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New Drugs: Cosentyx, Ibrance, Lenvima, and Unituxin

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Goal. The goal of this lesson is to provide information on four new drugs: dinutuximab (Unituxin™), lenvatinib (Lenvima™), palbociclib (Ibrance®), and secukinumab (Cosentyx™).

Objectives. At the completion of this activity, the participant will be able to:

1. recognize signs and symptoms, and key features of targeted pathologies for these new drugs, including information on their prevalence in the population;
2. recognize important therapeutic uses for the drugs and their applications in specified pathologies;
3. select the indication(s), pharmacologic action(s), clinical applications, dosing regimens, mode of administration, and availability for each drug;
4. demonstrate an understanding of adverse effects and toxicity, warnings, precautions, contraindications, and significant drug-drug or drug-food interactions reported for each agent; and
5. list important counseling information to convey to patients and/or their caregivers.

The four new-molecular entity drugs discussed in this lesson have been approved to treat a wide variety of pathologies (Table 1). The lesson provides a brief introduction to the therapeutic agents, and its depth is not intended to extend beyond an overview of the topic. The reader is, therefore, encouraged to consult the products' full prescribing information leaflet (package insert), FDA-approved *Medication Guide* when available, and other reliable sources for more detailed information.

Dinutuximab (Unituxin)

Unituxin (yu-ni-TUX-in) is the first approved drug aimed specifically for treatment of patients with high-risk neuroblastoma. It fulfills a critical need by providing a treatment option that prolongs survival in children with this high-risk cancer.

Indications and Use. Unituxin is indicated for use in combination with granulocyte-macrophage colony-stimulating factor, interleukin (IL)-2 (IL-2), and 13-cis-retinoic acid (RA) for treatment of pediatric patients with high-risk neuroblastoma who achieve at least a partial response to prior first-line multiagent, multimodality therapy. Multimodality regimens include surgery, autologous stem cell transplantation, chemotherapy, and radiotherapy.

Neuroblastoma. Neuroblastoma is the most common extracranial solid tumor in childhood, accounting for 6 percent of all childhood cancers in the United States. It is cancer that forms from embryonic (immature) nerve cells, often developing in the adrenal glands, but may also form in the abdomen, chest, or nerves that run alongside the spine. Neuroblastoma typically occurs in children younger than five years of age. According to the National Cancer Institute, neuroblastoma occurs in approximately one in 100,000 live births. About 90 percent of children are younger than five years at diagnosis. It is slightly more common in boys.

The five-year overall survival for all infants and children with neuroblastoma has increased from 46 percent when diagnosed between 1974 and 1989, to 71 percent when diagnosed between 1999 and 2005. Neuroblastoma has a worse prognosis in adolescents older than 10 years or in adults, regardless of stage or site; and in many cases, it has a more prolonged course when treated with standard doses of chemotherapy. There are racial differences in tumor biology, with African-Americans more likely to have high-risk disease and fatal outcome when compared with Caucasians.

Mechanism of Action. Dinutuximab is a monoclonal antibody that binds to the glycolipid GD2. This glycolipid is expressed on neuroblastoma cells and on normal cells of neuroectodermal origin, including the central nervous system and peripheral nerves. Dinutuximab binds to cell surface GD2 and induces cell lysis.

Efficacy and Safety. Efficacy and safety of Unituxin were evaluated in a clinical trial of 226 pediatric participants (median age 3.8 years) with high-risk neuro-

