities (ARIA) with edema/effusion (ARIA-E) or with microhemorrhage/hemosiderosis (ARIA-H); therefore, brain magnetic resonance imaging (MRI) is required within 1 year before initiating therapy and before the 6th, 7th, 9th, and 12th IV infusions.<br><br>If ARIA is identified on the MRI based on the clinical symptom severity, dosing may need to be suspended or permanently discontinued until the MRI demonstrates radiographic resolution and symptoms resolve. Continuation of treatment should be guided by clinical judgment.<br><br>In patients who develop intracerebral hemorrhage >1 cm in diameter during treatment, suspend dosing until MRI demonstrates radiographic stabilization and until symptoms, if present, resolve. Use clinical judgment in considering whether to continue treatment or permanently discontinue treatment. |
| Warnings and Precautions | Enhanced clinical vigilance for ARIA is recommended during the first 8 doses of treatment.<br><br>Testing for ApoE ε4 carrier status may be considered when initiating treatment as patients in studies 1 and 2 who were ApoE ε4 carriers had a higher incidence of ARIA.<br><br>In Study 1 (NCT02484547 [EMERGE]) and Study 2 (NCT02477800 [ENGAGE]), patients were excluded if they were using antiplatelet or anticoagulant medications other than aspirin ≤325 mg/day. There are limited data regarding the risk of ARIA in patients receiving antiplatelet or anticoagulant medications other than aspirin ≤325 mg/ day, and no specific recommendations were provided.<br><br>Seizure, including status epilepticus, which can be serious and life-threatening, has been associated with ARIA.<br><br>Hypersensitivity reactions, angioedema, and urticaria were reported during infusion of aducanumab. Therapy should be stopped immediately at the first observation of any signs or symptoms consistent with a hypersensitivity reaction. |

Aduhelm® [Package Insert]. Cambridge, MA; Biogen and Eisai. April 2022.

# Clinical Trials

- PRIME, a phase 1b study, demonstrated that aducanumab treatment resulted in a dose- and time-dependent reduction in Aβ plaques.
  - A placebo-controlled period through week 54, followed by a long-term extension study to week 518; the extension study was terminated early based on the futility analysis of phase 3 trials

- The ENGAGE and EMERGE studies were identically designed phase 3 studies; their objectives were to assess the efficacy and safety of aducanumab in patients with MCI due to Alzheimer's disease and mild dementia associated with Alzheimer's disease.

- The ENGAGE and EMERGE studies were terminated early based on a prespecified futility analysis to predict the future unobserved treatment effect from pooled data from the participants who had completed their week 78 visit.

Haeberlein SB et al. *J Prev Alz Dis*. 2022. http://dx.doi.org/10.14283/jpad.2022.30

# Phase 3 Clinical Trials: Study Design

| | |
|---|---|
| Study Design | A Phase 3 Multicenter, Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Study |
| Inclusion Criteria | Age 50-85 years; and<br>Must meet all of the following clinical criteria for MCI due to Alzheimer's disease or mild Alzheimer's disease and must have:<br>• A CDR-Global Score of 0.5;<br>• Objective evidence of cognitive impairment at screening;<br>• An Mini-Mental State Examination score between 24 and 30 (inclusive);<br>• Positive amyloid PET scan;<br>• Consent to ApoE genotyping; and<br>• A reliable informant or caregiver.<br>If using drugs to treat symptoms related to Alzheimer's disease, doses must be stable for at least 8 weeks before screening visit 1. |
| Exclusion Criteria | • Any medical or neurological condition (other than Alzheimer's disease) that might be a contributing cause of the subject's cognitive impairment;<br>• Have had a stroke or transient ischemic attack or unexplained loss of consciousness in the past 1 year;<br>• Clinically significant unstable psychiatric illness in the past 6 months;<br>• History of unstable angina, myocardial infarction, advanced chronic heart failure, or clinically significant conduction abnormalities within 1 year before screening;<br>• Indication of impaired renal or liver function;<br>• Have human immunodeficiency virus infection;<br>• Have a significant systematic illness or infection in the past 30 days;<br>• Relevant brain hemorrhage, bleeding disorder, and cerebrovascular abnormalities;<br>• Any contraindications to brain MRI or PET scans;<br>• Alcohol or substance abuse in the past 1 year; and<br>• Taking blood thinners (except for aspirin at a prophylactic dose or less). |

ApoE=apolipoprotein E; *ApoE*ε4=apolipoprotein E epsilon 4 allele; CDR=Clinical Dementia Rating; CDR-SB=Clinical Dementia Rating-Sum of Boxes; MCI=mild cognitive impairment; MRI=magnetic resonance imaging; PET=positron emission tomography

ClinicalTrials.gov. 221AD302 Phase 3 Study of Aducanumab (BIIB037) in Early Alzheimer's Disease - Full Text View - ClinicalTrials.gov.
ClinicalTrials.gov. 221AD301 Phase 3 Study of Aducanumab (BIIB037) in Early Alzheimer's Disease - Full Text View - ClinicalTrials.gov.

# Phase 3 Clinical Trials: Study Design (continued)

| | |
|---|---|
| Interventions | 1:1:1 randomization<br>• Aducanumab low dose: 3 mg/kg for ApoE ε4carriers and 6 mg/kg for noncarriers,<br>• Aducanumab high dose: Initially 6 mg/kg for ApoE ε4 carriers and 10 mg/ kg for noncarriers, later increasing to 10 mg/kg for both groups, or<br>• Placebo<br><br>Participants were allowed to continue other medications to treat their cognitive symptoms if they had been on a stable dose for ≥8 weeks. |
| Primary Outcome | To evaluate the efficacy of monthly doses of aducanumab in slowing cognitive and functional impairment as measured by changes at week 78 in the CDR-SB score as compared with placebo in participants with early Alzheimer's disease. |

ApoE=apolipoprotein E; ApoE ε4=apolipoprotein E epsilon 4 allele; CDR=Clinical Dementia Rating; CDR-SB=Clinical Dementia Rating-Sum of Boxes

ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/record/NCT02484547?term=nct02484547&draw=2&rank=1.
ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/results/NCT02477800?term=NCT02477800&draw=2&rank=1.

# Phase 3 Clinical Trials: Results

Selected Characteristics of Participants in EMERGE and ENGAGE

| | EMERGE (n=1638) | | | ENGAGE (n=1647) | | |
|---|---|---|---|---|---|---|
| Characteristic | Placebo (n=548) | Low Dose (n=543) | High Dose (n=547) | Placebo (n=545) | Low Dose (n=547) | High Dose (n=555) |
| Age, mean ±SD, years | 70.8±7.4 | 70.6±7.4 | 70.6±7.5 | 69.8±7.7 | 70.4±7.0 | 70.0±7.7 |
| Female, n (%) | 290 (53%) | 269 (50%) | 284 (52%) | 287 (53%) | 284 (52%) | 292 (53%) |
| AD medication used, n (%) | 282 (51%) | 281 (52%) | 285 (52%) | 299 (55%) | 317 (58%) | 313 (56%) |
| *ApoE* ε4 carriers, n (%)* | 368 (67%) | 362 (67%) | 365 (67%) | 376 (69%) | 391 (71%) | 378 (68%) |
| *ApoE* ε4 **non**carriers, n (%)* | 178 (32%) | 178 (33%) | 181 (33%) | 167 (31%) | 156 (29%) | 176 (32%) |

- The primary endpoint was achieved in the EMERGE study in the aducanumab 10 mg/kg (high dose) study group (n=547 participants) based on the final data set that included additional observations.
  - The change in CDR-SB score from baseline to 78 weeks, when compared to placebo, was -0.39 (-22% [95% CI -0.69 to -0.09] p=0.012).

Haeberlein SB et al. *J Prev Alz Dis*. 2022. http://dx.doi.org/10.14283/jpad.2022.30

# Phase 3 Clinical Trials: Adverse Event Rate

| Adverse Events | EMERGE (n=1638) | | | ENGAGE (n=1647) | | |
|---|---|---|---|---|---|---|
| | Placebo (n=548) | Low Dose (n=543) | High Dose (n=547) | Placebo (n=545) | Low Dose (n=547) | High Dose (n=555) |
| ARIA-E TOTAL | 13 (2%) | 140 (26%) | 188 (35%) | 16 (3%) | 141 (26%) | 199 (36%) |
| *ARIA-E in ApoE* ε4 carriers | 7/371 (2%) | 109/366 (30%) | 156/362 (43%) | 9/371 (2%) | 114/390 (29%) | 159/378 (42%) |
| *ARIA-E in ApoE* ε4 **non**carriers | 6/173 (4%) | 31/171 (18%) | 32/179 (18%) | 7/161 (4%) | 27/155 (17%) | 40/176 (23%) |
| | | | | | | |
| Brain microhemorrhage | 37 (7%) | 87 (16%) | 108 (20%) | 34 (6%) | 89 (16%) | 104 (19%) |
| Localized superficial siderosis | 14 (3%) | 52 (10%) | 73 (13%) | 10 (2%) | 51 (9%) | 89 (16%) |

Haeberlein SB et al. *J Prev Alz Dis*. 2022. http://dx.doi.org/10.14283/jpad.2022.30

NEW YORK STATE Department of Health | Office of Health Insurance Programs

SUNY The State University of New York

# Suggested Coverage Parameters

- American Academy of Neurology (AAN) Guideline Subcommittee suggests the following criteria for the appropriate use of aducanumab:
  - Appropriate identification of individuals with symptomatic, early Alzheimer's disease that includes:
    - Detailed patient history;
    - Use of standardized scales and tests to corroborate cognitive decline;
    - Neurological and physical exams;
    - A medication drug list review;
    - Laboratory testing to exclude other concomitant disorders that can cause cognitive decline; and
    - MRI to rule out other conditions that can present with cognitive decline.
  - Confirmation of Aβ deposits in the brain via amyloid positive PET scan or an analysis of the CSF.
  - A pretreatment brain MRI is recommended to avoid the administration of the drug to patients with:
    - Cerebrovascular disease and/or
    - Patients with localized superficial siderosis, >4 microhemorrhages, or brain hemorrhage >1 cm.
  - Because of the risk of ARIA, patients who have a clotting disorder or are receiving anticoagulant therapy other than low-dose aspirin (i.e., ≤325 mg/day) should not receive aducanumab treatment.
  - ApoE genotyping should be considered as it may affect the aducanumab dosing.

