continuing education for pharmacists

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# New Drugs: Briviact, Cinqair, Nuplazid, Taltz

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*Dr. Mona T. Thompson has no relevant financial relationships to disclose.*

**Goal.** The goal of this lesson is to provide information on brivaracetam (Briviact®), reslizumab (Cinqair®), pimavanserin (Nuplazid™) and ixekizumab (Taltz™).

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

1. demonstrate an understanding of the pathogenesis and pathophysiology of the disease states for which these new drugs are indicated;
2. select the indication(s), pharmacologic action(s), clinical applications, dosing regimens, mode of administration, and availability for each drug;
3. recall adverse effects and toxicities, warnings, precautions, contraindications, and significant drug-drug or drug-food interactions reported for each agent; and
4. list important counseling information to convey to patients and/or their caregivers.

## Brivaracetam (Briviact)

Brivaracetam (Briviact [briv-ee-akt]) is a new anticonvulsant approved for add-on therapy for the treatment of partial-onset seizures in patients aged 16 years and older with epilepsy. Brivaracetam is a third-generation antiepileptic drug (AED) characterized by high-affinity binding to synaptic vesicle protein 2A (SV2A) in the brain which is thought to contribute to the anticonvulsant effect.

***Epilepsy and Partial-Onset Seizures.*** Epilepsy, defined as the occurrence of at least two unprovoked seizures separated by at least 24 hours, is one of the most common debilitating neurologic disorders. Data from the Centers for Disease Control and Prevention (CDC) indicate that about 5.1 million people in the United States have a history of epilepsy, with 2.5 million people having active epilepsy. A seizure results from an excessive discharge of cortical neurons and is characterized by changes in electrical activity as measured by the electroencephalogram (EEG). Various mechanisms contribute to the hyperexcitability that results in seizure activity. These include alterations of ion channels in neuronal membranes; biochemical modification of receptors; changes in extracellular ion concentrations; and local imbalances between the main neurotransmitters (e.g., glutamate and gaba-aminobutyric acid [GABA]) and neuromodulators (e.g., acetylcholine, norepinephrine, and serotonin).

Not all individuals who experience a seizure will be diagnosed with epilepsy. Other causes of seizures include high fever, low blood sugar, and alcohol or drug withdrawal. Several conditions that affect a person's brain may cause epilepsy such as stroke, brain tumor, traumatic brain injury, loss of oxygen to the brain, genetic disorders such as Down syndrome, or other neurological diseases such as Alzheimer's Disease. In two out of three cases of epilepsy, the cause is unknown.

Seizures are classified into two main groups: *generalized*, which affects both hemispheres of the brain, and *focal*, which affects only one hemisphere. Focal seizures are also called partial seizures. Focal or partial seizures can be further classified as simple, complex, and secondary generalized seizures. In complex partial seizures, an impairment of consciousness occurs which is not exhibited with simple partial seizures. Secondary generalized seizures occur when the seizure begins in one hemisphere of the brain, but then spreads to both sides of the brain. These are also referred to as secondary generalized tonic-clonic seizures (SGTC). The indication for use of brivaracetam is limited to partial-onset seizures. Therefore, discussion of other types of seizures will not be covered in this lesson.

Secondary generalized tonic-clonic seizures are associated with increased morbidity and mortality, including an increased risk of falls, head trauma, and fractures. A lower quality of life has been observed in patients with SGTC, captured by lower scores related to work/social function, energy/fatigue, health discouragement, emotional well-being, seizure worry, social isolation, health perception, bodily pains, social support, overall

health, and overall quality of life. Intractable convulsive seizures are regarded as one of the strongest risk factors for sudden unexpected death in epilepsy (SUDEP). Most cases of SUDEP occur during or immediately following a seizure, and are believed to be related to apnea or arrhythmias that occur as a result of the seizure. It is estimated that there are 1.16 cases of SUDEP for every 1,000 people with epilepsy. Risk factors for SUDEP include uncontrolled seizures and generalized seizures.