Table 1
Selected new drugs

Generic (Trade Name)	Distributor	Indication	Dose*	Dosage Form	Most Common Side Effects	Medication Guide‡
Dinutuximab (Unituxin)	United Therapeutics Corp	neuroblastoma	17.5 mg/m^2/ day x 4 days	single-use vials for IV infusion 17.5 mg/5mL	(≥25%): pain, pyrexia, thrombocytopenia, lymphopenia, infusion reactions, hypotension, hyponatremia, increased alanine aminotransferase, anemia, vomiting, diarrhea, hypokalemia, urticaria, hypoalbuminemia, increased aspartate aminotransferase, hypocalcemia, capillary leak syndrome, neutropenia	No
Lenvatinib (Lenvima)	Eisai, Inc.	thyroid cancer	24 mg PO daily	4 mg, 10 mg capsules	(≥30%): hypertension, fatigue, diarrhea, arthralgia/myalgia, decreased appetite, weight loss, nausea, stomatitis, headache, vomiting, proteinuria, palmar-plantar erythrodysesthesia syndrome, abdominal pain, dysphonia	No
Palbociclib (Ibrance)	Pfizer Labs	breast cancer	125 mg PO daily x 21 days; off 7 days	75 mg, 100 mg, 125 mg capsules	(≥10%)δ: neutropenia, leukopenia, fatigue, anemia, URI, nausea, stomatitis, alopecia, diarrhea, thrombocytopenia, decreased appetite, vomiting, asthenia, peripheral neuropathy, epistaxis	No
Secukinumab (Cosentyx)	Novartis Pharmaceuticals Corp	psoriasis	300 mg @ weeks 0, 1, 2, 3, 4; then every 4 weeks	single-use pen, pre-filled syringes, vials for SC injection, 150 mg	(>1%): nasopharyngitis, URI, diarrhea	Yes

*Recommended dose for most patients ‡Availability at the time of publication of this lesson
δreported in patients taking Ibrance plus letrozole

blastoma whose tumors shrunk or disappeared after treatment with multiple-drug chemotherapy and surgery followed by additional intensive chemotherapy and who subsequently received bone marrow transplantation support and radiotherapy. Participants were randomly assigned to receive either an oral retinoid drug (RA; isotretinoin), or Unituxin in combination with interleukin-2 and granulocyte-macrophage colony-stimulating factor, both of which are believed to enhance the activity of Unituxin by stimulating the immune system, and RA.

Three years after treatment assignment, 63 percent of participants receiving the Unituxin combination were alive and free of tumor growth or recurrence, compared to 46 percent of participants treated with RA alone. In an updated analysis of survival, 73 percent of participants who received the Unituxin combination were alive compared with 58 percent of those receiving RA alone.

The most common adverse effects are listed in Table 1. The most common serious adverse reactions (≥5 percent) are infections, infusion reactions, hypokalemia, hypotension, pain, fever, and capillary leak syndrome. Unituxin carries a *Boxed Warning* alerting patients and health care professionals that Unituxin irritates nerve cells, causing severe pain that requires treatment with intravenous narcotics before, during, and after Unituxin infusion, and can also cause nerve damage and life-threatening infusion reactions.

Warnings and Precautions. The following **warnings** and **precautions** are listed:

- *Capillary leak syndrome and*

Table 2
Patient counseling information for Unituxin*

Inform patients and/or caregivers:
- that there is a risk of serious infusion reactions and anaphylaxis and to immediately report any signs or symptoms, such as facial or lip swelling, urticaria, difficulty breathing, lightheadedness, or dizziness that occur during or within 24 hours following the infusion;
- of the risk of severe pain and peripheral sensory and motor neuropathy, and to promptly report severe or worsening pain and signs and symptoms of neuropathy such as numbness, tingling, burning, or weakness;
- of the risk of capillary leak syndrome and to immediately report any signs or symptoms;
- of the risk of hypotension during the infusion and to immediately report any signs or symptoms;
- of the risk of infection following treatment, and to immediately report any signs or symptoms;
- of the risk of neurological disorders of the eye and to promptly report signs or symptoms such as blurred vision, photophobia, ptosis, diplopia, or unequal pupil size;
- of the risk of bone marrow suppression, and to promptly report signs or symptoms of anemia, thrombocytopenia, or infection;
- of the risk of electrolyte abnormalities including hypokalemia, hyponatremia, and hypocalcemia, and to report any signs or symptoms such as seizures, heart palpitations, and muscle cramping;
- of the risk of hemolytic uremic syndrome and to report any signs or symptoms such as fatigue, dizziness, fainting, pallor, edema, decreased urine output, or hematuria;
- (females of reproductive potential) that there is a potential risk to the fetus if Unituxin is administered during pregnancy and the need for use of effective contraception during, and for at least two months after completing therapy.

