New Drug Update 2023

Presentation by Daniel A. Hussar, Ph.D.
Dean Emeritus and Remington Professor Emeritus
Philadelphia College of Pharmacy

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:

After attending this program, the participant will be able to:
1. Identify the new therapeutic agents and explain their appropriate use.
2. Identify the indications and mechanisms of action of the new drugs.
3. Identify the most important adverse events and other risks of the new drugs.
4. State the route of administration for each new drug and the most important considerations regarding dosage and administration.
5. Compare the new therapeutic agents with older medications to which they are most similar in properties and/or use, and identify the most important advantages and disadvantages of the new drugs.

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)

Diabetes **Tirzepatide (Mounjaro – Lilly) – 2022**

Description: A glucagon-like peptide-1 (GLP-1) receptor and glucose-dependent insulinotropic polypeptide (GIP) receptor agonist;

Indication: Administered subcutaneously as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus;

Comparable drugs: Dulaglutide (Trulicity), semaglutide (Ozempic);

Recommended dosage:
- 2.5 mg injected once a week to start;
- after 4 weeks, increase to 5 mg once a week;
- dosage may be further increased in 2.5 mg increments after at least 4 weeks on the current dose to the maximum dosage of 15 mg once a week;

Products: Injection: Single-dose pens – 2.5 mg, 5 mg, 7.5 mg, 10 mg, 12.5 mg, or 15 mg per 0.5 mL;

Contraindications/most important risks:
- Contraindicated in patients with a personal or family history of medullary thyroid carcinoma or in patients with Multiple Endocrine Neoplasia syndrome type2 (boxed warning);
- Pancreatitis;
- Severe gastrointestinal disease;
- Acute kidney injury;
- Acute gallbladder disease;
- Diabetic retinopathy;
- Pregnancy – may cause adverse developmental effects (based on animal studies);
- Hypoglycemia with concurrent use of insulin or insulin secretagogues;
- May alter absorption of oral medications;

Most common adverse events (with dosage of 10 mg once a week): Nausea (15%), diarrhea (13%), decreased appetite (10%), dyspepsia (8%), constipation (6%), vomiting (5%), abdominal pain (5%);

Comparison with dulaglutide and semaglutide:

Advantages:
- Is more effective in reducing hemoglobin A1c and causing weight loss than semaglutide, insulin degludec, and insulin glargine (based on comparative studies);
- Has dual-targeted mechanisms of action;

Disadvantages:
- Is not indicated in pediatric patients (compared with dulaglutide);
- Labeled indications are more limited.

New Drug Comparison Rating (NDCR) =

Insomnia **Daridorexant hydrochloride (Quviviq – Idorsia) – 2022**

Description: An orexin receptor antagonist;

Indication: Administered orally for the treatment of adult patients with insomnia, characterized by difficulties with sleep onset and/or sleep maintenance;

Comparable drugs: Suvorexant (Belsomra), lemborexant (Dayvigo);

Recommended dosage:

- Should administer apart from food;
- 25 to 50 mg once a night, taken within 30 minutes before going to bed, with at least 7 hours remaining prior to planned awakening;
- reduce dosage in patients with moderate hepatic impairment or those being treated with moderate CYP3A4 inhibitors;

Products: Film-coated tablets – 25 mg, 50 mg;

Contraindications/most important risks:

- Contraindicated in patients with narcolepsy;
- CNS depressant effects and daytime impairment (Schedule IV);
- Worsening of depression/suicidal ideation;
- Sleep paralysis;
- Complex sleep behaviors;
- Compromised respiratory function;
- Hepatic impairment – not recommended in patients with severe impairment;
- Concurrent use with strong CYP3A4 inhibitors or moderate or strong CYP3A4 inducers should be avoided;
- Alcohol consumption should be avoided;

Most common adverse events: Headache (6%), fatigue (6%);

Comparison with suvorexant and lemborexant:

Advantages:

- May be used in a lower dosage in patients being treated concurrently with a moderate CYP3A4 inhibitor (compared with lemborexant);

Disadvantages:

- Concurrent use with strong or moderate CYP3A4 inducers should be avoided (compared with suvorexant);
- Has not been directly compared with other hypnotics in clinical studies.