The goals of epilepsy treatment are to control or reduce the frequency and severity of seizures, minimize side effects, and ensure compliance while allowing the patient to live as normal a life as possible. Complete suppression of seizures is balanced against tolerability of side effects and the patient's quality of life. Patients with drug-resistant focal epilepsy are at an increased risk for a number of physical and psychosocial complications.

According to the National Institute for Health and Care Excellence's (NICE) 2012 clinical guidelines, carbamazepine or lamotrigine should be offered as first-line treatment in adults with newly diagnosed focal seizures. If these agents are not tolerated or are unsuitable, levetiracetam, oxcarbazepine, or sodium valproate may be used. If the first AED utilized is ineffective, any of these five AEDs may be trialed. Adjunctive or add-on treatment may be considered after a second well-tolerated AED is found to be ineffective.

Brivaracetam, the latest AED to be approved by FDA, has a chemical structure similar to levetiracetam and may be a potentially useful treatment for patients with drug-resistant focal seizures.

***Efficacy and Safety.*** The effectiveness of brivaracetam as adjunct therapy in partial-onset seizures, with or without generalization, was established in three fixed-dose, randomized, double-blind, placebo-controlled, multicenter studies. Enrolled patients were inadequately controlled with one to two AEDs. In each trial, patients had an eight-week baseline in which patients were required to have at least eight partial-onset seizures, followed by a 12-week treatment period. Doses between 50 mg and 200 mg per day were used in the treatment arm of each study with no dose titration. The percent reduction in partial-onset seizure frequency in patients taking brivaracetam over placebo was significant. Additional studies are needed to determine the efficacy of brivaracetem in comparison to levetiracetam, its role in patients who are levetiracetam treatment naïve, and its long-term safety profile.

***Contraindications, Warnings, and Precautions.*** Brivaracetam is contraindicated in patients with a history of a hypersensitivity to the agent, or any of the inactive ingredients in the AED. Bronchospasm and angioedema have been reported with use. As with other AEDs, patients should be monitored for suicidal behavior or ideation; somnolence and fatigue; and advised not to drive or operate machinery until they are treatment-experienced and can gauge the adverse effects the drug may have on them to complete these tasks. Briviact may cause psychiatric adverse reactions, as observed in 13 percent of adult patients in Phase 3 controlled trials. Brivaracetam should be gradually withdrawn when possible to minimize risk of increased seizure frequency. Briviact is listed as a Schedule V controlled substance due to potential for abuse.

***Adverse Reactions.*** The most common adverse reactions observed in clinical trials were somnolence/sedation, dizziness, fatigue, and nausea and vomiting. Fatigue-related adverse reactions appeared to increase dose-dependently.

***Drug Interactions.*** Increasing the dose of brivaracetam by up to 100 percent (i.e., double the dose) is recommended when used concomitantly with rifampin, a potent inducer. Brivaracetam can also interact with other AEDs. When prescribed with carbamazepime, increased exposure to carbamazepine metabolite may occur affecting tolerability. In this instance, clinicians should consider reducing the dose of carbamazepine. Phenytoin levels should be closely monitored as well. Brivaracetem has no added benefit when used with levetiracetam; therefore, the combination should be avoided.

***Administration, Dosing, and Availability.*** Briviact is available as an oral tablet, oral solution (can also be administered via nasogastric or gastrostomy tube), and an injectable solution for intravenous use. The recommended

**Table 1**
**Patient counseling information for Briviact***

Inform patients, their caregivers, and/or families:
- to read the *Medication Guide* for Briviact;
- that antiepileptic drugs, including Briviact, may increase the risk of suicidal thoughts and behaviors; be alert for new or worsening signs of depression, changes in mood/behaviors, or thoughts and behaviors about self-harm;
- that Briviact can cause somnolence, fatigue, dizziness, and gait disturbance. These are more likely to occur early in treatment, but can occur at any time. Patients should not drive or operate machinery until they are treatment-experienced and know the effects the medication may have on them;
- that hypersensitivity reactions such as bronchospasm and angioedema can occur and to seek immediate medical care should this occur;
- not to stop Briviact without consulting their healthcare provider. It should be slowly withdrawn to reduce potential for increased seizure frequency and status epilepticus;
- to notify their healthcare provider if they become pregnant or intend to become pregnant. Encourage patients to enroll in the North American Antiepileptic Drug Pregnancy Registry if they become pregnant.

