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New Drug Update 2025

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This presentation considers the properties and uses of selected new therapeutic agents. The indications and routes of administration for these new drugs are reviewed, as are the most important precautions and practical considerations regarding their use. Where possible, the properties of the new drugs are compared with those of older drugs marketed for the same indications. A New Drug Comparison Rating (NDCR) is provided for each of the new drugs considered.

Learning Objectives:

1. Identify new therapeutic agents marketed within the last 12 months.
2. Describe the new therapeutic agents' indications, mechanism of action and appropriate use.
3. Identify the new therapeutic agents' adverse events, risks, and considerations regarding dosage and administration.
4. Compare the new therapeutic agents with older medications that have similar properties and uses.

New Drug Comparison Rating (NDCR) system

5 = important advance
4 = significant advantage(s) (e.g., with respect to use/effectiveness, safety, administration)
3 = no or minor advantage(s)/disadvantage(s)
2 = significant disadvantage(s) (e.g., with respect to use/effectiveness, safety, administration)
1 = important disadvantage(s)

Alzheimer's disease **Donanemab-azbt (Kisunla – Lilly)**

Description: An amyloid beta-directed antibody that reduces amyloid beta plaques;

Indication: Administered intravenously for the treatment of Alzheimer's disease; should be initiated in patients with mild cognitive impairment or mild dementia stage of disease;

Donanemab was evaluated in a placebo-controlled study in patients with confirmed presence of amyloid pathology and mild cognitive impairment or mild dementia stage of disease. Patients treated with donanemab demonstrated a statistically significant reduction in clinical decline in the integrated Alzheimer's Disease Rating Scale (iADRS), as well as the Clinical Dementia Rating Scale – Sum of Boxes (CDR-SB), compared to placebo at Week 76. The drug also significantly reduced amyloid beta plaques.

Comparable drug: Lecanemab (Leqembi);

Recommended dosage: 700 mg administered as an intravenous infusion over approximately 30 minutes every 4 weeks for the first 3 doses, followed by 1400 mg every 4 weeks; a recent baseline brain MRI should be obtained prior to initiating treatment, and prior to the 2nd, 3rd, 4th, and 7th infusions if radiographically observed amyloid related imaging abnormalities (ARIA) occur;

Product: Injection: Single-dose vials – 350 mg/20 mL (should be stored in a refrigerator); should be diluted to a final concentration of 4 mg/mL to 10 mg/mL with 0.9% Sodium Chloride Injection;

Contraindications/most important risks:

- Amyloid related imaging abnormalities (ARIA, including ARIA with edema [ARIA-E] and ARIA with hemosiderin deposition [ARIA-H]); (boxed warning);
- ApoE4 carrier status (patients who are ApoE4 homozygotes have a higher incidence of ARIA compared to heterozygotes and noncarriers);
- Infusion-related reactions (pre-treatment with antihistamines, acetaminophen, or corticosteroids should be considered prior to subsequent dosing);

Most common adverse events: ARIA-H microhemorrhage (25%), ARIA-E (24%); ARIA-H superficial siderosis (15%), headache (13%), infusion-related reactions (9%);

Comparison with lecanemab

Advantages:

- Has data to support stopping therapy based on reduction of amyloid plaques to minimal levels;
- Is administered every 4 weeks (whereas lecanemab is administered every 2 weeks);
- Infusion is administered over approximately 30 minutes (whereas lecanemab is administered over approximately 1 hour)**;**

Disadvantages:

- Clinical benefit with either donanemab or lecanemab is limited;

New Drug Comparison Rating (NDCR) =

Schizophrenia **Xanomeline/Trospium chloride (Cobenfy – Bristol-Myers Squibb)**

Description: A combination of a muscarinic (cholinergic) agonist (xanomeline) and a peripheral muscarinic antagonist (trospium); xanomeline is a new drug and trospium (e.g., Sanctura) has been previously marketed for the treatment of overactive bladder;

Indication: Administered orally for the treatment of schizophrenia in adults;

The combination product was evaluated in two placebo-controlled clinical trials. The primary efficacy measure was the change from baseline in the Positive and Negative Syndrome Scale (PANSS) total score at Week 5. The PANSS is a 30-item scale that measures symptoms of schizophrenia, and each item is rated by a clinician on a seven-point scale. Patients receiving the new product experienced a meaningful reduction in symptoms from baseline to Week 5 compared to those in the placebo group.