Day GS et al. *Neurology*. 2022. https://doi.org/10.1212/WNL.0000000000200176

# Update

- The Observational Study of Aducanumab-avwa in Participants with Alzheimer's Disease in the US (NCT05097131) has been terminated as it is expected there will be limited usage of the drug in clinical practice making the study not feasible for enrollment.

- A Study To Evaluate Safety and Tolerability of Aducanumab in Participants with Alzheimer's Disease who had Previously Participated in the Aducanumab Studies 221AD103, 221AD301, 221AD302, and 221AD205 (EMBARK [NCT04241068]) will continue.

- A Study to Verify the Clinical Benefit of Aducanumab in Participants with Early Alzheimer's Disease (ENVISION [NCT05310071]) will begin recruitment.

- The manufacturer has stated that it would "*substantially eliminate its commercial infrastructure supporting Aduhelm, retaining minimal resources to manage patient access programs, including a continued free drug program for patients currently on treatment in the United States*".

Biogen. May 2022. Earnings Press Release (biogen.com).
ClinicalTrials.gov An Observational Study of Aducanumab-avwa in Participants With Alzheimer's Disease in the US - Full Text View - ClinicalTrials.gov.
ClinicalTrials.gov. A Study to Evaluate Safety and Tolerability of Aducanumab in Participants With Alzheimer's Disease Who Had Previously Participated in the Aducanumab Studies 221AD103, 221AD301, 221AD302 and 221AD205 - Full Text View - ClinicalTrials.gov.
ClinicalTrials.gov. A Study to Verify the Clinical Benefit of Aducanumab in Participants With Early Alzheimer's Disease - Full Text View - ClinicalTrials.gov.

# Summary

- Aducanumab is FDA approved for the treatment of Alzheimer's disease.
  - Treatment should be initiated in patients with MCI or mild dementia stage of Alzheimer's disease, the population in which treatment was initiated in clinical trials.
  - Approved under the FDA accelerated approval process based on the surrogate endpoint of reducing Aβ plaques in people with MCI or mild dementia stage of Alzheimer's disease. To maintain approval, the manufacturer of aducanumab must conduct a randomized controlled trial confirming the efficacy of aducanumab compared to an appropriate control for the treatment of Alzheimer's disease.

- The Centers for Medicare and Medicaid Services encourage state Medicaid programs to subject aducanumab to utilization management techniques, such as prior authorization (PA) or medical necessity criteria.

# Recommendations for Aduhelm® (aducanumab) Clinical Coverage Policy

The following coverage parameters should be considered:

1. Evidence exists of mild cognitive impairment (MCI) due to Alzheimer's disease (AD) or mild Alzheimer's dementia by a Clinical Dementia Rating (CDR)-Global Score of 0.5 to 1, Mini-Mental Status Exam (MMSE) score between 24 and 30, and/or a Montreal Cognitive Assessment (MoCA) score of at least 18; AND

2. Apolipoprotein E ε4 carrier status has been evaluated; AND

3. An positron emission tomography (PET) scan or cerebrospinal fluid (CSF) analysis was completed that was positive for amyloid beta deposits; AND

4. The patient does not have evidence of any medical or neurological condition other than Alzheimer's disease that might be a contributing cause of the subject's cognitive impairment, including, but not limited to, stroke/vascular dementia, tumor, dementia with Lewy bodies, or frontotemporal dementia;

5. The patient does not have a history of a clotting disorder or is taking any form of antiplatelet or anticoagulant medications other than aspirin ≤325 mg/ day; AND

6. The use of aducanumab is consistent with the FDA-approved product information.

NEW YORK STATE | Department of Health | Office of Health Insurance Programs

SUNY The State University of New York

# Drug Utilization Review: Botulinum Toxins

## Drug Utilization Review Board

## July 14, 2022

NEW YORK STATE | Department of Health | Office of Health Insurance Programs

SUNY The State University of New York

# Purpose

- The primary objective is to develop clinical criteria for botulinum toxins for members in the New York State (NYS) Medicaid program.
- Utilization of botulinum toxins across the entire NYS Medicaid population, including the fee-for-service (FFS) and managed care (MC) programs, will also be reviewed.

# Background

- Botulinum toxins are neuromuscular blocking agents and acetylcholine release inhibitors.
- Botulinum toxins covered by the NYS Medicaid FFS program:
  - AbobotulinumtoxinA (Dysport®)
  - IncobotulinumtoxinA (Xeomin®)
  - OnabotulinumtoxinA (Botox®)
  - RimabotulinumtoxinB (Myobloc®)

*See end of slide presentation for references*

# Background – Covered Indications

| Botulinum toxins* | AH | Blepharo-spasm | CD | CM** | CS | NDO | OAB | Spasticity | Strabismus | UI*** |
|---|---|---|---|---|---|---|---|---|---|---|
| AbobotulinumtoxinA (Dysport®) | | | X | | | | | X (≥2 years) | | |
| IncobotulinumtoxinA (Xeomin®) | | X | X | | X (≥2y) | | | X (≥2 years)⁺ | | |
| OnabotulinumtoxinA (Botox®) | Xα | X# (≥12y) | X | X | | X∞ (≥5y) | X∞ | X (≥2 years) | X | X∞ |
| RimabotulinumtoxinB (Myobloc®) | | | X | | X | | | | | |

*Indicated for adults only unless otherwise specified in the table; only includes covered indications (e.g., excludes cosmetic indication for glabellar lines); **prophylaxis of chronic migraines (≥15 days per month with headache lasting >4 hours); ***urinary incontinence due to detrusor overactivity associated with a neurologic condition; ⁺upper limb spasticity in pediatric patients 2 to 17 years of age, excluding spasticity caused by cerebral palsy; ∞indicated for patients who have an inadequate response to or are intolerant of an anticholinergic medication; αindicated for patients with severe AH with inadequate response to topical agents; #indicated for blepharospasm associated with dystonia. AH=axillary hyperhidrosis, CD=cervical dystonia, CM=chronic migraine, CS=chronic sialorrhea, NDO=neurogenic detrusor overactivity, OAB=overactive bladder, UI=urinary incontinence, y=years.

*See end of slide presentation for references*

# Guideline/Consensus Statement Recommendations

| Covered indication | Drug(s) with indication | Guideline/consensus statement recommendations |
|---|---|---|
| Axillary hyperhidrosis (AH) | onabotulinumtoxinA | • First-line treatment should consist of topical 20% aluminum chloride or onabotulinumtoxinA injection for AH; if both treatments are not successful, combination treatment with both is recommended. If these are unsuccessful, oral anticholinergics may be considered alone or in combination with the above.<br>• The remaining treatment options include microwave therapy, local surgery, or sympathetic denervation. |
| Blepharospasm | incobotulinumtoxinA, onabotulinumtoxinA | • AAN guidelines* (2016) assert that incobotulinumtoxinA and onabotulinumtoxinA are probably effective and should be considered for treatment of blepharospasm (level B recommendation). These products are considered first-line by specialists and have equivalent efficacy.<br>• AbobotulinumtoxinA is considered possibly effective and may be considered (level C recommendation; note: abobotulinumtoxinA is not FDA approved for treatment of blepharospasm).<br>• The NIH National Eye Institute recommends onabotulinumtoxinA injections; surgery is recommended if injections fail. |
| Cervical dystonia (CD) | abobotulinumtoxinA, incobotulinumtoxinA, onabotulinumtoxinA, rimabotulinumtoxinB | • AAN guidelines (2016) assert that abobotulinumtoxinA and rimabotulinumtoxinB are considered effective and should be offered for treatment of CD (level A recommendation); onabotulinumtoxinA and incobotulinumtoxinA are probably effective and should be considered (level B recommendation).<br>• EFNS guidelines (2011) recommend onabotulinumtoxinA as first-line for CD; pallidal deep brain stimulation may also be considered. |

*AAN guidelines evidence definitions: level A recommendation for effectiveness signifies intervention should be offered; level B recommendation for effectiveness signifies intervention should be considered; level C recommendation for effectiveness signifies intervention may be considered. AAN=American Academy of Neurology, AH=axillary hyperhidrosis, CD=cervical dystonia, EFNS=European Federation of Neurological Societies, FDA=Food and Drug Administration, NIH=National Institutes of Health.

*See end of slide presentation for references*

# Guideline/Consensus Statement Recommendations

| Covered indication | Drug(s) with indication | Guideline/consensus statement recommendations |
|---|---|---|
| Chronic sialorrhea (CS) | incobotulinumtoxinA, rimabotulinumtoxinB | • National German guideline for hypersalivation recommends glycopyrrolate as first-line for children, adolescents, and adult patients in palliative care; the botulinum toxin (only addresses incobotulinumtoxinA, not rimabotulinumtoxinB) is considered an alternative treatment, but is recommended as first-line for patients with Parkinson's and other neurodegenerative diseases. |
| Migraine prevention – chronic migraine (CM)* | onabotulinumtoxinA | AHS (2021): asserts that onabotulinumtoxinA has established efficacy for migraine prevention.<br>• For patients with ICHD-3 CM (≥15 headache days per month for >3 months): recommends an 8-week trial of 2 or more of the following: topiramate, divalproex sodium/valproate sodium, beta-blocker (metoprolol, propranolol, timolol, atenolol, nadolol), TCA (amitriptyline, nortriptyline), or SNRI (venlafaxine, duloxetine) OR inability to tolerate or inadequate response to a minimum of 2 quarterly injections (6 months) of onabotulinumtoxinA prior to using a CGRP antagonist.<br>NICE (2021)**: asserts that onabotulinumtoxinA is recommended for patients with CM (≥15 headache days per month of which 8 days are with migraine) that have not responded to at least 3 previous preventive pharmacologic treatments (e.g., topiramate, propranolol, amitriptyline).<br>AAN (2016): recommends use of onabotulinumtoxinA for treatment of CM as it is safe, effective (decreases headache days), and may improve QOL. |

*Only includes FDA-approved agents for migraine prevention, **published in 2012 and updated in 2021. AAN=American Academy of Neurology, AHS=American Headache Society, CGRP=calcitonin gene-related peptide, CM=chronic migraine, CS=chronic sialorrhea, ICHD-3=International Classification of Headache Disorders - 3rd edition, NICE=National Institute for Health and Care Excellence, QOL=quality of life, SNRI=selective norepinephrine reuptake inhibitor, TCA=tricyclic antidepressant.