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

starting dosage for brivaracetam is 50 mg twice daily. Based on the patient's response and tolerability, the dose may be adjusted down to 25 mg twice daily or up to 100 mg twice daily. However, gradual dose escalation is not required. In the presence of hepatic impairment, the recommended starting dose is 25 mg twice daily with a maximum dose of 75 mg twice daily. The intravenous formulation may be used at the same dose and frequency when oral administration is not feasible, and is infused over two to 15 minutes. Briviact is available as 10 mg, 25 mg, 50 mg, 75 mg, and 100 mg tablets, as well as a 10mg/mL oral solution and a 50 mg/5 mL single-dose vial for injection. Patient counseling information for brivaracetam is summarized in Table 1.

## Reslizumab (Cinqair)

Reslizumab (Cinqair [sink-ayr']) is an interleukin-5 (IL-5) antagonist monoclonal antibody (IgG4 kappa) indicated for add-on maintenance treatment of patients with severe asthma aged 18 years and older, and with an eosinophilic phenotype. IL-5 is the major cytokine responsible for the growth and differentiation, recruitment, activation, and survival of eosinophils. Eosinophils are among the many cell types (also mast cells, neutrophils, macrophages, and lymphocytes), along with mediators such as histamine, leukotrienes, and cytokines, that are involved in inflammation and are a component in the pathogenesis of asthma. Therefore, antagonizing IL-5 reduces the production and survival of eosinophils and offers another mechanism for treating asthma.

***Eosinophilic Asthma.*** Asthma is a chronic disease of the airways of the lungs characterized by airflow obstruction and airway hyper-responsiveness and inflammation. CDC estimates that 17.1 million adults and 6.3 million children have asthma in the U.S, which is approximately 8 percent of the U.S. population. Guidelines from the National Asthma Education and Prevention Program detail a stepwise approach to treating adults and children with asthma. Treatment is individualized based on the severity of the disease, which is classified as either intermittent or persistent, ranging from mild, to moderate or severe. Reporting of symptoms, nighttime awakening, use of short-acting beta agonists, interference with normal activity, lung function, and asthma exacerbations are utilized to place patients into severity levels corresponding with treatment recommendations. While most patients are able to gain control of asthma symptoms with bronchodilators and low to moderate doses of inhaled corticosteroids, some remain uncontrolled.

Patients with severe asthma represent only about 5 to 10 percent of asthma patients. Severe asthma is difficult to treat and difficult to define due to patient presentation, type of inflammatory process, comorbidities, and the affects of treatment adherence in each patient. Beyond the initial asthma therapies such as bronchodilators and inhaled corticosteroids, alternative treatments may be used to target other inflammatory pathways. These include leukotriene modifiers such as montekulast or zafirkulast, or omalizumab which targets immunoglobulin-E (IgE) for severe allergic asthma.

As previously stated, there are many cells and mediators involved in the inflammatory pathways that lead to asthma. Eosinophilic asthma is a phenotype of asthma characterized by the persistence of eosinophils in the lung and sputum. The number of eosinophils in the blood and bronchial fluid can correlate with asthma severity. IL-5 has been recognized as the most specific cytokine in the eosinophilic lineage and has been identified as a key common denominator in inflammatory pathways in asthma.

Mepolizumab was the first IL-5 antagonist for the treatment of severe asthma with an eosinophilic phenotype to be approved. Another IL-5 antagonist, benralizumab, is being studied in phase III trials. While reslizumab and mepolizumab are indicated for select patients with severe asthma, recommendations for use of these agents have not yet been incorporated into national asthma treatment recommendations.