New Drug Comparison Rating (NDCR) =

Fungal infection **Oteseconazole (Vivjoa – Mycovia) – 2022**

Description: An azole antifungal agent;

Indication: Administered orally to reduce the incidence of recurrent vulvovaginal candidiasis (RVVC) in females with a history of RVVC who are NOT of reproductive potential;

Comparable drug: Fluconazole

Recommended dosage:
- Should be administered with food;
- Oteseconazole-only regimen: 600 mg (4 capsules) on Day 1; 450 mg (3 capsules) on Day 2; then beginning on Day 14 – 150 mg once a week (every 7 days) for 11 weeks;
- Fluconazole/oteseconazole regimen: Fluconazole 150 mg on Days 1, 4, and 7; oteseconazole 150 mg once a day on Days 14 – 20; then beginning on Day 28 – 150 mg once a week (every 7 days) for 11 weeks;

Product: Capsules – 150 mg;

Contraindications/most important risks:
- Contraindicated in pregnant and lactating patients;
- Contraindicated in females of reproductive potential;
- Hepatic impairment – not recommended in patients with moderate or severe impairment;
- Renal impairment – not recommended in patients with severe impairment;
- May increase the exposure and activity of breast cancer resistance protein (BCRP) substrates;

Most common adverse events: Headache (7%), nausea (4%);

Comparison with fluconazole:

Advantages:
- May be more effective, and activity may include species of *Candida* that are resistant to fluconazole;
- Is the first drug to be approved with a labeled indication for RVVC;
- Is less likely to interact with other medications;

Disadvantages:
- Is more likely to cause adverse developmental effects if used during pregnancy and use is contraindicated;
- Labeling is more restrictive in limiting use to females with a history of RVVC who are NOT of reproductive potential;
- Labeled indications are more limited;

New Drug Comparison Rating (NDCR) =

Bacterial infection **Vonoprazan fumarate/amoxicillin/clarithomycin (Voquezna – Phathom)**

Description: Vonoprazan – a potassium competitive acid blocker (PCAB);

Indication: Administered orally (with amoxicillin and with or without clarithromycin) for the treatment of *Helicobacter pylori* infection in adults;

Comparable drugs: Lansoprazole/amoxicillin/clarithromycin triple therapy;

Products:

- Voquezna Dual Pak – co-package containing vonoprazan tablets (20 mg) and amoxicillin capsules (500 mg);
- Voquezna Triple Pak – co-package containing vonoprazan tablets (20 mg), amoxicillin capsules (500 mg), and clarithromycin tablets (500 mg);

Recommended dosage:

- Voquezna Dual Pak – vonoprazan 20 mg twice a day (morning and evening) plus amoxicillin 1,000 mg three times a day (morning, mid-day, and evening) for 14 days;
- Voquezna Triple Pak – vonoprazan 20 mg plus amoxicillin 1,000 mg plus clarithromycin 500 mg, each administered twice a day (morning and evening, 12 hours apart) for 14 days;

Contraindications/most important risks (for vonoprazan):

- Contraindicated in patients being treated with rilpivirine;
- Lactation – breastfeeding is not recommended;
- May reduce absorption and activity of drugs which are dependent on an acidic medium for optimum absorption;
- May increase chromogranin A levels and cause false positive results in diagnostic investigations for neuroendocrine tumors;
- Is a CYP2C19 inhibitor and may reduce conversion of clopidogrel to its active metabolite;
- Is a weak CYP3A inhibitor and may increase exposure and risks of CYP3A substrates;
- Action may be reduced by strong or moderate CYP3A4 inducers and concurrent use should be avoided;

Most common adverse events (and incidence with triple and dual combinations, respectively): Diarrhea (4%, 5%), dysgeusia (5%, 1%), vulvovaginal candidiasis (3%, 2%), abdominal pain (2%, 3%);

Comparison with lansoprazole/amoxicillin/clarithromycin triple therapy:

Advantages:

- Regimens are more effective in patients who have a clarithromycin resistant strain of *Helicobacter pylori* at baseline;
- Vonoprazan has a unique mechanism of action;

Disadvantages:

- Vonoprazan is not indicated or available for use as a single agent.

New Drug Comparison Rating (NDCR) =

Irritable bowel syndrome **Tenapanor hydrochloride (Ibsrela – Ardelyx) – 2022**

Description: A sodium/hydrogen exchanger 3 (NHE3) inhibitor:

Indication: Administered orally for the treatment of irritable bowel syndrome with constipation (IBS-C) in adults;

Comparable drugs: Linaclotide (Linzess), plecanatide (Trulance);

Recommended dosage:
- Should be administered immediately prior to breakfast or the first meal of the day and immediately prior to dinner;
- 50 mg twice a day;

Product: Tablets – 50 mg;