*A complete list of counseling information is available in the product's Prescribing Information leaflet.

hypotension: Administer required prehydration and monitor patients closely during treatment. Depending upon severity, manage by interruption, infusion rate reduction, or permanent discontinuation;

- *Infection*: Temporarily interrupt until resolution of systemic infection;
- *Neurological disorders of the eye*: Interrupt for dilated pupil with sluggish light reflex or other visual disturbances and permanently discontinue for recurrent eye disorders or loss of vision;
- *Bone marrow suppression*: Monitor peripheral blood counts during Unituxin therapy;
- *Electrolyte abnormalities*: Monitor serum electrolytes closely each day during therapy with Unituxin;
- *Atypical hemolytic uremic syndrome*: Permanently discontinue Unituxin and institute supportive management;
- *Embryo-fetal toxicity*: Based on its mechanism of action, may cause fetal harm when given to a pregnant woman. Advise females of reproductive potential of potential risks to a fetus and to use effective contraception during and for two months after the last dose of Unituxin.

A history of anaphylaxis to dinutuximab is the only **contraindication**.

Drug Interactions. No drug-drug interaction studies have been conducted with dinutuximab.

Administration, Dosing, and Availability. The recommended dose of dinutuximab is 17.5 mg/m^2/day administered as a diluted intravenous infusion over 10 to 20 hours for four consecutive days for up to five cycles. Prior to initiation of each dose of dinutuximab, administer required intravenous hydration and premedication with antihistamines, analgesics, and antipyretics.

Unituxin is available as an intravenous injection containing 17.5 mg/5 mL in a single-use vial. Vials should be stored in a refrigerator at 2°C to 8°C (36°F to 46°F), protected from light by storing in the outer carton, and neither be frozen nor shaken.

Patient Counseling. Specific points for patient counseling are summarized in Table 2.

Lenvatinib (Lenvima)

Development of new therapies to assist patients with refractory disease is of primary importance. Lenvima's approval offers patients an additional therapeutic option to help slow the progression of differentiated thyroid cancer (DTC).

Indications and Use. Lenvima (lehn-VEEMA) is indicated for the treatment of patients with locally recurrent or metastatic, progressive, radioactive iodine-refractory differentiated thyroid cancer.

Differentiated Thyroid Cancer. Carcinoma of the thyroid is an uncommon cancer but the most common malignancy of the endocrine system. Over the past three decades, thyroid cancer has been increasing in the United States, Canada, and some European countries. In the United States, its incidence has increased more than any other cancer. DTC accounts for more than 90 percent of all thyroid malignancies and includes papillary, follicular, and Hürthle cell histologies. Thyroid cancer affects women more commonly than men, estimated to be 9.1 per 100,000 females and 2.9 per 100,000 males. Onset usually occurs between 25 and 65 years of age.

DTC is ordinarily highly treatable and usually curable. Standard therapies for patients with advanced DTC include surgery, radioactive iodine, and thyroid-stimulating hormone (TSH) suppression. Although DTC is associated with low mortality, disease recurrence is high, at 20 to 30 percent, or even higher in some subgroups of patients. In most patients with DTC, however, recurrence is low.

The National Cancer Institute estimates that 62,450 Americans will be diagnosed with thyroid cancer with 1,950 deaths from the disease in 2015. Although most patients with DTC have a favorable prognosis with standard treatments, 10 to 15 percent of patients will develop disease refractory to

radioactive iodine therapy. For decades, standard therapy for radioactive iodine-refractory DTC consisted of cytotoxic chemotherapy with doxorubicin (Adriamycin, Doxil), with unsatisfactory results and serious side effects. These patients have a median overall survival of 2.5 to 3.5 years.

Mechanism of Action. Lenvatinib is a receptor tyrosine kinase (RTK) inhibitor that inhibits the kinase activities of vascular endothelial growth factor (VEGF) receptors VEGFR1 (FLT1), VEGFR2 (KDR), and VEGFR3 (FLT4). It also inhibits other RTKs that have been implicated in pathogenic angiogenesis (formation and development of blood vessels), tumor growth, and cancer progression. Interference with blood supply into a cancerous growth is a deterrent to continued tumor growth.

Efficacy and Safety. Efficacy and safety were demonstrated in 392 participants with progressive, radioactive iodine-refractory DTC who were randomly assigned to receive either Lenvima or placebo. Study results showed Lenvima-treated participants lived a median of 18.3 months without their disease progressing (progression-free survival), compared to a median of 3.6 months for participants who received placebo. Additionally, 65 percent of participants treated with Lenvima experienced a reduction in tumor size, compared to 2 percent of participants who received placebo. A majority of participants randomly assigned to receive the placebo were treated with Lenvima upon disease progression.