*See end of slide presentation for references*

# Guideline/Consensus Statement Recommendations

| Covered indication | Drug(s) with indication | Guideline/consensus statement recommendations |
|---|---|---|
| Overactive bladder (OAB) | onabotulinumtoxinA | • AUA/SUFU guidelines (2019) assert that onabotulinumtoxinA (intradetrusor) may be offered as a third-line treatment option for patients with non-neurogenic OAB who are refractory to first- and second-line treatments. First-line treatment consists of behavioral therapy (e.g., bladder training) and second-line treatments include antimuscarinics or beta-3-adrenoceptor agonists. |
| Neurogenic detrusor overactivity (NDO) | onabotulinumtoxinA | • EAU guidelines (2016) recommend antimuscarinics (e.g., oxybutynin, trospium, tolterodine) as first-line treatment of NDO. For minimally invasive treatment in MS or spinal cord injury, use of botulinum toxin injection in the detrusor is the most effective treatment to reduce neurogenic detrusor overactivity. |
| Spasticity | abobotulinumtoxinA, incobotulinumtoxinA, onabotulinumtoxinA | • The Interdisciplinary Working Group for Movement Disorders recommendations (2017) for treatment of spasticity in MS assert that specialists may consider botulinum treatment for patients with MS (although robust data are lacking).<br>• Per AAN guidelines (2016), onabotulinumtoxinA, abobotulinumtoxinA, and incobotulinumtoxinA are effective and should be considered for upper-limb spasticity; abobotulinumtoxinA and onabotulinumtoxinA are established as effective and should be offered for lower-limb spasticity.<br>• The Canadian practice guidelines for stroke rehabilitation (2015) assert that botulinum toxin may be used to treat spasticity (allows for increased range of motion, decreased pain, and improved gait); other treatment options include tizanidine and baclofen. |

AAN=American Academy of Neurology, AUA=American Urological Association, EAU=European Association of Urology, MS=multiple sclerosis, NDO=neurogenic detrusor overactivity, OAB=overactive bladder, SUFU=Society of Urodynamics.

*See end of slide presentation for references*

# Guideline/Consensus Statement Recommendations

| Covered indication | Drug(s) with indication | Guideline/consensus statement recommendations |
|---|---|---|
| Strabismus | onabotulinumtoxinA | • The Pediatric Ophthalmology/Adult Strabismus Preferred Practice Pattern® Panel of the American Association for Pediatric Ophthalmology and Strabismus Adult Strabismus Task Force guidelines (2020) for adults assert that patients not responding to initial treatment with prism to manage diplopia may consider use of onabotulinumtoxinA or surgery for cases that do not resolve.<br>• The American Optometric Association issued guidelines for strabismus in adults and children in 2011. They assert that onabotulinumtoxinA may be considered as an alternative or as adjunctive treatment to surgery. |
| Urinary incontinence (UI) | onabotulinumtoxinA | • AUA/SUFU guidelines for UI (2019) assert that onabotulinumtoxinA (intradetrusor) may be offered as a third-line treatment option for patients who are refractory to first- and second-line treatments. First-line treatment consists of behavioral therapy (e.g., bladder training) and second-line treatments include antimuscarinics or beta-3-adrenoceptor agonists. |

AUA=American Urological Association, SUFU=Society of Urodynamics, UI=urinary incontinence.

*See end of slide presentation for references*

# Utilization Analysis - Methodology

- Data source: Medicaid Data Warehouse
- Timeframe: April 1, 2020 – June 30, 2021
- Sample: Members enrolled in the NYS Medicaid Program (FFS+MC) with either a medical or pharmacy claim for a botulinum toxin during the timeframe.
  - Diagnosis look-back: 365 days from the index clam for each drug.
- Exclusions:
  1. NDCs for cosmetic purposes (e.g., treatment of glabellar lines), including prabotulinumtoxinA-xvfs (Jeuveau®);
  2. Null NDC on the J code;
  3. J code/NDC mismatch;
  4. Duplicate pharmacy claims.
- Limitations:
  - While time periods analyzed take into account inherent delays in claim/encounter submissions, data may not be fully complete.

# Utilization Analysis - Methodology

| Generic name (brand name/manufacturer) | Units | NDCs for products included in the analysis |
|---|---|---|
| OnabotulinumtoxinA (Botox®/Allergan) | 50 units | 0023-3920-50 |
| | 100 units | 0023-1145-01 |
| AbobotulinumtoxinA (Dysport®/Galderma Laboratories, LP) | 500 units | 15054-0500-01 |
| | | 15054-0500-02 |
| | 300 units | 15054-0530-06 |
| IncobotulinumtoxinA (Xeomin®/Merz Pharmaceuticals, LLC) | 50 units | 00259-1605-01 |
| | 100 units | 00259-1610-01 |
| | 200 units | 00259-1620-01 |
| RimabotulinumtoxinB (Myobloc®/Solstice Neurosciences, LLC) | 2500 units | 10454-0710-10 |
| | 5000 units | 10454-0711-10 |
| | 10000 units | 10454-0712-10 |

- Note: the Medicaid Confidential Data Cell Size Policy (OHIP-0001) requires that no cell containing a value of 1 to 30 be reported. The cell size value must be reported as ≤30 in all public-facing documents. Additionally, no cell can be reported that allows a value of 1 to 30 to be derived from other reported cells or information.

# Utilization in FFS+MC

| Drug | # Members* | # Services** | # Services/Member |
|---|---|---|---|
| Botox® (onabotulinumtoxinA) | 11,898 | 37,247 | 3.1 |
| Dysport® (abobotulinumtoxinA) | 96 | 230 | 2.4 |
| Myobloc® (rimabotulinumtoxinB) | 63 | 158 | 2.5 |
| Xeomin® (incobotulinumtoxinA) | 341 | 925 | 2.7 |

Source: MDW; timeframe: April 1, 2020 – June 30, 2021; extract date: December 21, 2021. Note: includes both medical and pharmacy claims; excludes products for cosmetic purposes (e.g., glabellar lines).
*Number of members is not additive. **Number of services reported is the number of lines reported for all claims included in the analysis; for this analysis, there is only one line reported on a pharmacy claim; however, there may be multiple lines reported on a procedure claim.
FFS=fee-for-service, MC=managed care.

# Members With a CMS-Approved Diagnosis – FFS+MC

| | OnabotulinumtoxinA (Botox®) | | IncobotulinumtoxinA (Xeomin®) | |
|---|---|---|---|---|
| Indication | # Members | % Members | # Members | % Members |
| # Members | 11,898 | 100.0% | 341 | 100.0% |
| | | | | |
| CMS-approved CM diagnosis* | 5,598 | 47.0% | - | - |
| Other CMS-approved non-CM diagnoses⁺ | 4,763 | 40.0% | 260 | 76.2% |
| CMS-approved ICD-10 diagnoses | **10,361** | **87.1%** | **260** | **76.2%** |

Source: MDW; timeframe: April 1, 2020 – June 30, 2021; diagnosis look-back: July 1, 2019 – June 30, 2021; extract date: December 21, 2021 and January 17, 2022.
*Only identified for Botox® ⁺For members not included in CMS-approved CM diagnosis. Excludes Dysport® and Myobloc® products due to small sample size.CM=chronic migraine, CMS=Centers for Medicare and Medicaid Services, FFS=fee-for-service, ICD-10=International Classification of Diseases, tenth revision, MC=managed care.

- 87.1% (n=10,361) and 76.2% (n=260) of members who received onabotulinumtoxinA (Botox®) and incobotulinumtoxinA (Xeomin®), respectively, had a CMS-approved ICD-10 diagnosis supporting medical necessity.

# Members Without a CMS-Approved Diagnosis - FFS+MC

| | OnabotulinumtoxinA (Botox®) | | IncobotulinumtoxinA (Xeomin®) | |
|---|---|---|---|---|
| Indication | # Members | % Members | # Members | % Members |
| # Members | 11,898 | 100.0% | 341 | 100.0% |
| | | | | |
| Migraine/headache diagnoses NOT accepted by CMS* | 613 | 5.2% | - | - |
| Other diagnoses NOT accepted by CMS⁺ | 350 | 2.9% | - | - |
| No indication¥ | **574** | **4.8%** | **81** | **23.8%** |

Source: MDW; timeframe: April 1, 2020 – June 30, 2021; diagnosis look-back: July 1, 2019 – June 30, 2021; extract date: December 21, 2021 and January 17, 2022. *Only identified for Botox®; included migraine/headache diagnoses not accepted by CMS. ⁺Excluded members from the Botox®-only group (previous row). ¥Not included in the above rows. Excludes Dysport® and Myobloc® products due to small sample size. CMS=Centers for Medicare and Medicaid Services, FFS=fee-for-service, MC=managed care.

- 12.9% (n=1,537) of members who received onabotulinumtoxinA (Botox®) did not have a CMS-approved ICD-10 diagnosis supporting medical necessity.

# Members Who Received Step Therapy for Chronic Migraine – FFS+MC

| Members with at least 1 claim for a step therapy agent prior to starting onabotulinumtoxinA (Botox®) | | | |
|---|---|---|---|
| | OnabotulinumtoxinA | With Step Drug* | |
| **Indication** | **# Members** | **# Members** | **% Members** |
| # Members on onabotulinumtoxinA (4/1/2020-6/30/2021) | 11,898 | | |
| # Members starting onabotulinumtoxinA (7/1/2020-6/30/2021) | 7,413 | 2,077 | 28.0% |
| | | | |
| CMS-approved CM diagnosis** | 2,887 | 1374 | 47.6% |
| Other CMS-approved non-CM diagnoses[+] | 3,409 | 453 | 13.3% |
| CMS-approved ICD-10 diagnoses | 6,296 | 1,827 | 29.0% |
| | | | |
| Migraine/headache diagnoses NOT accepted by CMS*** | 402 | 179 | 44.5% |
| Other diagnoses NOT accepted by CMS[¥] | 276 | 31 | 11.2% |
| No indication[£] | 439 | 40 | 9.1% |

Source: MDW; timeframe: April 1, 2020 – June 30, 2021; diagnosis look-back: July 1, 2019 – June 30, 2021; extract date: December 21, 2021 – March 20, 2022. CM=chronic migraine, CMS=Centers for Medicare and Medicaid Services, FFS=fee-for-service, MC=managed care.