Comparable drugs: Aripiprazole (e.g., Abilify) and other atypical antipsychotic dopamine antagonists;

Recommended dosage: Should be administered at least 1 hour before a meal or 2 hours after a meal; initial dosage - 50 mg/20 mg twice a day for at least 2 days, then increased to 100 mg/20 mg twice a day for at least 5 days; may be increased to 125 mg/30 mg twice a day based on patient tolerability and response; for geriatric patients, a slower dosage titration should be considered and the maximum recommended dosage is 100 mg/20 mg twice a day;

Products: Capsules – 50 mg/20 mg, 100 mg/20 mg, 125 mg/30 mg;

Contraindications/most important risks:

- Contraindicated in patients with gastric retention, urinary retention, or untreated narrow-angle glaucoma;
- Angioedema;
- Increased heart rate (should be assessed at baseline and as clinically indicated during treatment);
- Decreased gastrointestinal motility;
- Central nervous system effects (patients should be advised to not drive or operate machinery until they know how the product affects them);
- Hepatic impairment (contraindicated in patients with moderate or severe impairment, and is not recommended in patients with mild impairment);
- Renal impairment (is not recommended in patients with moderate or severe impairment);
- Interactions: activity and adverse events may be increased by the concurrent use of strong CYP2D6 inhibitors or drugs that are eliminated by active tubular secretion; concurrent use with sensitive substrates of CYP3A4 or P-glycoprotein may increase the risk of adverse events of these substrates; concurrent use with antimuscarinic drugs may increase the risk of anticholinergic adverse events;

Most common adverse events: Nausea (19%), dyspepsia (18%), constipation (17%), vomiting (15%), hypertension (11%);

Comparison with aripiprazole (as representative of the atypical antipsychotic dopamine antagonists)
Advantages:

- Has a novel mechanism of action in targeting cholinergic receptors;
- May be effective in some patients in whom other antipsychotic agents are not effective or not tolerated;
- Labeling does not include a boxed warning regarding use in the elderly with dementia-related psychosis;
- Is not likely to cause extrapyramidal reactions and weight gain;

Disadvantages:

- Is more likely to cause cholinergic/anticholinergic adverse events;
- Is administered twice a day (whereas aripiprazole is administered once a day);
- Labeled indications are more limited (compared with most antipsychotic dopamine antagonists);
- Has not been directly compared with other antipsychotic drugs in clinical trials;

New Drug Comparison Rating (NDCR) =

Pain **Suzetrigine (Journavx – Vertex)**

Description: A sodium channel blocker;

Indication: Administered orally for the treatment of moderate to severe acute pain in adults;

Suzetrigine was evaluated in two placebo and active-controlled trials, one following full abdominoplasty and the other following bunionectomy. Patients received suzetrigine (100 mg loading dose followed by 50 mg every 12 hours), placebo, or hydrocodone/acetaminophen (5 mg/325 mg every 6 hours) for a duration of 48 hours. Ibuprofen (400 mg every 6 hours as needed for pain relief) was permitted as a rescue medication. Pain intensity was measured using a patient-reported 11-point numeric pain rating scale (NPRS), ranging from 0 to 10. Suzetrigine provided superior reduction in pain intensity compared with placebo in both studies. Compared with hydrocodone/acetaminophen, the reduction of pain intensity was similar with suzetrigine in one study, but significantly smaller in the study in patients with bunionectomy

Comparable drugs: Hydrocodone/acetaminophen;

Recommended dosage: Starting dose – 100 mg on an empty stomach at least 1 hour before or 2 hours after food; 12 hours after the starting dose – 50 mg every 12 hours with or without food; use has not been studied beyond 14 days;