***Efficacy and Safety.*** While the exact mechanism of action of reslizumab has not been established, reduction in blood eosinophil counts was observed in clinical trials following the first dose and was maintained throughout treatment. However, eosinophils did return to baseline after the treatment period had ended. Systemic exposure to reslizumab appeared to be unaffected by the presence of treatment-emergent anti-reslizumab antibodies. Literature in animal models suggests that IL-5 and eosinophils are part of an early inflammatory reaction at the site of tumorigenesis and can promote tumor rejection. This conflicts with other animal reports indicating that eosinophils can promote tumor growth. Therefore, the malignancy risk in humans from an antibody to IL-5 is unknown.

Reslizumab was approved following four randomized, double-blind, placebo-controlled studies 16 to 52 weeks in duration involving 981 patients. All subjects continued their current asthma regimen throughout the duration of the study. The primary endpoint for studies I and II was the frequency of asthma exacerbations for each patient during the 52-week treatment period. Patients receiving Cinqair experienced significant reductions in the rate of all asthma exacerbations compared to placebo. The time to first asthma exacerbation was also significantly longer for the groups receiving Cinqair and improvements in lung function were observed based on forced expiratory volumes (FEV1).

***Contraindications, Warnings, and Precautions.*** In clinical trials, 6/1028 (0.6 percent) patients receiving the reslizumab treatment dose reported malignancies follow-

**Table 2**
**Patient counseling information for Cinqair**

Inform patients:
- that hypersensitivity reactions, including anaphylaxis, have occurred with the administration of Cinqair. Educate patients on the signs and symptoms of hypersensitivity reactions and anaphylaxis, such as skin or mucous involvement, airway compromise, and reduced blood pressure;
- that Cinqair does not treat acute asthma symptoms or acute exacerbations. Patients should seek medical attention if asthma remains uncontrolled or worsens after initiating Cinqair;
- about the risk of malignancies; and
- not to discontinue systemic or inhaled corticosteroids except under the direction of a physician. This may be associated with withdrawal symptoms and/or unmask conditions previously masked by corticosteroid use.

ing exposure compared to 2/730 (0.3 percent) in the placebo group. The observed malignancies were diverse in nature without a clustering of any particular type. Upon initiation of therapy with Cinqair, patients should not discontinue systemic or inhaled corticosteroids abruptly. If appropriate, corticosteroids may be gradually decreased under the direction of a physician. Eosinophils may be involved in the immunological response to some helminth infections, and it is unknown if Cinqair will interfere with the immune response against parasitic infections. Therefore, patients with pre-existing helminth infections must be treated prior to initiation of Cinqair.

***Adverse Reactions.*** In clinical studies, the most common adverse reaction noted for Cinqair was oropharyngeal pain. Anaphylaxis has been observed in placebo-controlled studies in 0.3 percent of patients, and was reported as early as the second dose. The events occurred during infusion or within 20 minutes after completion.

***Drug Interactions.*** No formal drug interaction studies have been performed with Cinqair.

***Administration, Dosing, and Availability.*** The recommended dosing regimen for Cinqair is 3 mg/kg by intravenous infusion once every four weeks. Administration directions call for the weight-based dosage to be further diluted in 50 mL of 0.9 percent sodium chloride and infused, immediately after preparation, over 20 to 50 minutes using an in-line 0.2 micron filter. It should never be given as an intravenous push or bolus, and must be administered in a healthcare setting where patients can be monitored throughout the infusion and for a period following infusion. Healthcare professionals must be prepared to manage anaphylaxis. Reslizumab is available as a 100 mg/10 mL solution in single-use vials. Patient counseling information for Cinqair is summarized in Table 2.

## **Pimavanserin** (Nuplazid)

Nuplazid (noo-plá-zid) is an atypical antipsychotic indicated for the treatment of hallucinations and delusions associated with Parkinson's disease psychosis. It is a selective serotonin 5-$HT_{2A}$ inverse agonist and, unlike other atypical antipsychotics, lacks dopaminergic, adrenergic, histaminergic, or muscarinic affinity. At the time of writing, a phase II study to evaluate the efficacy of pimavanserin as treatment for Alzheimer's disease psychosis is currently recruiting patients.