Contraindications/most important risks:
- Contraindicated in patients with known or suspected mechanical gastrointestinal obstruction;
- Contraindicated in pediatric patients less than 6 years of age (boxed warning regarding serious dehydration); use should be avoided in patients 6 years to less than 18 years of age;
- Severe diarrhea;
- May reduce the exposure and activity of OATP2B1 substrates (e.g., enalapril);

Most common adverse events: Diarrhea (16%), abdominal distension (3%), flatulence (3%), dizziness (2%);

Comparison of tenapanor with linaclotide and plecanatide:

Advantages:
- Has a unique mechanism of action;

Disadvantages:
- Is administered more frequently (twice a day);
- Instructions for use in patients with swallowing difficulties are not provided;
- May reduce the effectiveness of OATP2B1 substrates;
- Has not been directly compared with previous agents in clinical studies;
- Labeled indications are more limited.

New Drug Comparison Rating (NDCR) =

Hypercholesterolemia **Inclisiran sodium (Levqio – Novartis) – 2022**

Description: A small interfering RNA (siRNA) directed to proprotein convertase subtilisin kexin type 9 (PCSK9) messenger RNA (mRNA);

Indication: Administered subcutaneously as an adjunct to diet and maximally tolerated statin therapy for the treatment of adults with heterozygous familial hypercholesterolemia (HeFH) or clinical atherosclerotic cardiovascular disease (ASCVD), who require additional lowering of low-density lipoprotein cholesterol (LDL-C);

Comparable drugs: Alirocumab (Praluent), evolocumab (Repatha);

Recommended dosage:
- 284 mg as a single injection initially, again at 3 months, and then every 6 months;
- Should be administered by a healthcare professional;

Product: Injection: Single-dose prefilled syringes – 284 mg/1.5 mL;

Contraindications/most important risks:
- Pregnancy - may cause adverse developmental effects;

Most common adverse events: Injection site reaction (8%), arthralgia (5%), urinary tract infection (4%), diarrhea (4%), bronchitis (4%), pain in extremity (3%), dyspnea (3%);

Comparison with alirocumab and evolocumab:

Advantages:
- Has a longer duration of action and is administered every 6 months during maintenance treatment;
- Has a unique mechanism of action;

Disadvantages:
- Reduction in risk of adverse cardiovascular events has not yet been determined;
- Effectiveness and safety in pediatric patients have not been established (compared with evolocumab);
- Should be administered by a healthcare professional;
- Has not been directly compared with other LDL-C lowering drugs in clinical studies;
- Labeled indications are more limited.

New Drug Comparison Rating (NDCR) =

Hypertrophic cardiomyopathy **Mavacamten (Camzyos – Bristol-Myers Squibb) – 2022**

Description: A cardiac myosin inhibitor;

Indication: Administered orally for the treatment of adults with symptomatic New York Heart Association (NYHA) class II-III obstructive hypertrophic cardiomyopathy to improve functional capacity and symptoms;

Comparable drugs: Beta-adrenergic blocking agents (e.g., metoprolol);

Recommended dosage:

- 5 mg once a day initially;
- may be adjusted to 2.5 mg, 10 mg and 15 mg based on response, adverse events, left ventricular ejection fraction (LVEF) and Valsalva left ventricular outflow tract (LVOT) gradient assessment;
- algorithms for dosage adjustment in product labeling should be consulted;

Products: Capsules – 2.5 mg, 5 mg, 10 mg, 15 mg; available only through a restricted Risk Evaluation and Mitigation Strategy (REMS) program;

Contraindications/most important risks:

- Concurrent use with a moderate to strong CYP2C19 inhibitor or strong CYP3A4 inhibitor is contraindicated (boxed warning);
- Concurrent use with a moderate to strong CYP2C19 inducer or moderate to strong CYP3A4 inducer is contraindicated (boxed warning);
- Risk of heart failure (boxed warning) – initiation of treatment in patients with a LVEF less than 55% is not recommended; treatment should be interrupted if LVEF is less than 50% or if clinical status worsens;
- Pregnancy – may cause adverse developmental effects; patients of reproductive potential must use effective contraception until 4 months after the last dose;
- Concurrent use of a weak CYP2C9 inhibitor or a moderate CYP3A4 inhibitor may increase activity and risk;
- Concurrent use with a negative inotrope may increase activity and risk;

Most common adverse events: Dizziness (27%), syncope (6%);

Comparison with beta-blockers (e.g., metoprolol):

Advantages:

- Is more effective than previous treatments and may reduce need for surgery;
- Has a unique mechanism of action and is the first drug to target the underlying pathology of the disease;

Disadvantages:

- May cause serious adverse events and interact with many other medications;
- Monitoring treatment is more complex;
- May cause adverse developmental effects if used during pregnancy;
- Availability and use are restricted by a REMS program.