Product: Tablets – 50 mg;

Contraindications/most important risks:

- Hepatic impairment (use should be avoided in patients with severe impairment, and should be used in a reduced dosage in patients with moderate impairment);
- Concomitant use with strong CYP3A inhibitors (contraindicated); dosage should be reduced when used concurrently with a moderate CYP3A inhibitor; food or drink containing grapefruit should be avoided;
- Concomitant use with strong or moderate CYP3A inducers should be avoided;
- Concomitant use may reduce the action of sensitive CYP3A substrates or CYP3A substrates for which minimal concentration changes may result in reduced efficacy;
- Hormonal contraceptives: patients using hormonal contraceptives containing progestins other than levonorgestrel and norethindrone should use additional nonhormonal contraceptives, or use alternative contraceptives (such as a combined oral contraceptive containing ethinyl estradiol with levonorgestrel or norethindrone) during concurrent treatment and for 28 days after discontinuation of suzetrigine;

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Most common adverse events: Pruritus (2%), muscle spasms (1%), rash (1%);

Comparison with hydrocodone/acetaminophen

Advantages:

- Is a non-opioid oral analgesic with a novel mechanism of action (sodium channel blocker);
- Has not been observed to have addictive potential;
- Has a longer duration of action (administered every 12 hours compared with every 6 hours with hydrocodone/acetaminophen);

Disadvantages:

- May be less effective in some patients;
- Labeled indications are more limited (e.g., is not indicated for the treatment of chronic pain);

New Drug Comparison Rating (NDCR) =

Hypertension **Aprocitentan (Tryvio – Idorsia)**

Description: An endothelin receptor antagonist (ERA); inhibits the binding of endothelin (ET)-1 to ET_A and ET_B receptors;

Indication: Administered orally for the treatment of hypertension in combination with other antihypertensive drugs, to lower blood pressure in adult patients who are not adequately controlled on other drugs;

Aprocitentan was evaluated in a clinical trial in adults with systolic blood pressure (SBP) of 140 mmHg or higher who were prescribed at least three antihypertensive medications. Patients were switched to standard background antihypertensive therapy consisting of an angiotensin receptor blocker, a calcium channel blocker, and a diuretic. Patients with concomitant use of beta-blockers continued this treatment throughout the study. The primary efficacy endpoint was the change in sitting SBP from baseline to Week 4. Aprocitentan was statistically superior to placebo in reducing sitting SBP at Week 4, and most of the blood pressure lowering effect occurred within the first two weeks of treatment. The treatment effect was consistent for sitting diastolic blood pressure.

Comparable drugs: Angiotensin receptor blockers, calcium channel blockers, diuretics;

Recommended dosage: 12.5 mg once a day;

Product: Film-coated tablets – 12.5 mg;

Contraindications/most important risks:

- Pregnancy (may cause major birth defects (contraindicated during pregnancy; boxed warning; available only through a restricted distribution program [Tryvio REMS] – **requirement deleted 4/25**);
- Hepatotoxicity and liver failure (serum aminotransferases and total bilirubin should be monitored);
- Fluid retention;
- Decreases in hemoglobin;
- Decreased sperm count;
- Hepatic impairment (not recommended in patients with moderate or severe impairment);

Most common adverse events: Edema/fluid retention (9%); anemia (4%);

Comparison with other oral antihypertensive drugs

Advantages:

- Has a novel mechanism of action among antihypertensive drugs (antagonism of endothelin receptors);
- Increases the effectiveness of combination antihypertensive drug regimens;
- Is less likely to interact with other drugs;

Disadvantages:

- Is not a first-line treatment for hypertension;
- Has greater risk of causing embryo-fetal toxicity;
- Has greater risk of causing hepatotoxicity;
- Is available only through a restricted distribution program **(requirement deleted 4/25)**;

New Drug Comparison Rating (NDCR) =

Chronic obstructive pulmonary disease **Ensifentrine (Ohtuvayre – Verona)**

Description: A phosphodiesterase 3 (PDE3) inhibitor and phosphodiesterase 4 (PDE4) inhibitor;