The most common adverse effects noted in clinical trials are listed in Table 1. Serious adverse effects included cardiac failure; arterial thromboembolic events; hepatotoxicity; renal failure and impairment; gastrointestinal perforation in the wall of the stomach or intestines, or fistula formation (abnormal connection between two parts of the stomach or intestines); QT interval prolongation; hypocalcemia; the simultaneous occurrence of headache, confusion, seizures and visual changes (Reversible Posterior Leukoencephalopathy Syndrome); hemorrhage; risks to an unborn child if a patient becomes pregnant during treatment; and impaired suppression of production of TSH.

Warnings and Precautions. The following **warnings** and **precautions** are listed:

- *Hypertension*: Control blood pressure prior to treatment with Lenvima. Withhold Lenvima for Grade 3 hypertension despite optimal antihypertensive therapy. Discontinue for life-threatening hypertension;
- *Cardiac failure*: Monitor for clinical symptoms or signs of cardiac decompensation. Withhold Lenvima for Grade 3 cardiac dysfunction. Discontinue for Grade 4 cardiac dysfunction;
- *Arterial thromboembolic events*: Discontinue Lenvima following an arterial thromboembolic event;
- *Hepatotoxicity*: Monitor liver function tests before initiation of Lenvima, and periodically throughout treatment. Withhold Lenvima for Grade 3 or greater liver impairment. Discontinue for hepatic failure;
- *Proteinuria*: Monitor for proteinuria before initiation of, and periodically throughout treatment with Lenvima. Withhold Lenvima for ≥2 grams of proteinuria per 24 hours. Discontinue for nephrotic syndrome;
- *Renal failure and impairment*: Withhold Lenvima for Grade 3 or 4 renal failure/impairment;
- *Gastrointestinal perforation and fistula formation*: Discontinue Lenvima in patients who develop gastrointestinal perforation or life-threatening fistula;
- *QT interval prolongation*: Monitor and correct electrolyte abnormalities in all patients. Withhold Lenvima for development of Grade 3 or greater QT interval prolongation;
- *Hypocalcemia*: Monitor blood calcium levels at least monthly and replace calcium as necessary;
- *Reversible posterior leukoencephalopathy syndrome (RPLS)*: Withhold Lenvima for RPLS until fully resolved;
- *Hemorrhagic events*: Withhold Lenvima for Grade 3 hemorrhage. Discontinue for Grade 4 hemorrhage;
- *Impairment of thyroid stimulating hormone suppression*: Monitor TSH levels monthly and adjust thyroid replacement medication as needed in patients with DTC;
- *Embryofetal toxicity*: Based

Table 3
Patient counseling information for Lenvima*

Inform patients:
- to undergo regular blood pressure monitoring and to contact their healthcare provider if blood pressure is elevated;
- that Lenvima can cause cardiac dysfunction and to immediately contact their healthcare provider if they experience any clinical symptoms of cardiac dysfunction such as shortness of breath or swelling of ankles;
- to seek immediate medical attention for new onset chest pain or acute neurologic symptoms consistent with heart attack or stroke;
- that they will need to undergo lab tests to monitor for liver function and to report any new symptoms indicating hepatic toxicity or failure;
- that they will need to undergo regular lab tests for kidney function and protein in the urine;
- that Lenvima can increase the risk of gastrointestinal perforation or fistula and to seek immediate medical attention for severe abdominal pain;
- that Lenvima can increase the risk for bleeding and to contact their healthcare provider for bleeding or symptoms of severe bleeding;
- (females of reproductive potential) of the risk to a fetus and to inform their healthcare provider of a known or suspected pregnancy. Advise them to use effective contraception during treatment with Lenvima and for at least two weeks following completion of therapy. If breastfeeding, they should discontinue breastfeeding during treatment with Lenvima.

*A complete list of counseling information is available in the product's Prescribing Information leaflet.

on its mechanism of action, Lenvima may cause fetal harm. Advise females of potential risk to a fetus and use of effective contraception during Lenvima use and for at least two weeks following completion of therapy.

There are no **contraindications** listed.

Drug Interactions. No dose adjustment of lenvatinib is recommended when co-administered with CYP3A, P-glycoprotein (P-gp), and breast cancer resistance protein (BCRP) inhibitors, and CYP3A and P-gp inducers.