*Step therapy agents (FDA-approved or Compendia-supported): amitriptyline, atenolol, divalproex (Depakote®), metoprolol, nadolol, propranolol, timolol, betimol, topiramate (Topamax®, Trokendi®), venlafaxine; **Only identified for Botox®; [+]for members not included in CMS-approved CM diagnosis (e.g., axillary hyperhidrosis, overactive bladder, etc.); ***only identified for Botox® and included migraine/headache diagnoses not accepted by CMS; [¥]excluded members from the Botox®-only group (previous row); [£]not included in the above rows

# Conclusions

- Per FDA-approved labeling and guideline/consensus statement recommendations, the following indications have other agents recommended as first-line prior to using a botulinum toxin product: axillary hyperhidrosis, chronic sialorrhea, headache prevention in chronic migraine, overactive bladder, neurogenic detrusor overactivity, strabismus, and urinary incontinence.
- In FFS+MC, most of the utilization was for onabotulinumtoxinA (Botox®), followed by incobotulinumtoxinA (Xeomin®).
- Most members (87.1%) in FFS+MC who received onabotulinumtoxinA (Botox®) had a CMS-approved ICD-10 diagnosis supporting medical necessity.
- 47.6% of members with a CMS-approved chronic migraine diagnosis attempted step therapy with at least 1 migraine agent prior to onabotulinumtoxinA (Botox®).

# UB Recommendations to DOH

1. Recommend a diagnosis requirement for covered indications, excluding coverage for indications which involve cosmetic purposes (e.g., glabellar lines associated with procerus and corrugator muscle activity).

# UB Recommendations to DOH

2. Consider implementation of step therapy for botulinum toxins for the following indications:

   a) Chronic sialorrhea: require a trial with glycopyrrolate (note: excludes patients with Parkinson's and other neurodegenerative diseases as the botulinum toxin is recommended as first-line)
   b) Headache prevention in patients with chronic migraine: require a trial with 2 FDA approved oral preventive agents (amitriptyline, beta-blockers [atenolol, metoprolol, nadolol, propranolol, timolol], divalproex sodium/valproate sodium/valproic acid, topiramate, or venlafaxine)
   c) Overactive bladder: require a trial with an antimuscarinic or beta-3-adrenoceptor agonist
   d) Neurogenic detrusor overactivity: require a trial with an antimuscarinic agent (e.g., oxybutynin, trospium, tolterodine) (note: excludes patients with multiple sclerosis or spinal cord injury as botulinum toxin injection is the most effective treatment to reduce neurogenic detrusor overactivity)
   e) Urinary incontinence due to detrusor overactivity: require a trial with an antimuscarinic or beta-3-adrenoceptor agonist

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1. Botox® [package insert]. Madison, NJ: Allergan, Inc.; 2021. Accessed February 24, 2022.
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# Drug Utilization Review: Remicade® (infliximab), Inflectra® (infliximab-dyyb), Renflexis® (infliximab-abda), and Avsola® (infliximab-axxq)

## Drug Utilization Review Board

## July 14, 2022

NEW YORK STATE | Department of Health | Office of Health Insurance Programs
SUNY The State University of New York

# Background

- The purpose of the presentation is to develop a clinical policy for infliximab products based on currently available literature and peer-reviewed guidelines.

- Infliximab is a practitioner-administered drug and is covered as a medical benefit in the fee-for-service program.

- Utilization of the following infliximab products across the NYS Medicaid Program will be evaluated:
  - Reference product: Remicade® and
  - Biosimilar products:
    - Inflectra® [infliximab-dyyb],
    - Renflexis® [infliximab-abda], and
    - Avsola® [infliximab-axxq]).

# Infliximab FDA-labeled Indications

| Condition | FDA-labeled indication |
|---|---|
| **Crohn's disease in patients ≥6 years of age** | • Reduce the signs and symptoms and induce and maintain clinical remission in patients with moderately to severely active CD who have had an inadequate response to conventional therapy.<br>• Reduce the number of draining enterocutaneous and rectovaginal fistulas and maintain fistula closure in adult patients with fistulizing CD. |
| **Ulcerative colitis in patients ≥6 years of age** | • Reduce the signs and symptoms, induce and maintain clinical remission and mucosal healing, and eliminate corticosteroid use in adult patients with moderately to severely active UC who have had an inadequate response to conventional therapy.<br>• For pediatric patients ≥6 years of age, reduce the signs and symptoms and induce and maintain clinical remission in patients with moderately to severely active UC who have had an inadequate response to conventional therapy. |
| **Rheumatoid arthritis in adults** | • In combination with MTX, reduce the signs and symptoms, inhibit the progression of structural damage, and improve the physical function in patients with moderately to severely active RA. |
| **Ankylosing spondylitis in adults** | • Reduce the signs and symptoms of active AS. |
| **Psoriatic arthritis in adults*** | • Reduce the signs and symptoms of active arthritis, inhibit the progression of structural damage, and improve the physical function in patients with PsA. |
| **Plaque psoriasis in adults** | • Treatment of chronic, severe (extensive and/or disabling) plaque psoriasis in patients who are candidates for systemic therapy and when other systemic therapies are medically less appropriate. |

AS=ankylosing spondylitis; CD=Crohn's disease; FDA=Food and Drug Administration; MTX=methotrexate; PsA=psoriatic arthritis; RA=rheumatoid arthritis; UC=ulcerative colitis
*For the treatment of PsA, infliximab can be used with or without MTX.

Remicade® (infliximab) [product insert]. Janssen Biotech. Inc. Horsham. PA. October 2021

# Tumor Necrosis Factor Inhibitors (TNFi): Current Coverage in NYS Medicaid

| TNFi<br>Preferred on the PDL | Reference product | Biosimilar products: FDA-approved | FDA-approved indications | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | RA | JIA | PsA | Ps | AS | nr-axSpA | CD | UC | HS | UV |
| **Subject to the Preferred Drug Program (PDP)** | | | | | | | | | | | | |
| Adalimumab | Humira® | YES | YES | YES | YES | YES | YES | NO | YES | YES | YES | YES |
| Certolizumab Pegol | Cimzia® | NO | YES | NO | YES | YES | YES | YES | YES | NO | NO | NO |
| Etanercept | Enbrel® | YES | YES | YES | YES | YES | YES | NO | NO | NO | NO | NO |
| Golimumab | Simponi® | NO | YES | NO | YES | NO | YES | NO | NO | YES | NO | NO |
| **Practitioner-administered product and NOT subject to the PDP** | | | | | | | | | | | | |
| Infliximab | Remicade® | YES | YES | NO | YES | YES | YES | NO | YES | YES | NO | NO |

AS=ankylosing spondylitis; CD=Crohn's disease; FDA=Food and Drug Administration; HS=hidradenitis suppurativa; JIA=juvenile idiopathic arthritis; nr-axSpA=non-radiographic axial spondyloarthritis; PDP=Preferred Drug Program; PDL=Preferred Drug List; Ps=plaque psoriasis; PsA=psoriatic arthritis; RA=rheumatoid arthritis; TNFi=tumor necrosis factor inhibitor; UC=ulcerative colitis; UV=uveitis

Current clinical criteria associated with TNFi subject to the PDP in the immunomodulators – systemic category:

1. Confirm diagnosis for FDA- or compendia-supported use

**AND**

2. Trial of a DMARD prior to treatment with an immunomodulator.

Humira® (adalimumab) [product insert]. AbbVie Inc. North Chicago. IL December 2021.
Enbrel® (etanercept) [product insert]. Immunex Corporation. Thousand Oaks. CA. April 2021.
Cimzia® (certolizumab pegol) [product insert]. UCB Inc. Smyrna. GA. March 2019.
Simponi® (golimumab) [product insert]. Janssen Biotech Inc. Horsham. PA. September 2019.
Remicade® (infliximab) [product insert]. Janssen Biotech. Inc. Horsham. PA. October 2021.

# Comparison of TNFi to Infliximab

| TNF Inhibitor | Reference product | FDA approved indications | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | RA | JIA | PsA | Ps | AS | nr-axSpA | CD | UC | HS | UV |
| **Self-administered products** | | | | | | | | | | | |
| Adalimumab | Humira® | Adults | ≥2 yrs of age | Adults | Adults | Adults | NO | ≥6 yrs of age | ≥5 yrs of age | ≥12 yrs of age | ≥2 yrs of age |
| Certolizumab Pegol | Cimzia® | Adults | NO | Adults | Adults | Adults | Adults | Adults | NO | NO | NO |
| Etanercept | Enbrel® | Adults | ≥2 yrs of age | Adults | ≥4 yrs of age | Adults | NO | NO | NO | NO | NO |
| Golimumab | Simponi® | Adults | NO | Adults | NO | Adults | NO | NO | Adults | NO | NO |
| **Practitioner-administered product** | | | | | | | | | | | |
| Infliximab | Remicade® | Adults | NO | Adults | Adults | Adults | NO | ≥6 yrs of age* | ≥6 yrs of age* | NO¥ | NO¥ |

AS=ankylosing spondylitis; CD=Crohn's disease; FDA=Food and Drug Administration; HS=hidradenitis suppurativa; JIA=juvenile idiopathic arthritis; nr-axSpA=non-radiographic axial spondyloarthritis; Ps=plaque psoriasis; PsA=psoriatic arthritis; RA=rheumatoid arthritis; TNFi=tumor necrosis factor infliximab; UC=ulcerative colitis; UV=uveitis; yrs=years

*Infliximab is FDA approved for reducing signs and symptoms and inducing and maintaining clinical remission for patients with moderately to severely active CD or UC *who have had an inadequate response to conventional therapy*.
¥There is compendia support for the use of infliximab for the treatment of HS and UV.

Humira® (adalimumab) [product insert]. AbbVie Inc. North Chicago. IL December 2021.
Enbrel® (etanercept) [product insert]. Immunex Corporation. Thousand Oaks. CA. April 2021.
Cimzia® (certolizumab pegol) [product insert]. UCB Inc. Smyrna. GA. March 2019.
Simponi® (golimumab) [product insert]. Janssen Biotech Inc. Horsham. PA. September 2019.
Remicade® (infliximab) [product insert]. Janssen Biotech. Inc. Horsham. PA. October 2021.