Indication: Administered by oral inhalation for the maintenance treatment of chronic obstructive pulmonary disease (COPD) in adult patients;

Ensifentrine was evaluated in two 24-week placebo-controlled clinical trials in adult patients with moderate to severe COPD. Most patients were taking concurrent therapy (i.e., LABA, LAMA, ICS). The drug was administered by oral inhalation via standard jet nebulizer such as PARI LC Sprint. The primary endpoint for both trials was the change from baseline in forced expiratory volume in one second (FEV_1) $AUC_{0\text{-}12h}$ post dose at Week 12. Ensifentrine demonstrated a statistically significant improvement in this endpoint compared with placebo.

Comparable drugs: Roflumilast (e.g., Daliresp) is a selective PDE4 inhibitor that is administered orally to reduce the risk of COPD exacerbations in patients with severe COPD associated with chronic bronchitis and a history of exacerbations. Long-acting beta adrenergic agonists (LABA), long-acting muscarinic antagonists (LAMA; anticholinergics), and/or inhaled corticosteroids (ICS) are often used in combination via oral inhalation for the maintenance treatment of COPD.

Recommended dosage: 3 mg (one ampule) twice a day, once in the morning and once in the evening, administered by oral inhalation using a standard jet nebulizer with a mouthpiece connected to an air compressor;

Product: Inhalation suspension – 3 mg/2.5 mL for oral inhalation in unit-dose ampules; ampule should be removed from the foil pouch immediately before use and shaken vigorously;

Contraindications/most important risks:

- Should not be used to treat acute symptoms of bronchospasm;
- Paradoxical bronchospasm;
- Psychiatric adverse events including suicidality;
- Hepatic impairment (exposure is increased and should be used with caution);

Most common adverse events: Back pain (2%), hypertension (2%); urinary tract infection (1%), diarrhea (1%);

Comparison with roflumilast

Advantages:

- Is the first agent to selectively inhibit both PDE3 and PDE4;
- Is less likely to cause systemic adverse events and interact with other medications;

Disadvantages:

- Route of administration is less convenient (oral inhalation using a nebulizer [roflumilast is administered orally in the treatment of COPD]);
- Is administered twice a day (whereas roflumilast is administered once a day);

New Drug Comparison Rating (NDCR) =

Liver disease **Resmetirom (Rezdiffra – Madrigal)**

Description: A partial agonist of the thyroid hormone receptor-beta (THR-beta); activation in the liver reduces liver fat accumulation;

Indication: Administered orally, in conjunction with diet and exercise, for the treatment of adults with noncirrhotic, nonalcoholic steatohepatitis (NASH) with moderate to advanced liver fibrosis (consistent with stages F2 to F3 fibrosis);

The condition being treated has been recently renamed to metabolic dysfunction-associated steatohepatitis (MASH). Resmetirom was evaluated in a placebo-controlled trial in which a surrogate endpoint (extent of liver inflammation and scarring) was analyzed at month 12 in a 54-month trial. Two doses of the drug, 80 mg and 100 mg, were evaluated based on the patient's weight. In the patients treated with a dosage of 80 mg once daily, 26%-27% experienced NASH resolution and no worsening of liver scarring, compared with 24%-36% of patients treated with 100 mg once daily and 9%-13% of those receiving placebo. In addition, 23% of those receiving the 80 mg dose and 24%-28% of those receiving the 100 mg dose experienced an improvement in liver scarring and no worsening of NASH, compared with 13%-15% of those who received placebo. Accelerated approval was provided based on the improvement of surrogate markers and continuing studies are being conducted.