Administration, Dosing, and Availability. The recommended dose of Lenvima is 24 mg once daily taken with or without food. In patients with severe renal or hepatic impairments, the dose is 14 mg once daily. Dosing may continue until disease progression or until unacceptable toxicity occurs.

Lenvima is available in 4 mg and 10 mg capsules.

Patient Counseling. Specific points for patient counseling are summarized in Table 3.

Palbociclib (Ibrance)

The addition of targeted agents to current therapy has provided the potential for significant clinical benefit for patients with metastatic breast cancer. Several novel therapies have been developed that offer affected women renewed hope for healing. Palbociclib selectively interferes with the critical components of the cell cycle regulatory machinery in breast cancer.

Indications and Use. Ibrance (EYE-brans) is indicated in combination with letrozole (Femara) for the treatment of postmenopausal women with estrogen receptor (ER)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced breast cancer as initial endocrine-based therapy for their metastatic disease.

Breast Cancer. Breast cancer is the most frequent female malignancy worldwide, and the second most common cancer in the U.S. after prostate cancer. Breast cancer forms in the breast tissue and in advanced cases, spreads to surrounding normal tissue. The median age at diagnosis is 61 years. The National Cancer Institute estimates that 232,670 American women were diagnosed with breast cancer and 40,000 died from the disease in 2014. Approximately 12.3 percent of women will have a positive diagnosis at some point during their lifetime.

Three major therapeutic approaches used today to treat or control breast cancer are surgical removal of primary tumors, irradiation of cancer cells to control their growth, and anticancer drugs to kill cancer cells or inhibit their proliferation. Notably, surgery or radiotherapy still requires chemotherapy to eradicate remaining malignancy cells and impede relapses.

Anticancer drugs are based on three therapeutic approaches: (1) classical chemotherapy to stop cell proliferation by the indiscriminate targeting of rapid cell division in the body, (2) hormone therapy that stops cancer cell growth by targeting the receptors and downstream signaling molecules of hormones pivotal for proliferation of these cells, and (3) targeted therapy where signaling pathways deregulated in primary breast tumors are specifically targeted. Interestingly, frequent advances in the understanding of breast cell microbiology spotlight the tumor microenvironment as a significant player in breast carcinogenesis and have provided new avenues for targeted therapy.

Mechanism of Action. Palbociclib is an orally available inhibitor of cyclin-dependent kinase (CDK) 4 and 6. Cyclin D1 and CDK4/6 are downstream of signaling pathways that lead to cellular proliferation contributing to sustained tumor growth.

Efficacy and Safety. Efficacy and safety were demonstrated in 165 postmenopausal women with ER-positive, HER2-negative advanced breast cancer who had not received previous treatment for advanced disease. Clinical study participants were randomly assigned to receive Ibrance in combination with letrozole or letrozole alone. Participants treated with Ibrance plus letrozole lived about 20.2 months without their disease progressing (progression-free survival), compared to about 10.2 months seen in participants receiving only letrozole. Information on overall survival is not available at this time.

The most common adverse effects are listed in Table 1. The most frequently reported serious adverse reactions in patients receiving palbociclib plus letrozole are pulmonary embolism (4 percent) and diarrhea (2 percent).

Warnings and Precautions. The following **warnings** and **precautions** are listed:

- *Neutropenia*: Monitor complete blood count prior to start of Ibrance therapy and at the beginning of each cycle as well as on Day 14 of the first two cycles, and as clinically indicated;
- *Infections*: Monitor for signs and symptoms of infection and withhold dosing as medically appropriate;
- *Pulmonary embolism*: Monitor patients for signs and symptoms of pulmonary embolism and treat as medically appropriate;
- *Embryo-fetal toxicity*: The drug can cause fetal harm. Advise females of potential risk to a fetus and to use effective contraception.

There are no **contraindications** listed.

Drug Interactions. Palbociclib is metabolized primarily by CYP3A and sulfotransferase (SULT) enzyme SULT2A1. Avoid coadministration with strong CYP3A *inhibitors* (e.g., clarithromycin, indinavir, itraconazole, ketoconazole, lopinavir/ritonavir, nefazodone, nelfinavir, posaconazole, ritonavir, saquinavir, telaprevir, telithromycin, verapamil, voriconazole). Avoid grapefruit or grapefruit juice during Ibrance treatment. If coadministration of Ibrance with a strong CYP3A inhibitor cannot be avoided, reduce the dose of Ibrance.