New Drug Comparison Rating (NDCR) =

Asthma **Tezepelumab-ekko (Tezspire – AstraZeneca) – 2022**

Description: A monoclonal antibody that acts as a thymic stromal lymphopoietin (TSLP) blocker;

Indication: Administered subcutaneously for the add-on maintenance treatment of adult and pediatric patients aged 12 years and older with severe asthma;

Comparable drugs: Interleukin-5 (IL-5) antagonists (mepolizumab [Nucala], reslizumab [Cinqair], benralizumab [Fasenra]);

Recommended dosage: 210 mg administered once every 4 weeks;

Products: Injection: Single-dose vials and single-dose prefilled syringes – 210 mg/1.91 mL (should be stored in a refrigerator);

Contraindications/most important risks:

- Risk with abrupt dosage reduction or discontinuation of systemic or inhaled corticosteroids;
- Hypersensitivity reactions;
- Helminth infections – should be effectively treated prior to initiation of therapy;
- Vaccines – use of live attenuated vaccines should be avoided during treatment;

Most common adverse events: Pharyngitis (4%), arthralgia (4%), back pain (4%), injection site reaction (3%);

Comparison with IL-5 antagonists (mepolizumab is used for comparison):

Advantages:

- Use is not limited to patients with an eosinophilic phenotype;
- Has a unique mechanism of action;

Disadvantages:

- Safety in patients less than 12 years of age has not been established;
- Has not been directly compared with previous agents in clinical studies;
- Labeled indications are more limited.

New Drug Comparison Rating (NDCR) =

Atopic dermatitis **Tralokinumab-ldrm (Adbry – LEO) – 2022**

Description: A monoclonal antibody that acts as an interleukin-13 (IL-13) antagonist;

Indication: Administered subcutaneously 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;

Comparable drug: Dupilumab (Dupixent);

Recommended dosage:
- 600 mg (four 150 mg injections) for the initial dose, 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 weighing less than 100 kg who achieve clear or almost clear skin after 16 weeks of treatment;

Product: Injection: Single-dose prefilled syringes – 150 mg/mL (should be stored in a refrigerator);

Contraindications/most important risks:
- Hypersensitivity reactions;
- Conjunctivitis and keratitis;
- Helminth infections – should be effectively treated prior to initiation of therapy;
- Vaccines – use of live vaccines should be avoided during treatment;

Most common adverse events: Upper respiratory tract infections (24%), conjunctivitis (8%), injection site reactions (7%), eosinophilia (1%);

Comparison with dupilumab:

Advantages:
- May be administered every 4 weeks in selected patients;

Disadvantages:
- May be less effective (based on results of noncomparative clinical trials);
- Multiple injections are needed for each dose;
- Safety has not been established in pediatric patients;
- Labeled indications are more limited.

New Drug Comparison Rating (NDCR) =

Atopic dermatitis **Abrocitinib (Cibinqo – Pfizer) -2022**

Description: A Janus kinase (JAK) inhibitor;

Indication: Administered orally 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 not advisable;

Comparable drug: Upadacitinib (Rinvoq);

Recommended dosage:
- 100 mg once a day;
- 200 mg once a day for patients who are not responding to 100 mg daily dose;
- reduce dosage in patients who are CYP2C19 poor metabolizers, are taking a strong CYP2C19 inhibitor, have moderate renal impairment, or with the occurrence of certain adverse events;

Products: Film-coated tablets – 50 mg, 100 mg, 200 mg;

Contraindications/most important risks:
- Use of antiplatelet therapies except for low-dose aspirin (81 mg daily or less) during the first 3 months of treatment is contraindicated;
- Serious infections, major adverse cardiovascular events, thrombosis, higher rate of all-cause mortality, and malignancies (boxed warning);
- Laboratory abnormalities (potential changes in platelets, lymphocytes, lipids);
- Lactation – breastfeeding is not recommended;
- Hepatic impairment – not recommended in patients with severe impairment;
- Renal impairment – not recommended in patients with severe impairment;
- Vaccines – use of live vaccines should be avoided prior to, during, or immediately after treatment;
- Concurrent use with moderate to strong inhibitors of both CYP2C19 and CYP2C9, or strong inducers of CYP2C19 or CYP2C9, should be avoided;
- May increase the activity and risk of P-gp substrates;
- Concurrent use with other JAK inhibitors, biologic immunomodulators, or other immunosuppressants is not recommended;

Most common adverse events (with dosage of 100 mg once a day): Nasopharyngitis (12%), nausea (6%), headache (6%), herpes simplex (3%), dizziness (2%), acne (2%), increased blood creatinine phosphokinase (2%);

Comparison with upadacitinib:

Advantages:
- Is less likely to interact with CYP3A4 inhibitors or inducers;

Disadvantages:
- Is more likely to interact withCYP2C19 and CYP2C9 inhibitors or inducers;
- Use is not recommended in patients with severe renal impairment;
- Safety in pediatric patients has not been established;
- Labeled indications are more limited.