# TNFi Maintenance Dosing Schedule

| TNF Inhibitors | Reference product | Manufacturer-recommended dosage frequency |
|---|---|---|
| **Self-administered products** | | |
| Adalimumab | Humira® | Every other week subcutaneous injection for all FDA-approved indications |
| Certolizumab Pegol | Cimzia® | Every 4-week subcutaneous injection for CD, RA, PsA, AS, and nr-axSpA, and every other week for Ps |
| Etanercept | Enbrel® | Weekly subcutaneous injections for all FDA-approved indications |
| Golimumab | Simponi® | Every 4-week subcutaneous injection for all FDA-approved indications |
| **Practitioner-administered product** | | |
| Infliximab | Remicade® | An intravenous infusion for a minimum of a 2-hour period every 8 weeks for CD, UC, RA, PsA, and Ps, and every 6 weeks for AS |

AS=ankylosing spondylitis; CD=Crohn's disease; FDA=Food and Drug Administration; nr-axSpA=non-radiographic axial spondyloarthritis; Ps=plaque psoriasis; PsA=psoriatic arthritis; RA= rheumatoid arthritis; TNFi=tumor necrosis factor inhibitor; UC=ulcerative colitis

Humira® (adalimumab) [product insert]. AbbVie Inc. North Chicago. IL December 2021.
Enbrel® (etanercept) [product insert]. Immunex Corporation. Thousand Oaks. CA. April 2021.
Cimzia® (certolizumab pegol) [product insert]. UCB Inc. Smyrna. GA. March 2019.
Simponi® (golimumab) [product insert]. Janssen Biotech Inc. Horsham. PA. September 2019.
Remicade® (infliximab) [product insert]. Janssen Biotech. Inc. Horsham. PA. October 2021.

# ACR Recommendations for RA

| First-line therapy | Treatment for patients who do not achieve the target despite first-line treatment |
|---|---|
| <u>For DMARD-naïve patients:</u><br>• Start DMARD therapy as soon as possible.<br>  ○ Reevaluate efficacy and tolerability within 3 months.<br>• For DMARD-naïve patients with moderate to high disease activity:<br>  ○ MTX monotherapy<br>• For DMARD-naïve patients with low disease activity:<br>  ○ Hydroxychloroquine > sulfasalazine > MTX > leflunomide | <u>For patients receiving DMARDs who are not at target:</u><br>• For patients taking maximally tolerated MTX doses:<br>  ○ Add bDMARD or tsDMARD instead of triple csDMARD therapy.<br>• For patients with moderate to high disease activity who received csDMARD but are MTX naïve:<br>  ○ Switch to MTX monotherapy instead of MTX + bDMARD or tsDMARD.<br>• For patients taking a bDMARD or tsDMARD who are not at target:<br>  ○ Switch to a bDMARD or tsDMARD in a different class. |

ACR=American College of Rheumatology; bDMARD=biologic disease-modifying anti-rheumatic drug; csDMARD=conventional synthetic disease-modifying anti-rheumatic drug; MTX=methotrexate; RA=rheumatoid arthritis; TNFi=tumor necrosis factor inhibitor; tsDMARD=targeted synthetic disease-modifying anti-rheumatic drug

csDMARDs include hydroxychloroquine, sulfasalazine, MTX, leflunomide
bDMARDs include TNFi (etanercept, adalimumab, infliximab, golimumab, certolizumab pegol), T cell costimulatory inhibitor (abatacept), IL-6 receptor inhibitors (tocilizumab, sarilumab)
tsDMARDs: JAK inhibitors (tofacitinib, baricitinib, upadacitinib)
Triple csDMARD therapy: MTX + hydroxychloroquine + sulfasalazine

Fraenkel L et al. Arthritis Care Res (Hoboken). 2021;73(7):924-939.

# AGA Recommendations for Adult Outpatients with Moderate to Severe Luminal and Fistulizing CD

| Induction of remission |
| --- |
| • Suggests corticosteroids > no treatment.<br>• Start a biologic with or without an immunomodulator > wait until after failure of 5-ASA and/or corticosteroids.<br>• For patients naïve to biologics: recommends infliximab/adalimumab/ustekinumab > certolizumab pegol and suggests vedolizumab > certolizumab pegol. Recommends biologic monotherapy > thiopurine monotherapy.<br>• For patients with primary nonresponse[a] to TNFi: recommends ustekinumab. Suggests vedolizumab.<br>• For patients with secondary nonresponse[b]: recommends adalimumab or ustekinumab. Suggests vedolizumab. (If adalimumab was used previously, indirect evidence suggests infliximab used as second-line).<br>• Induction of fistula remission in patients with CD and active perianal fistula without perianal abscess: recommends biologic + antibiotic > biologic alone. Use of antibiotic alone is not suggested |

5-ASA=5-aminosalicylic acid (includes mesalamine, olsalazine, balsalazide); AGA=American Gastroenterological Association; CD=Crohn's disease; thiopurine includes azathioprine; TNFi=tumor necrosis factor inhibitor

[a]Primary nonresponse: inadequate response
[b]Secondary nonresponse: relapse after an initial response to infliximab

Feuerstein JD, Ho EY, Shmidt E, et al. 2021;160(7):2496-2508.

# AGA Recommendations for Adult Outpatients with Moderate to Severe Luminal and Fistulizing CD (*continued*)

| Induction and maintenance of remission | Maintenance of remission |
|---|---|
| • Recommends TNFi (infliximab or adalimumab > certolizumab pegol) or ustekinumab<br><br>• Suggests vedolizumab or MTX (SUBQ or IM) monotherapy.<br><br>• Use of oral MTX, natalizumab, 5-ASA, or sulfasalazine is not suggested.<br><br>• For patients naïve to biologics and immunomodulators:<br>  ○ Suggests infliximab + thiopurines or adalimumab + thiopurines > infliximab or adalimumab monotherapy (indirect evidence suggests infliximab + MTX or adalimumab + MTX > infliximab or adalimumab monotherapy)<br><br>• Induction and maintenance of fistula remission in patients with CD and active perianal fistula: recommends infliximab. Suggests adalimumab, ustekinumab or vedolizumab. | • Use of corticosteroids is not recommended.<br><br>• Maintenance of remission in quiescent moderate to severe CD or corticosteroid-induced remission: suggests thiopurines. |

5-ASA=5-aminosalicylic acid (includes mesalamine, olsalazine, balsalazide); AGA=American Gastroenterological Association; CD=Crohn's disease; IM=intramuscular; MTX=methotrexate; SUBQ=subcutaneous; thiopurine includes azathioprine

Feuerstein JD, Ho EY, Shmidt E, et al. 2021;160(7):2496-2508.

# AGA Recommendations for Adult Outpatients with Moderate to Severe UC

| Induction of remission |
| --- |
| • For patients naïve to biologics: Infliximab or vedolizumab > the standard dose of adalimumab or golimumab and there is limited evidence to inform appropriate positioning of tofacitinib. (Patients with less severe disease may choose self-administered SUBQ adalimumab for convenience).<br><br>• For patients who previously received infliximab (particularly those with primary nonresponse): recommends ustekinumab or tofacitinib > vedolizumab or adalimumab.<br><br>• Use of thiopurine or MTX monotherapy is not suggested. |

AGA=American Gastroenterological Association; MTX=methotrexate; SUBQ=subcutaneous; UC=ulcerative colitis; thiopurine includes azathioprine

Feuerstein JD, Isaacs KL, Schneider Y, et al. 2020;158(5):1450-1461.

# AGA Recommendations for Adult Outpatients with Moderate to Severe UC (*continued*)

| Induction and maintenance of remission | Maintenance of remission |
|---|---|
| • Suggests introducing biologic with or without immunomodulator early > gradual step up after failure of 5-ASA, except in patients with less severe disease.<br><br>• Use of infliximab, adalimumab, golimumab, vedolizumab, ustekinumab, or tofacitinib (only after failure of or intolerance to TNFi) is recommended over no treatment.<br><br>• Suggests TNFi/vedolizumab/ustekinumab + a thiopurine or MTX > biologic or thiopurine monotherapy. MTX monotherapy is not suggested. | • Use of thiopurine monotherapy over no treatment is suggested.<br><br>• No recommendation made for biologic or tofacitinib monotherapy vs. thiopurine monotherapy.<br><br>• Achieved remission with biologics and/or immunomodulators or tofacitinib: continuing 5-ASA is not suggested.<br><br>• Use of MTX monotherapy is not suggested. |

5-ASA=5-aminosalicylic acid (includes mesalamine, olsalazine, balsalazide); AGA=American Gastroenterological Association; MTX=methotrexate; UC=ulcerative colitis; thiopurine includes azathioprine; TNFi=tumor necrosis factor inhibitor

Feuerstein JD, Isaacs KL, Schneider Y, et al. 2020;158(5):1450-1461.

# Utilization Analysis - Methodology

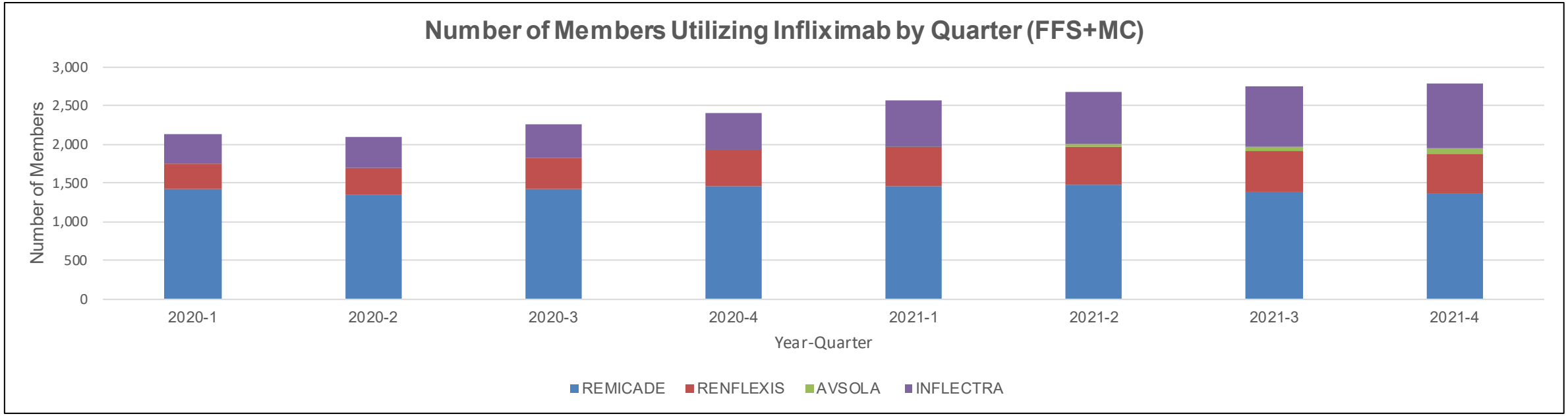
- Data source: Medicaid Data Warehouse (MDW)
- Timeframe: January 1, 2020, through December 31, 2021
- Sample: members who received infliximab during the timeframe of the analysis. Both pharmacy claims and Healthcare Common Procedure Coding System (HCPCS) codes specific to infliximab were included.
- Exclusion: infliximab-specific HCPCS codes with an incorrect national drug code (NDC) for infliximab.