Comparable drug: None; glucagon-like peptide-1 (GLP-1) receptor agonists and pioglitazone have been reported to improve steatohepatitis, but not fibrosis;

Recommended dosage: 80 mg once a day in patients weighing less than 100 kg; 100 mg once a day in patients weighing 100 kg or more; dosage should be reduced in patients treated concurrently with a moderate CYP2C8 inhibitor (e.g., clopidogrel);

Products: Film-coated tablets – 60 mg, 80 mg, 100 mg;

Contraindications/most important risks:

- Decompensated cirrhosis (use should be avoided);
- Hepatotoxicity (liver function tests and liver-related adverse events should be monitored);
- Hepatic impairment (use should be avoided in patients with moderate to severe impairment);
- Gallbladder-related adverse events (cholelithiasis, cholecystitis);
- Is a CYP2C8 substrate and concurrent use with a strong CYP2C8 inhibitor (gemfibrozil) is not recommended;
- Is a weak CYP2C8 inhibitor and may increase the activity of CYP2C8 substrates (e.g., pioglitazone);
- Is an OATP1B1 and OATP1B3 substrate and activity may be increased by inhibitors of these transporters (e.g., cyclosporine); concurrent use is not recommended;
- May increase concentrations and activity of some statins; daily dosage of rosuvastatin and simvastatin should not exceed 20 mg; daily dosage of atorvastatin and pravastatin should not exceed 40 mg;

Most common adverse events (incidence with 80 mg once daily dosage): Diarrhea (23%), nausea (18%), vomiting (7%), pruritus (6%);

Comparison with other options

Advantages:

- Is the first drug to be approved for the treatment of patients with fatty liver disease;
- Reduces the extent of both liver inflammation and scarring (fibrosis);

Disadvantages:

- Has been approved under the accelerated approval program and additional studies are required;

New Drug Comparison Rating (NDCR) =

Bacterial infection **Pivmecillinam hydrochloride (Pivya – Utility)**

Description: A penicillin class antibacterial agent that is a prodrug that is converted to mecillinam;

Indication: Administered orally for the treatment of female patients 18 years of age and older with uncomplicated urinary tract infections (uUTI) caused by susceptible isolates of *Escherichia coli, Proteus mirabilis,* and *Staphylococcus saprophyticus*;

Mecillinam is primarily active against gram-negative bacteria. Its effectiveness was evaluated in three clinical trials in which it was compared with placebo, cephalexin, and ibuprofen. The endpoint was the composite response rate of clinical cure and microbiological response. The composite response was achieved in 62%, 72%, and 66% of the patients treated with pivmecillinam compared with, respectively, 10% (placebo), 76% (cephalexin), and 22% (ibuprofen).

Comparable drug: Cephalexin;

Recommended dosage: 185 mg 3 times a day for 3 to 7 days as clinically indicated;

Product: Film-coated tablets – 185 mg (pivmecillinam);

Contraindications/most important risks:

- Serious hypersensitivity reactions to beta-lactam antibacterial drugs (contraindicated);
- Primary or secondary carnitine deficiency from inherited disorders and other inborn errors of metabolism (contraindicated);
- Acute porphyria (contraindicated);
- Severe cutaneous adverse reactions (e.g., Stevens-Johnson Syndrome);
- Carnitine depletion (alternative treatment should be considered in patients with significant renal impairment, decreased muscle mass, and/or those requiring long-term antimicrobial treatment);
- *Clostridioides difficile*-associated diarrhea;
- Interference with newborn screening test (treatment of a pregnant woman prior to delivery may cause a false positive test for isovaleric acidemia in the newborn);
- Concurrent use with valproic acid, valproate, or other pivalate-generating drugs should be avoided because of the increased risk of carnitine depletion;
- May reduce the clearance of methotrexate and increase its activity (alternative therapy should be considered);

Most common adverse events: Nausea (4%), diarrhea (2%); vulvovaginal candidiasis (2%); genital pruritus (2%);

Comparison with cephalexin and other urinary tract antibacterial agents

Advantages:

- Has higher specificity against penicillin-protein binding-2 (PBP-2) in the cell wall of gram-negative bacteria than most other beta-lactam antibiotics;
- May be effective in certain patients with uUTI for which other treatments are not effective;

Disadvantages:

- Use is limited to adult female patients;
- Is administered 3 times a day (whereas most comparable agents are administered less frequently);
- Has a greater risk of carnitine depletion and concurrent use with pivalate-generating drugs (e.g., valproate) is not recommended;

New Drug Comparison Rating (NDCR) =

Bacterial infection **Sulopenem etzadroxil/Probenecid (Orlynvah – Iterum)**

Description: A combination of a penem antibacterial agent and a renal tubular transport inhibitor; sulopenem etzadroxil is a prodrug that is converted to the beta-lactam antibacterial agent sulopenem following administration; probenecid inhibits the renal clearance and increases plasma concentrations of sulopenem;

Indication: Administered orally for the treatment of uncomplicated urinary tract infections (uUTI) caused by *Escherichia coli, Klebsiella pneumoniae,* or *Proteus mirabilis*, in adult women who have limited or no alternative oral antibacterial treatment options;

Is not indicated for the treatment of complicated UTI or as step-down treatment after intravenous antibacterial of cUTI, or for the treatment of complicated intra-abdominal infections (cIAI) or as step-down treatment after intravenous antibacterial treatment of cIAI.

Sulopenem/probenecid was evaluated in two noninferiority trials. The first trial was conducted in patients with amoxicillin/clavulanate-susceptible pathogens and the composite response rate (combined microbiological response and clinical response) was 62% compared to 55% in the amoxicillin/clavulanate group. In the second trial in patients with ciprofloxacin-resistant pathogens, the composite response rate was 48% compared to 33% in the ciprofloxacin group

Comparable drugs: Amoxicillin/clavulanate (e.,g., Augmentin), ciprofloxacin (e.g., Cipro), and other urinary tract antibacterial drugs;

Recommended dosage: 500 mg/500 mg twice a day with food for 5 days;

Product: Tablets – 500 mg sulopenem etzadroxil/500 mg probenecid;

Contraindications/most important risks:

- Hypersensitivity reactions including anaphylaxis (contraindicated in patients with a history of hypersensitivity reactions to other beta-lactam antibacterial drugs (e.g., penicillins, cephalosporins);
- Exacerbation of gout (contraindicated in patients with known uric acid kidney stones);
- Patients with known blood dyscrasias (contraindicated);
- *Clostridioidies difficile*-associated diarrhea;
- Concurrent use with ketorolac tromethamine is contraindicated and concurrent use with ketoprofen is not recommended;

Most common adverse events: Diarrhea (10%); nausea (4%); vulvovaginal mycotic infection (2%);

Comparison with other urinary tract antibacterial drugs

Advantages:

- Is the first penem (carbapenem) antibacterial drug to be approved for oral administration;
- May be more effective than other antibacterial agents in treating certain patients with uUTI;

Disadvantages:

- Use is limited to adult female patients;
- Labeled indication is restricted to women who have limited or no alternative oral antibacterial treatment options;
- Inclusion of probenecid increases the risk of certain adverse events and drug interactions;

New Drug Comparison Rating (NDCR) =

Atopic Dermatitis **Lebrikizumab-lbkz (Ebglyss – Lilly)**

Description: A monoclonal antibody that is an interleukin-13 (IL-13) antagonist and inhibits IL-13 signaling;

Indication: Administered subcutaneously for the treatment of adults and pediatric patients 12 years of age and older who weigh at least 40 kg with moderate-to-severe atopic dermatitis whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable;

Lebrikizumab was evaluated in three placebo-controlled trials. At Week 16 of treatment the Investigator's Global Assessment (IGA) score of 0 (clear) or 1 (almost clear) was attained in 43% and 33% of patients treated with lebrikizumab in the first two studies, compared with 13% and 11%, respectively of those receiving placebo. The Eczema Area and Severity Index-75 (EASI-75; at least a 75% improvement in EASI score from baseline) was attained in 59% and 52% of those treated with lebrikizumab, respectively, compared with 16% and 18% of those receiving placebo, EASI-90 was attained in 38% and 31% of patients, compared with 9% and 10% of those receiving placebo.