Avoid concomitant use of

Table 4
Patient counseling information for Ibrance*

Inform patients:
- to immediately report any signs or symptoms of myelosuppression or infection, such as fever, chills, dizziness, shortness of breath, weakness or any increased tendency to bleed and/or to bruise;
- to immediately report any signs or symptoms of pulmonary embolism, such as shortness of breath, chest pain, tachypnea, and tachycardia;
- to take Ibrance with food and swallow the capsules whole. No capsule should be ingested if it is broken, cracked, or otherwise not intact;
- that Ibrance may interact with grapefruit, thus patients should not consume grapefruit products while on treatment with Ibrance;
- to avoid strong CYP3A inhibitors and strong CYP3A inducers;
- to inform their healthcare providers of all concomitant medications, including prescription medicines, over-the-counter drugs, vitamins, and herbal products;
- that if they vomit or miss a dose, an additional dose should not be taken that day. The next prescribed dose should be taken at the usual time;
- (females of reproductive potential) to use effective contraception during Ibrance therapy and for at least two weeks after the last dose. Advise females to contact their healthcare provider if they become pregnant, or if pregnancy is suspected, during treatment with Ibrance.

*A complete list of counseling information is available in the product's Prescribing Information leaflet.

strong CYP3A *inducers* (e.g., phenytoin, rifampin, carbamazepine, St. John's Wort). Coadministration of moderate CYP3A inducers may also decrease the plasma exposure of Ibrance; thus, avoid concomitant use of moderate CYP3A *inducers* (e.g., bosentan, efavirenz, etravirine, modafinil, nafcillin).

Coadministration of midazolam with multiple doses of Ibrance increased the midazolam plasma exposure by 61 percent in healthy subjects, compared with administration of midazolam alone. The dose of a sensitive CYP3A substrate with a narrow therapeutic index (e.g., alfentanil, cyclosporine, dihydroergotamine, ergotamine, everolimus, fentanyl, pimozide, quinidine, sirolimus, tacrolimus) may need to be reduced as palbociclib may increase their exposure.

Administration, Dosing, and Availability. The recommended starting dose of Ibrance is 125 mg daily taken with food for 21 days, followed by seven days off treatment to comprise a complete cycle of 28 days, in combination with letrozole 2.5 mg once daily given continuously throughout the 28-day cycle. Patients should be encouraged to take their dose at approximately the same time each day. Dosing interruption and/or dose reduction are recommended based on individual safety and tolerability.

Ibrance is available in 75 mg, 100 mg, and 125 mg capsules.

Patient Counseling. Specific points for patient counseling are summarized in Table 4.

Secukinumab (Cosentyx)

Conventional systemic therapies for plaque psoriasis have not fully met the needs of patients, and current biologic treatments, although generally well tolerated, have a still-developing long-term safety profile. Studies conducted in patients with plaque psoriasis have provided evidence that secukinumab may be safe and efficacious as a potential treatment for this disorder.

Indications and Use. Cosentyx (koe-SEN-tix) is indicated for treatment of moderate to severe plaque psoriasis in adult patients who are candidates for systemic therapy or phototherapy.

Psoriasis. Psoriasis is a common skin condition that causes patches of skin redness and irritation. It is an autoimmune disorder of genetic basis, and thus occurs more commonly in persons with a family history of the disease, and most often begins in people between the ages of 15 and 35. The estimated worldwide population prevalence is 1 to 3 percent.

The most common form is plaque psoriasis, which accounts for 90 percent of cases. In plaque psoriasis, patients develop thick, red skin with flaky, silver-white patches called scales. Patches frequently occur on the elbows, knees, palms of the hands and soles of the feet, and midsection of the trunk; but can appear anywhere, including on the scalp. The lesions may vary in severity from minor localized patches to complete body coverage. Lesions may be accompanied by intense itching, swelling, and pain. While psoriasis may appear to be contagious, it is not. It is a life-long condition that may regress for long periods and then reappear later.