# Utilization Analysis - Methodology

- Limitations:
  - The Medicaid Confidential Data Cell Size Policy (OHIP-0001) requires that no cell containing a value of 1 to 30 be reported. The cell size value must be reported as ≤30 in all public-facing documents. Additionally, no cell can be reported that allows a value of 1 to 30 to be derived from other reported cells or information. Due to the small sample size, reporting the raw numbers or the percentages of patients would violate the Medicaid Confidential Data Cell Size Policy.

  - While analyzed time periods account for inherent delays in claim/encounter submissions, data may not be fully complete.

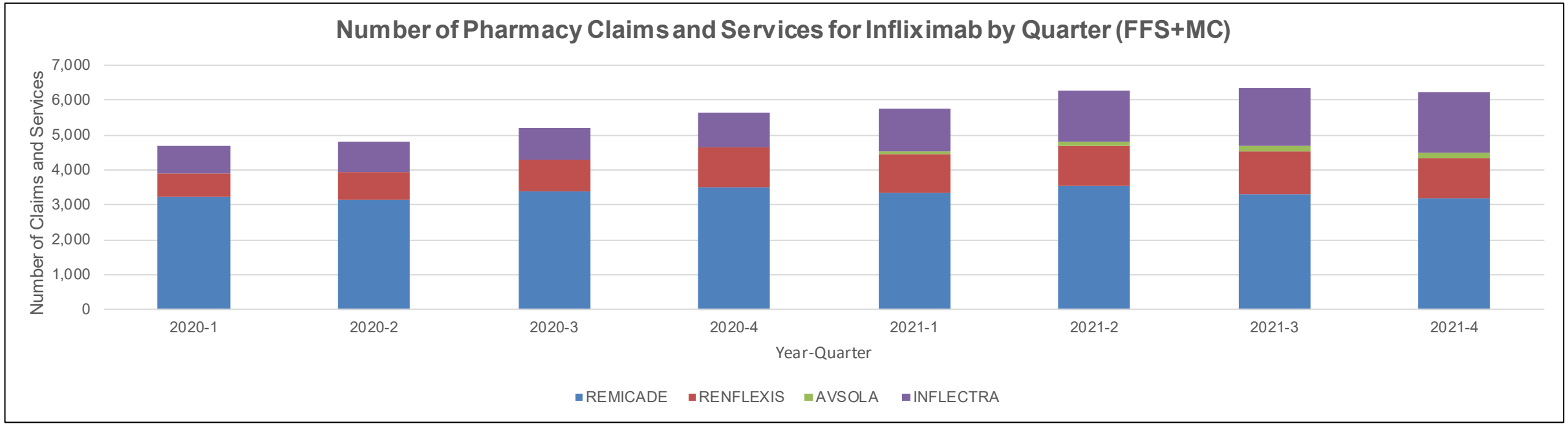
# Results: Utilization




Source: MDW Extract date: May 25, 2022. FFS=fee-for-service; MC=managed care

- During the 2-year period, 4,225 members (FFS+MC) received infliximab.
- From 2020 to 2021, the number of members utilizing infliximab increased by 16.7%.

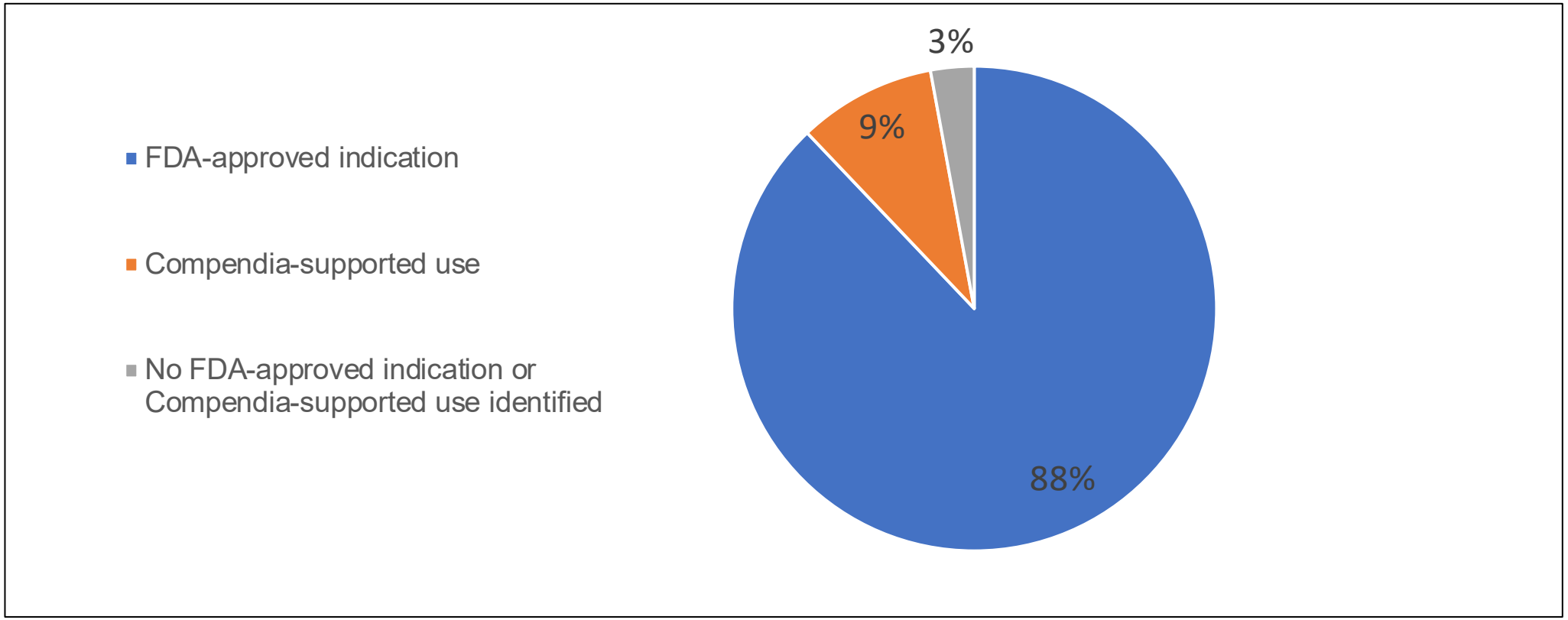
# Results: Utilization




Source: MDW Extract date: May 25, 2022. FFS=fee-for-service; MC=managed care

- During the 2-year period, there were 44,966 services/ pharmacy claims.
- From 2020 to 2021, there was a 21.0% increase in services/ pharmacy claims.

# Results: Diagnosis Evaluation




FDA=Food and Drug Administration
Source: MDW Extract date: May 25, 2022

- Members were included in the analysis if they started infliximab therapy during the timeframe of January 1, 2021, through December 31, 2021.
- To determine if the member had an FDA-approved or compendia-supported indication, an evaluation of the prior year (i.e., 2020) and evaluation year (i.e., 2021) was conducted.

# Conclusions

- Infliximab has FDA-approved indications for RA, PsA, plaque psoriasis, AS, CD, UC.
- Per FDA-approved labeling, treatment for CD and UC have other agents recommended as first-line prior to using infliximab.
- Per guideline recommendations, consider the implementation of step therapy of a csDMARD or an FDA-approved, self-administered TNFi before infliximab.
- In FFS+MC, most of the utilization was for members with the FDA-approved diagnosis of CD and/or UC.

# UB Recommendations to DOH for Infliximab Clinical Policy

- Recommend a diagnosis requirement for covered indications

AND

- Consider implementation of step therapy for infliximab: requiring the use of a DMARD OR a TNFi FDA approved for self-administration prior to initiation of infliximab therapy.

# References


1. Remicade® (infliximab) [product insert]. Janssen Biotech. Inc. Horsham. PA. October 2021.
2. Renflexis® (infliximab-abda) [product insert]. Merck Sharp & Dohme Corp. Kenilworth. NJ. January 2022.
3. Inflectra® (infliximab-dyyb) [product insert]. Manufactured by Celltrion. Inc. Distributed by Pfizer. New York. NY. June 2021.
4. Avsola® (infliximab-axxq) [product insert]. Amgen Inc. Thousand Oaks. CA. September 2021.
5. Humira® (adalimumab) [product insert]. AbbVie Inc. North Chicago. IL December 2021.
6. Cimzia® (certolizumab pegol) [product insert]. UCB Inc. Smyrna. GA. March 2019.
7. Enbrel® (etanercept) [product insert]. Immunex Corporation. Thousand Oaks. CA. April 2021.
8. Simponi® (golimumab) [product insert]. Janssen Biotech Inc. Horsham. PA. September 2019.
9. Fraenkel L, Bathon JM, England BR, et al. 2021 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. Arthritis Care Res (Hoboken). 2021;73(7):924-939. doi:10.1002/acr.24596
10. 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(7):2496-2508. doi:10.1053/j.gastro.2021.04.022
11. Feuerstein JD, Isaacs KL, Schneider Y, et al. AGA Clinical Practice Guidelines on the Management of Moderate to Severe Ulcerative Colitis. Gastroenterology. 2020;158(5):1450-1461. doi:10.1053/j.gastro.2020.01.006

NEW YORK STATE | Department of Health | Office of Health Insurance Programs

SUNY The State University of New York

# Drug Utilization Review: Entyvio® (vedolizumab)

## Drug Utilization Review Board
## July 14, 2022

NEW YORK STATE | Department of Health | Office of Health Insurance Programs

SUNY The State University of New York

# Background

- The purpose of the presentation is to develop a clinical policy for vedolizumab (Entyvio®) based on currently available literature and peer-reviewed guidelines.
  - Entyvio® (vedolizumab) is an integrin receptor antagonist indicated for the treatment of moderately to severely active ulcerative colitis (UC) and moderately to severely active Crohn's disease (CD) in adults.

- Utilization of vedolizumab across the NYS Medicaid Program will be evaluated.
  - Vedolizumab is a practitioner-administered drug and is covered as a medical benefit in the fee-for-service program.