Comparable drugs: Dupilumab (Dupixent; an IL-4 receptor antagonist);

Recommended dosage: Initial dosage – 500 mg (two 250 mg injections) at Week 0 and Week 2, followed by 250 mg (one injection) every 2 weeks until Week 16 or later, when adequate clinical response is achieved; the maintenance dosage is 250 mg every 4 weeks;

Product: Injection: single-dose prefilled pen and single-dose prefilled syringe with needle shield – 250 mg/2 mL;

Contraindications/most important risks:

- Hypersensitivity reactions;
- Conjunctivitis and keratitis;
- Parasitic (helminth) infections (pre-existing infections should be treated before initiating lebrikizumab);
- Use of live vaccines should be avoided during treatment;

Most common adverse events: Conjunctivitis (10%), injection site reactions (3%), herpes zoster (less than 1%);

Comparison with dupilumab

Advantages:

- Is administered less frequently for maintenance treatment (every 4 weeks rather than every 2 weeks);

Disadvantages:

- Labeled indications are more limited (dupilumab is indicated for the treatment of moderate-to-severe atopic dermatitis in adults and pediatric patients aged 6 months and older; dupilumab is also indicated for the add-on maintenance treatment of patients with moderate-to-severe asthma characterized by an eosinophilic phenotype or with corticosteroid-dependent asthma, inadequately controlled chronic obstructive pulmonary disease and an eosinophilic phenotype, and in the treatment of patients with chronic rhinosinusitis with nasal polyps, eosinophilic esophagitis, and prurigo nodularis);
- Has not been directly compared with dupilumab in clinical trials;

New Drug Comparison Rating (NDCR) =

Prurigo nodularis and atopic dermatitis **Nemolizumab-ilto (Nemluvio – Galderma)**

Description: A monoclonal antibody that is an interleukin-31 (IL-31) receptor antagonist and inhibits IL-31 signaling;

Indications: Administered subcutaneously: initially approved for the treatment of adults with prurigo nodularis; subsequently approved for the treatment of adults and pediatric patients 12 years of age and older with moderate-to-severe atopic dermatitis in combination with topical corticosteroids and/or calcineurin inhibitors when the disease is not adequately controlled with topical prescription therapies

Nemolizumab was evaluated in the treatment of atopic dermatitis in two placebo-controlled trials. Concomitant low and/or medium potency topical corticosteroids and/or topical calcineurin inhibitors were administered for at least 14 days prior to baseline and continued during the trials. At Week 16 of treatment, the Investigator's Global Assessment (IGA) score of 0 (clear) or 1 (almost clear) was attained in 36% of patients treated with nemolizumab (compared with 25% with placebo), the Eczema Area and Severity Index-75 (EASI-75; at least a 75% improvement in EASI score from baseline) was attained in 44% (compared with 29% with placebo), and a Peak Pruritus Numeric Rating Scale (PP-NRS) improvement was attained in 33% of patients (compared with 15% with placebo).

Comparable drug: Dupilumab (Dupixent; an IL-4 receptor antagonist);

Recommended dosage (for patients with atopic dermatitis): Initial dose of 60 mg (two 30 mg injections), followed by 30 mg given every 4 weeks; after 16 weeks of treatment, for patients who achieve clear or almost clear skin, a dosage of 30 mg every 8 weeks is recommended;

Product: For injection: single-dose prefilled dual-chamber pen containing 30 mg of nemolizumab lyophilized powder and diluent (water for injection); must be reconstituted prior to administration;

Contraindications/most important risks:

- Hypersensitivity reactions;
- Use of live vaccines should be avoided during treatment;

Most common adverse events (in patients with atopic dermatitis): Headache (5%), arthralgia (1%), urticaria (1%), myalgia (1%);

Comparison with dupilumab (for the treatment of atopic dermatitis)

Advantages:

- Is the first monoclonal antibody that specifically targets IL-31 receptors;
- Is administered less frequently for maintenance treatment (every 4 weeks for initial treatment, and every 8 weeks for maintenance treatment);

Disadvantages:

- Formulation requires reconstitution;
- Labeled indications are more limited (dupilumab is indicated for the treatment of moderate-to-severe atopic dermatitis in adult and pediatric patients aged 6 months and older and for the treatment of prurigo nodularis in adults; dupilumab is also approved for the add-on maintenance treatment of patients with moderate-to-severe asthma characterized by an eosinophilic phenotype or with oral corticosteroid dependent asthma, inadequately controlled chronic obstructive pulmonary disease and an eosinophilic phenotype, and chronic rhinosinusitis with nasal polyps, and for the treatment of patients with eosinophilic esophagitis);
- Has not been directly compared with dupilumab in clinical trials;

New Drug Comparison Rating (NDCR) =

Hyperhidrosis **Sofpironium bromide (Sofdra – Botanix)**

Description: An anticholinergic agent;

Indication: Applied topically for the treatment of primary axillary hyperhidrosis in adult and pediatric patients 9 years of age and older;

Sofpironium was evaluated in two vehicle-controlled clinical trials in patients who had symptoms of axillary hyperhidrosis for at least 6 months. The co-primary endpoints were the proportion of subjects having at least a 2-point improvement in the Hyperhidrosis Disease Severity Measure-Axillary, 7-item (HDSM-Ax-7) scale score, and the change in gravimetric sweat production (GSP) from Baseline to Day 43. The new agent provided statistically meaningful changes in both endpoints, compared to the vehicle.

Comparable drugs: Anticholinergic agents: Glycopyrronium (Qbrexxa; applied topically); onabotulinumtoxinA (Botox) is approved to treat severe primary axillary hyperhidrosis in patients who have an inadequate response with topical agents:

Recommended dosage: Apply one pump per underarm once a day at bedtime; patient should not shower or wash underarms for at least 8 hours following application; patient should not shave armpits at least 8 hours before application; patient should not shower at least 30 minutes before application;

Product: Topical gel – 12.45% (each pump delivers 72 mg of sofpironium in 0.67 mL of gel; product is flammable and fire, flame, and smoking should be avoided during and immediately after application;

Contraindications/most important risks:

- Contraindicated in patients with medical conditions that might be exacerbated by the anticholinergic effect (e.g., glaucoma, severe ulcerative colitis, myasthenia gravis);
- Urinary retention;
- Potential for lack of sweating and body temperature control in hot environmental conditions;
- Transient blurred vision (avoid operating a vehicle or machinery until symptoms resolve);
- Concurrent use with other agents with anticholinergic activity can cause additive effects and should be avoided;
- Concurrent use with a strong CYP2D6 inhibitor should be avoided;

Most common adverse events: Dry mouth (14%), blurred vision (9%), application site pain (8%), erythema (7%), mydriasis (7%), dermatitis (6%), pruritus (5%), urinary retention (2%), irritation (2%), exfoliation (2%);

Comparison with other topical agents

Advantages:

- May be more effective;

Disadvantages:

- Has not been directly compared with other agents in clinical trials;

New Drug Comparison Rating (NDCR) =

Pre-assessment questions

Which of the following agents is indicated for the treatment of patients with hypertension?

a. ensifentrine
b. donanemab
c. resmetirom
d. aprocitentan

Which of the following agents should be administered at least 1 hour before a meal or at least 2 hours after a meal?

a. sofpironium
b. xanomeline
c. pivmecillinam
d. sulopenem

Which of the following agents is administered by oral inhalation?

a. sofpironium
b. lebrikizumab
c. ensifentrine
d. resmetirom

When comparing pivmecillinam and sulopenem, which of the following statements is correct?

a. Pivmecillinam is administered three times a day and sulopenem is administered twice a day.
b. Pivmecillinam should be administered with food but sulopenem should be administered apart from food.
c. Pivmecillinam is indicated for the treatment of uncomplicated urinary tract infections and sulopenem is indicated for the treatment of complicated urinary tract infections.
d. Sulopenem is associated with a risk of carnitine depletion whereas pivmecillinam does not.