Psoriasis imposes a major impact on patient psychosocial status and quality of life. The disease also carries an increased risk of comorbidities including psoriatic arthritis, uveitis, cardiovascular disease, the metabolic syndrome as a whole and its individual components, and inflammatory bowel disease, which in severe cases, can reduce life expectancy. Recent studies also showed an increased prevalence of celiac disease, nonalcoholic fatty liver disease, and erectile dysfunction in patients suffering from psoriasis. Preliminary epidemiological data suggest that adequate treatment of psoriasis could reduce the incidence of these comorbidities.

Mechanism of Action. Secukinumab is a high affinity, fully human IgG1 monoclonal antibody that selectively binds with and neutralizes the protein interleukin 17A (IL-17A), a naturally occurring cytokine that is involved in inflammatory and immune responses. By binding to IL-17A, secukinumab prevents it from binding to its receptor, and thus inhibits its ability to trigger the inflammatory response that plays a role in development of plaque psoriasis.

Efficacy and Safety. Efficacy and safety were established in four clinical trials with a total of 2,403 participants with plaque psoriasis

Table 5
Patient counseling information for Cosentyx*

Inform patients:
- to read the FDA-approved *Medication Guide* before starting Cosentyx therapy and to reread it each time the prescription is renewed;
- that Cosentyx may lower the ability of their immune system to fight infections. Instruct patients of the importance of communicating any history of infections to their healthcare provider and contacting their healthcare provider if they develop any symptoms of infection after receiving Cosentyx ;
- to seek immediate medical attention if they experience any symptoms of serious hypersensitivity reactions;
- to refrigerate the Sensoready pens, prefilled syringes, and vials at 2°C to 8°C (36°F to 46°F). Keep the product in its original carton to protect from light until the time of use. Do not freeze. To avoid foaming, do not shake the product.

*A complete list of counseling information is available in the product's *Medication Guide*.

who were candidates for phototherapy or systemic therapy. Participants were randomly assigned to receive Cosentyx or placebo. The results showed that Cosentyx achieved greater clinical response than placebo, with skin that was clear or almost clear, as assessed by scoring of the extent, nature and severity of psoriatic changes of the skin.

Adverse effects are shown in Table 1. The most common ones included diarrhea and upper respiratory infections (URIs).

Warnings and Precautions. The following **warnings** and **precautions** are listed:

- *Infections*: Serious infections have occurred. Caution should be exercised when considering the use of Cosentyx in patients with a chronic infection or a history of recurrent infection. If a serious infection develops, discontinue Cosentyx until the infection resolves;
- *Tuberculosis (TB)*: Prior to initiating treatment with Cosentyx, evaluate for TB. Monitor closely for signs and symptoms of active TB during and after treatment;
- *Crohn's disease*: Exacerbations were observed in clinical trials. Caution should be exercised when prescribing Cosentyx to patients with active Crohn's disease;
- *Hypersensitivity reactions*: If an anaphylactic reaction or other serious allergic reaction occurs, discontinue Cosentyx immediately and initiate appropriate therapy. The removable cap of the Cosentyx Sensoready pen and the prefilled syringe contain natural rubber latex, which may cause an allergic reaction in latex-sensitive individuals;
- *Vaccinations*: Prior to initiating therapy with Cosentyx, consider completion of all age-appropriate immunizations according to current immunization guidelines. Patients treated with Cosentyx should not receive live vaccines. Non-live vaccinations received during a course of Cosentyx may not elicit an immune response sufficient to prevent disease.

Serious hypersensitivity reaction to secukinumab or to any of the product's excipients is a **contraindication** to Cosentyx.

Drug Interactions. Drug interaction trials have not been conducted with Cosentyx. See warnings/precautions above for coadministration with vaccines.

Administration, Dosing, and Availability. The recommended dose of Cosentyx is 300 mg by subcutaneous injection at weeks 0, 1, 2, 3, and 4; followed by 300 mg every four weeks. For some patients, a dose of 150 mg may be acceptable. Injections should be administered at a different anatomic location (such as upper arms, thighs or any quadrant of the abdomen) than the previous injection, and not into areas where the skin is tender, bruised, erythematous, indurated or affected by psoriasis.

The drug is available in a single-use Sensoready pen and prefilled syringe each containing 150 mg/mL, and in a single-use vial containing 150 mg lyophilized powder for reconstitution by a healthcare professional only.

Patient Counseling. An FDA-approved *Medication Guide* must be dispensed with each new or refill prescription for Cosentyx. Specific points for counseling are summarized in Table 5.