New Drug Comparison Rating (NDCR) =

Psoriasis **Deucravacitinib (Sotyktu – Bristol-Myers Squibb) – 2022**

Description: A tyrosine kinase 2 (TYK2; a Janus kinase) inhibitor;

Indication: Administered orally for the treatment of adults with moderate to severe plaque psoriasis who are candidates for systemic therapy or phototherapy;

Comparable drug: Apremilast (Otezla);

Recommended dosage: 6 mg once a day;

Product: Film-coated tablets – 6 mg;

Contraindications/most important risks:

- Hypersensitivity reactions;
- Infections;
- Rhabdomyolysis and increased creatine phosphokinase;
- Malignancies;
- Potential risks related to Janus kinase (JAK) inhibition;
- Laboratory abnormalities (triglycerides, liver enzymes);
- Vaccines – use of live vaccines should be avoided during treatment;
- Hepatic impairment – not recommended in patients with severe impairment;
- Concurrent use with other potent immunosuppressants is not recommended;

Most common adverse events: Upper respiratory tract infections (19%), increased blood creatine phosphokinase (3%), herpes simplex (2%), mouth ulcers (2%), folliculitis (2%), acne (1%);

Comparison with apremilast:

Advantages:

- Is more effective;
- Is less likely to cause adverse events;
- Is less likely to interact with other drugs;
- Dosage titration is not necessary;
- Is administered less frequently;
- Has a unique mechanism of action;

Disadvantages:

- May have greater risk of infection;
- Has been associated with infrequent occurrence of malignancies and rhabdomyolysis;
- Use is not recommended in patients with severe hepatic impairment;
- Labeled indications are more limited.

New Drug Comparison Rating (NDCR) =

Psoriasis **Tapinarof (Vtama – Dermavant) – 2022**

Description: An aryl hydrocarbon receptor agonist;

Indication: Applied topically for the treatment of plaque psoriasis in adults;

Comparable drugs: Topical corticosteroids (e.g., triamcinolone acetonide);

Recommended dosage: Apply a thin layer of cream to affected skin areas once a day;

Product: Cream -1%;

Contraindications/most important risks:

- Is not for oral, ophthalmic, or intravaginal use;

Most common adverse events: Folliculitis (20%), nasopharyngitis (11%), contact dermatitis (7%), headache (4%);

Comparison with topical corticosteroids:

Advantages:

- May be less likely to cause systemic adverse events;
- Has a unique mechanism of action;

Disadvantages:

- Has not been directly compared with previous agents in clinical studies;
- Labeled indications are more limited.

New Drug Comparison Rating (NDCR) =

Psoriasis **Spesolimab-sbzo (Spevigo – Boehringer Ingelheim) – 2022**

Description: A monoclonal antibody that acts as an interleukin-36 (IL-36) receptor antagonist;

Indication: Administered intravenously for the treatment of generalized pustular psoriasis (GPP) flares in adults;

Comparable drug: No other drugs have a labeled indication for GPP;

Recommended dosage:
- 900 mg as a single dose by intravenous infusion over 90 minutes;
- if flare symptoms persist, may administer an additional intravenous 900 mg dose one week after the first dose;

Product: Injection: Single-dose vials – 450 mg/7.5 mL (should be stored in a refrigerator);

Contraindications/most important risks;
- Infections;
- Hypersensitivity reactions including drug reaction with eosinophilia and systemic symptoms (DRESS);
- Infusion-related reactions;
- Vaccines – use of live vaccines should be avoided during treatment;

Most common adverse events: Asthenia/fatigue (9%), nausea/vomiting (9%), headache (9%), pruritus/prurigo (6%), infusion site hematoma/bruising (6%), urinary tract infection (6%);

Comparison: No other drugs to which comparisons are appropriate:

Advantages:
- Is the first drug to have a labeled indication for GPP;
- Has a unique mechanism of action;

Limitations:
- Must be administered intravenously.

New Drug Comparison Rating (NDCR) =