# FDA-Approved Indications and Current PDP Criteria

| TNF inhibitor<br>Preferred on the PDL | Reference product | Biosimilar products FDA-approved | FDA-approved indications | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | RA | JIA | PsA | Ps | AS | nr-axSpA | CD | UC | HS | UV |
| **TNFi subject to the PDP** | | | | | | | | | | | | |
| Adalimumab | Humira® | YES | YES | YES | YES | YES | YES | NO | YES | YES | YES | YES |
| Certolizumab Pegol | Cimzia® | NO | YES | NO | YES | YES | YES | YES | YES | NO | NO | NO |
| Etanercept | Enbrel® | YES | YES | YES | YES | YES | YES | NO | NO | NO | NO | NO |
| Golimumab | Simponi® | NO | YES | NO | YES | NO | YES | NO | NO | YES | NO | NO |
| **TNFi practitioner-administered product and NOT subject to the PDP** | | | | | | | | | | | | |
| Infliximab | Remicade® | YES | YES | NO | YES | YES | YES | NO | YES | YES | NO | NO |
| **Integrin receptor antagonist practitioner-administered product and NOT subject to the PDP** | | | | | | | | | | | | |
| Vedolizumab | Entyvio® | NO | NO | NO | NO | NO | NO | NO | YES | YES | NO | NO |

AS=ankylosing spondylitis; CD=Crohn's disease; FDA=Food and Drug Administration; HS=hidradenitis suppurativa; JIA=juvenile idiopathic arthritis; nr-axSpA=non-radiographic axial spondyloarthritis; PDL=Preferred Drug List; PDP=Preferred Drug Program; Ps=plaque psoriasis; PsA=psoriatic arthritis; RA=rheumatoid arthritis; TNFi=tumor necrosis factor inhibitor; UC=ulcerative colitis; UV=uveitis

Current clinical criteria associated with TNFi subject to the PDP in the immunomodulators – systemic category:

1. Confirm diagnosis for FDA- or compendia-supported use

**AND**

2. Trial of a DMARD prior to treatment with an immunomodulator.


Humira® (adalimumab) [product insert]. AbbVie Inc. North Chicago. IL December 2021.
Enbrel® (etanercept) [product insert]. Immunex Corporation. Thousand Oaks. CA. April 2021.
Cimzia® (certolizumab pegol) [product insert]. UCB Inc. Smyrna. GA. March 2019.
Simponi® (golimumab) [product insert]. Janssen Biotech Inc. Horsham. PA. September 2019.
Remicade® (infliximab) [product insert]. Janssen Biotech. Inc. Horsham. PA. October 2021.
Entyvio® (vedolizumab) [product insert]. Takeda Pharmaceuticals U.S.A., Inc. Lexington. MA. August 2021.

# Age Recommendations

| TNF Inhibitor | Reference product | FDA-approved indications | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | RA | JIA | PsA | Ps | AS | nr-axSpA | CD | UC | HS | UV |
| **Self-administered products** | | | | | | | | | | | |
| Adalimumab | Humira® | Adults | ≥2 yrs of age | Adults | Adults | Adults | NO | ≥6 yrs of age | ≥5 yrs of age | ≥12 yrs of age | ≥2 yrs of age |
| Certolizumab Pegol | Cimzia® | Adults | NO | Adults | Adults | Adults | Adults | Adults | NO | NO | NO |
| Etanercept | Enbrel® | Adults | ≥2 yrs of age | Adults | ≥4 yrs of age | Adults | NO | NO | NO | NO | NO |
| Golimumab | Simponi® | Adults | NO | Adults | NO | Adults | NO | NO | Adults | NO | NO |
| **Practitioner-administered product** | | | | | | | | | | | |
| Infliximab | Remicade® | Adults | NO | Adults | Adults | Adults | NO | ≥6 yrs of age* | ≥6 yrs of age* | NO¥ | NO¥ |
| **Integrin Receptor Antagonist Practitioner-Administered Product** | | | | | | | | | | | |
| Vedolizumab | Entyvio® | NO | NO | NO | NO | NO | NO | Adults | Adults | NO | NO |

AS=ankylosing spondylitis; CD=Crohn's disease; FDA=Food and Drug Administration; HS=hidradenitis suppurativa; JIA=juvenile idiopathic arthritis; nr-axSpA=non-radiographic axial spondyloarthritis; Ps=plaque psoriasis; PsA=psoriatic arthritis; RA=rheumatoid arthritis; UC=ulcerative colitis; UV=uveitis; yrs=years

*Infliximab is FDA approved for reducing signs and symptoms and inducing and maintaining clinical remission for patients with moderately to severely active CD or UC *who have had an inadequate response to conventional therapy*.
¥There is compendia support for the use of infliximab for the treatment of HS and UV.

Humira® (adalimumab) [product insert]. AbbVie Inc. North Chicago. IL December 2021.
Enbrel® (etanercept) [product insert]. Immunex Corporation. Thousand Oaks. CA. April 2021.
Cimzia® (certolizumab pegol) [product insert]. UCB Inc. Smyrna. GA. March 2019.
Simponi® (golimumab) [product insert]. Janssen Biotech Inc. Horsham. PA. September 2019.
Remicade® (infliximab) [product insert]. Janssen Biotech. Inc. Horsham. PA. October 2021.
Entyvio® (vedolizumab) [product insert]. Takeda Pharmaceuticals U.S.A., Inc. Lexington. MA. August 2021.

# Maintenance Dosing Schedule

| TNF Inhibitor | Reference product | Manufacturer-recommended dosage frequency |
|---|---|---|
| **Self-administered products** | | |
| Adalimumab | Humira® | Every other week subcutaneous injection for all FDA-approved indications |
| Certolizumab Pegol | Cimzia® | Every 4-week subcutaneous injection for CD, RA, PsA, AS, and nr-axSpA, and every other week for Ps |
| Etanercept | Enbrel® | Weekly subcutaneous injections for all FDA-approved indications |
| Golimumab | Simponi® | Every 4-week subcutaneous injection for all FDA-approved indications |
| **Practitioner-administered product** | | |
| Infliximab | Remicade® | An intravenous infusion for a minimum of a 2-hour period every 8 weeks for CD, UC, RA, PsA, and Ps, and every 6 weeks for AS |
| **Integrin Receptor Antagonist Practitioner-Administered Product** | | |
| Vedolizumab | Entyvio® | An intravenous infusion for a minimum of a 30-minute period every 8 weeks for CD and UC |

AS=ankylosing spondylitis; CD=Crohn's disease; FDA=Food and Drug Administration; nr-axSpA=non-radiographic axial spondyloarthritis; Ps=plaque psoriasis; PsA=psoriatic arthritis; RA=rheumatoid arthritis; UC=ulcerative colitis


Humira® (adalimumab) [product insert]. AbbVie Inc. North Chicago. IL December 2021.
Enbrel® (etanercept) [product insert]. Immunex Corporation. Thousand Oaks. CA. April 2021.
Cimzia® (certolizumab pegol) [product insert]. UCB Inc. Smyrna. GA. March 2019.
Simponi® (golimumab) [product insert]. Janssen Biotech Inc. Horsham. PA. September 2019.
Remicade® (infliximab) [product insert]. Janssen Biotech. Inc. Horsham. PA. October 2021.
Entyvio® (vedolizumab) [product insert]. Takeda Pharmaceuticals U.S.A., Inc. Lexington. MA. August 2021.

# AGA Recommendations for Adult Outpatients with Moderate to Severe Luminal and Fistulizing CD

| Induction of remission |
| --- |
| • Suggests corticosteroids > no treatment.<br>• Start a biologic with or without an immunomodulator > wait until after failure of 5-ASA and/or corticosteroids.<br>• For patients naïve to biologics: recommends infliximab/adalimumab/ustekinumab > certolizumab pegol and suggests vedolizumab > certolizumab pegol. Recommends biologic monotherapy > thiopurine monotherapy.<br>• For patients with primary nonresponse[a] to TNFi: recommends ustekinumab. Suggests vedolizumab.<br>• For patients with secondary nonresponse[b]: recommends adalimumab or ustekinumab. Suggests vedolizumab. (If adalimumab was used previously, indirect evidence suggests infliximab used as second-line).<br>• Induction of fistula remission in patients with CD and active perianal fistula without perianal abscess: recommends biologic + antibiotic > biologic alone. Use of antibiotic alone is not suggested. |

5-ASA=5-aminosalicylic acid (includes mesalamine, olsalazine, balsalazide); AGA=American Gastroenterological Association; CD=Crohn's disease; TNFi=tumor necrosis factor inhibitor; thiopurine includes azathioprine

[a]Primary nonresponse: inadequate response
[b]Secondary nonresponse: relapse after an initial response to infliximab

Feuerstein JD, Ho EY, Shmidt E, et al. 2021;160(7):2496-2508.

# AGA Recommendations for Adult Outpatients with Moderate to Severe Luminal and Fistulizing CD (*continued*)

| Induction and maintenance of remission | Maintenance of remission |
|---|---|
| • Recommends TNFi (infliximab or adalimumab > certolizumab pegol) or ustekinumab<br>• Suggests vedolizumab or MTX (SUBQ or IM) monotherapy.<br>• Use of oral MTX, natalizumab, 5-ASA, or sulfasalazine is not suggested.<br>• For patients naïve to biologics and immunomodulators:<br>  ○ Suggests infliximab + thiopurines or adalimumab + thiopurines > infliximab or adalimumab monotherapy (indirect evidence suggests infliximab + MTX or adalimumab + MTX > infliximab or adalimumab monotherapy)<br>• Induction and maintenance of fistula remission in patients with CD and active perianal fistula: recommends infliximab. Suggests adalimumab, ustekinumab or vedolizumab. | • Use of corticosteroids is not recommended.<br>• Maintenance of remission in quiescent moderate to severe CD or corticosteroid-induced remission: suggests thiopurines. |

5-ASA=5-aminosalicylic acid (includes mesalamine, olsalazine, balsalazide); AGA=American Gastroenterological Association; CD=Crohn's disease; IM=intramuscular; MTX=methotrexate; SUBQ=subcutaneous; thiopurine includes azathioprine

Feuerstein JD, Ho EY, Shmidt E, et al. 2021;160(7):2496-2508.

# AGA Recommendations for Adult Outpatients with Moderate to Severe UC

| Induction of remission |
| --- |
| • For patients naïve to biologics: infliximab or vedolizumab > the standard dose of adalimumab or golimumab and there is limited evidence to inform appropriate positioning of tofacitinib. (Patients with less severe disease may choose self-administered SUBQ adalimumab for convenience).<br><br>• For patients who previously received infliximab (particularly those with primary nonresponse): recommends ustekinumab or tofacitinib > vedolizumab or adalimumab.<br><br>• Use of thiopurine or MTX monotherapy is not suggested.<br><br>• Suggests monotherapy with biologic (TNFi/vedolizumab/ustekinumab) or tofacitinib > thiopurine. |

AGA=American Gastroenterological Association; MTX=methotrexate; SUBQ=subcutaneous; UC=ulcerative colitis; thiopurine includes azathioprine; TNFi=tumor necrosis factor inhibitor

Feuerstein JD, Isaacs KL, Schneider Y, et al. 2020;158(5):1450-1461.