Overview and Summary

The new drugs discussed in this lesson each share an important therapeutic option over previously available agents approved to treat their indicated pathologies. These new drugs are all targeted agents whose mechanism of action is directed to modulation of a specific intracellular reaction, versus activity upon less specific systems. They promise additional relief to patients experiencing these illnesses.

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The author, the Ohio Pharmacists Foundation and the Ohio Pharmacists Association disclaim any liability to you or your patients resulting from reliance solely upon the information contained herein. Bibliography for additional reading and inquiry is available upon request.

This lesson is a knowledge-based CPE activity and is targeted to pharmacists in all practice settings.

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continuing education quiz

New Drugs: Cosentyx, Ibrance, Lenvima, and Unituxin

1. Unituxin is indicated for use with all of the following EXCEPT:
   a. 13-cis-retinoic acid.
   b. letrozole.
   c. interleukin-2.
   d. granulocyte-macrophage colony-stimulating factor.

2. Neuroblastomas often develop in the:
   a. adrenal glands. c. liver.
   b. kidney. d. lung.

3. All of the following are characteristics of thyroid cancer EXCEPT:
   a. it is an uncommon cancer.
   b. it is the most common malignancy of the endocrine system.
   c. it affects men more commonly than women.
   d. onset usually occurs between the ages of 25 and 65.

4. The mechanism of action of lenvatinib is inhibition of:
   a. glycolipid GD2.
   b. cyclin-dependent kinase 4 and 6.
   c. vascular endothelial growth factor receptors.
   d. interleukin-17A.

5. All of the following are symptoms of Reversible Posterior Leukoencephalopathy Syndrome EXCEPT:
   a. visual changes. c. headache.
   b. hemorrhage. d. confusion.

6. The recommended daily dose of Lenvima in patients with severe renal impairment is:
   a. 5 mg. c. 14 mg.
   b. 8 mg. d. 24 mg.

7. Patients taking Lenvima should be informed that:
   a. it may increase the risk of capillary leak syndrome.
   b. females of reproductive potential should use effective contraception for at least two months following the final dose.
   c. it should not be taken on an empty stomach.
   d. it may increase the risk of gastrointestinal fistula formation.

Completely fill in the lettered box corresponding to your answer.

1. [a] [b] [c] [d]	6. [a] [b] [c] [d]	11. [a] [b] [c] [d]
2. [a] [b] [c] [d]	7. [a] [b] [c] [d]	12. [a] [b] [c] [d]
3. [a] [b] [c] [d]	8. [a] [b] [c] [d]	13. [a] [b] [c] [d]
4. [a] [b] [c] [d]	9. [a] [b]	14. [a] [b] [c] [d]
5. [a] [b] [c] [d]	10. [a] [b] [c] [d]	15. [a] [b] [c] [d]

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8. The most serious adverse effects reported in patients taking palbociclib and letrozole are:
   a. pulmonary embolism and diarrhea.
   b. decreased appetite and vomiting.
   c. lymphopenia and neutropenia.
   d. proteinuria and thrombocytopenia.

9. If coadministration of Ibrance with a strong CYP3A inhibitor cannot be avoided, reduce the Ibrance dose.
   a. True b. False

10. It is recommended that Ibrance be:
   a. taken on an empty stomach.
   b. taken daily for the 28-day cycle.
   c. taken with letrozole for half the cycle.
   d. taken at the same time each day.

11. Grapefruit products should not be consumed by patients taking:
   a. Ibrance. c. Unituxin.
   b. Cosentyx. d. Lenvima.

12. Which of the following forms of psoriasis accounts for 90 percent of the cases?
   a. Erythrodermic c. Plaque
   b. Gluttate d. Pustular

13. The proposed mechanism of action of secukinumab is thought to be due to antagonism of:
   a. glycolipid GD2.
   b. interleukin-17A.
   c. cyclin-dependent kinase.
   d. vascular endothelial growth factor.

14. Patients treated with which of the following drugs should not receive live vaccines?
   a. Palbociclib c. Lenvatinib
   b. Secukinumab d. Dinutuximab

15. Which of the following drug's labeling includes a *Boxed Warning* with an alert for nerve damage?
   a. Cosentyx c. Lenvima
   b. Ibrance d. Unituxin

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