# AGA Recommendations for Adult Outpatients with Moderate to Severe UC (*continued*)

| Induction and maintenance of remission | Maintenance of remission |
|---|---|
| • Suggests introducing biologic with or without immunomodulator early > gradual step up after failure of 5-ASA, except in patients with less severe disease.<br><br>• Use of infliximab, adalimumab, golimumab, vedolizumab, ustekinumab, or tofacitinib (only after failure of or intolerance to TNFi) is recommended over no treatment.<br><br>• Suggests TNFi/vedolizumab/ustekinumab + a thiopurine or MTX > biologic or thiopurine monotherapy. MTX monotherapy is not suggested. | • Use of thiopurine monotherapy over no treatment is suggested.<br><br>• No recommendation made for biologic or tofacitinib monotherapy vs. thiopurine monotherapy.<br><br>• Achieved remission with biologics and/or immunomodulators or tofacitinib: continuing 5-ASA is not suggested.<br><br>• Use of MTX monotherapy is not suggested. |

5-ASA=5-aminosalicylic acid (includes mesalamine, olsalazine, balsalazide); AGA=American Gastroenterological Association; MTX=methotrexate; TNFi=tumor necrosis factor inhibitor; UC=ulcerative colitis; thiopurine includes azathioprine

Feuerstein JD, Isaacs KL, Schneider Y, et al. 2020;158(5):1450-1461.

# Utilization Analysis - Methodology

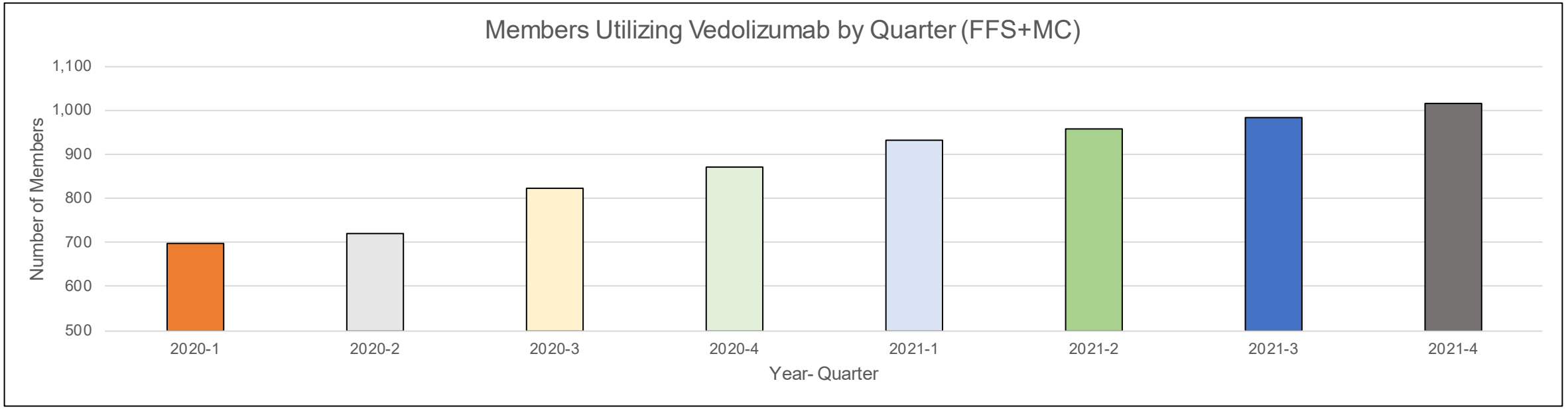
- Data source: Medicaid Data Warehouse (MDW)
- Timeframe: January 1, 2020, through December 31, 2021
- Sample: members who received vedolizumab during the timeframe of the analysis. Both pharmacy claims and Healthcare Common Procedure Coding System (HCPCS) codes specific to vedolizumab were included.
- Exclusion: vedolizumab-specific HCPCS codes with an incorrect national drug code (NDC) for vedolizumab.

# Utilization Analysis - Methodology

- Limitations:
  - The Medicaid Confidential Data Cell Size Policy (OHIP-0001) requires that no cell containing a value of 1 to 30 be reported. The cell size value must be reported as ≤30 in all public-facing documents. Additionally, no cell can be reported that allows a value of 1 to 30 to be derived from other reported cells or information. Due to the small sample size, reporting the raw numbers or the percentages of patients would violate the Medicaid Confidential Data Cell Size Policy.

  - While analyzed time periods account for inherent delays in claim/encounter submissions, data may not be fully complete.

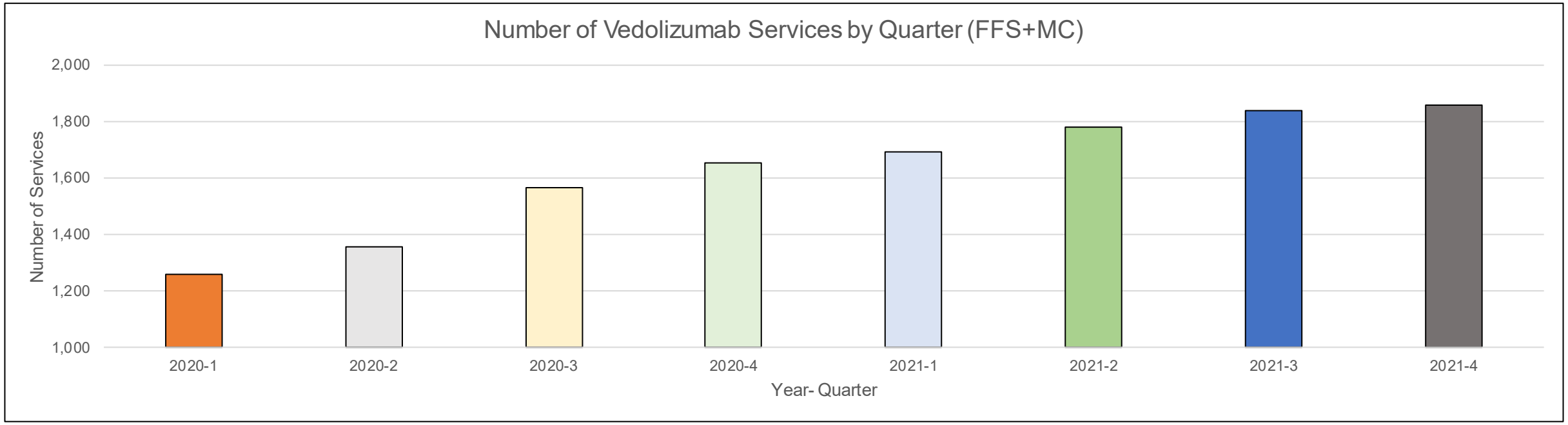
# Results: Utilization by Number of Members




Source: MDW Extract date: May 25, 2022. FFS=fee-for-service; MC=managed care

- During the 2-year period, 1,579 members (FFS+MC) received vedolizumab.
- From 2020 to 2021, the number of members utilizing vedolizumab increased by 16.4%.

# Results: Utilization by Number of Services




Source: MDW Extract date: May 25, 2022. FFS=fee-for-service; MC=managed care

- During the 2-year period, there were 13,005 vedolizumab services/ pharmacy claims.
- From 2020 to 2021, there was a 23.0% increase in vedolizumab services/ pharmacy claims.

# Results: Diagnosis Evaluation

- Members were included in the analysis if they started vedolizumab therapy during the timeframe of January 1, 2021, through December 31, 2021.

- To determine if the member had an FDA-approved or compendia-supported indication, an evaluation of the prior year (i.e., 2020) and evaluation year (i.e., 2021) was conducted.

- A total of 457 members were identified as starting vedolizumab therapy during the timeframe of the analysis.
  - The majority of members were using vedolizumab for an FDA-approved indication and ≤30 members did not have a documented FDA-approved indication for the use of vedolizumab.

# Conclusions

- Vedolizumab is approved by the FDA for the treatment of moderately to severely active CD and moderately to severely active UC.
- Per treatment guidelines for CD, a TNFi (infliximab or adalimumab) or ustekinumab is recommended for induction and maintenance of remission (vedolizumab or methotrexate is only suggested).
- Per treatment guidelines for UC, use of infliximab, adalimumab, golimumab, vedolizumab, ustekinumab, or tofacitinib (only after failure of or intolerance to a TNFi) is recommended over no treatment for induction and maintenance of remission.
- In FFS+MC, a majority of members were using vedolizumab for an FDA-approved indication.

# UB Recommendations to DOH for Vedolizumab Clinical Policy

- Recommend a diagnosis requirement for covered indications

AND

- Consider implementation of step therapy for vedolizumab: requiring the use of a DMARD OR a TNFi prior to initiation of vedolizumab therapy.

# References


1. Remicade® (infliximab) [product insert]. Janssen Biotech. Inc. Horsham. PA. October 2021.
2. Renflexis® (infliximab-abda) [product insert]. Merck Sharp & Dohme Corp. Kenilworth. NJ. January 2022.
3. Inflectra® (infliximab-dyyb) [product insert]. Manufactured by Celltrion. Inc. Distributed by Pfizer. New York. NY. June 2021.
4. Avsola® (infliximab-axxq) [product insert]. Amgen Inc. Thousand Oaks. CA. September 2021.
5. Humira® (adalimumab) [product insert]. AbbVie Inc. North Chicago. IL December 2021.
6. Cimzia® (certolizumab pegol) [product insert]. UCB Inc. Smyrna. GA. March 2019.
7. Enbrel® (etanercept) [product insert]. Immunex Corporation. Thousand Oaks. CA. April 2021.
8. Simponi® (golimumab) [product insert]. Janssen Biotech Inc. Horsham. PA. September 2019.
9. Entyvio® (vedolizumab) [product insert]. Takeda Pharmaceuticals U.S.A., Inc. Lexington. MA. August 2021.
10. 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(7):2496-2508. doi:10.1053/j.gastro.2021.04.022
11. Feuerstein JD, Isaacs KL, Schneider Y, et al. AGA Clinical Practice Guidelines on the Management of Moderate to Severe Ulcerative Colitis. Gastroenterology. 2020;158(5):1450-1461. doi:10.1053/j.gastro.2020.01.006