***Parkinson's Disease Psychosis.*** Parkinson's disease (PD) is a neurodegenerative disorder with a clinical presentation including motor deficits, and possibly followed by mental deterioration. As many as one million Americans live with PD, with approximately 60,000 new diagnoses each year. Worldwide, it is estimated that seven to 10 million people have PD. While the incidence of Parkinson's disease increases with age, a small percentage of people with PD are diagnosed before age 50.

Parkinson's disease is characterized by the death of dopaminergic neurons in the pars compacta, a portion of the substantia nigra located in the midbrain. PD slowly progresses and remains relatively asymptomatic until profound depletion of substantia nigra pars compacta neurons has occurred. Initial symptoms may be sensory, but as the disease progresses the classic primary features present as resting tremor, rigidity, bradykinesia, and postural instability. A positive diagnosis of PD can be made with a high level of confidence when clinical presentation is coupled with a positive response to dopaminergic medication.

PD has been increasingly recognized as having a multitude of non-motor symptoms, including psychosis, cognitive impairment and dementia, mood disturbances, fatigue, apathy, and sleep disorders. More than 50 percent of patients with Parkinson's disease have psychosis at some time. Psychosis affects up to 75 percent of patients with Parkinson's disease dementia. The primary psychosis symptoms expressed in Parkinson's disease are hallucinations and delusions which can cause distress for both patients and caregivers. Psychotic episodes are a challenge for treatment and care, are associated with increased morbidity and mortality, and increase the likelihood of nursing home placement.

Best-practice treatment guidelines have traditionally recommended consideration of comorbidities and reduction of dopaminergic therapy to treat psychosis. Typical antipsychotics can cause dopamine antagonism and worsen Parkinsonism and are, therefore, rarely used. Previously, clozapine was the "gold standard" treatment for PD psychosis, with efficacy in treating psychosis without worsening motor symptoms demonstrated in randomized clinical trials. Clozapine selectively binds to D1 mesolimbic receptors, sparing the striatal dopamine D2 receptors, which along with its greater serotonergic 5-$HT_{2A/2C}$ affinity, leads to its favorable motor profile in PD. It is the only antipsychotic medication that has consistently been found

to be efficacious in PD psychosis-randomized controlled trials. However, its use is limited due to the risk of agranulocytosis which can be very dangerous. Quetiapine is structurally similar to clozapine and is also frequently used for the treatment of PD psychosis, despite less consistently supportive data in clinical trials. Quetiapine also has a greater serotonergic affinity to 5-$HT_2$ receptors than to D2 receptors, which confers a more favorable motor profile in PD. Despite insufficient evidence for its use in PD psychosis, quetiapine is often used as it has an acceptable safety profile and doesn't require frequent blood testing.

In PD, the binding of 5-$HT_{2A}$ receptors is increased in the neocortex, and visual hallucinations are associated with increased numbers of 5-$HT_{2A}$ receptors in visual processing areas. Post-mortem and genetic studies suggest that in PD dementia, dementia with Lewy bodies and Alzheimer's disease, delusions and hallucinations are linked to alterations in the 5-HT system. While other atypical antipsychotics target the 5-$HT_{2A}$ system with varying levels, pimavanserin, with its high selectivity of 5-$HT_{2A}$, was developed to provide antipsychotic benefits without the adverse effects of current atypical antipsychotics.

***Efficacy and Safety.*** The efficacy of Nuplazid was demonstrated in a six-week, randomized, placebo-controlled, parallel group study. Study patients had a diagnosis of PD with psychotic symptoms warranting antipsychotic treatment, but without dementia. Patients were required to have a Mini-Mental State Examination (MMSE) score >/= 21 and be able to self report symptoms. The PD-adapted Scale for the Assessment of Positive Symptoms (SAPS-PD) was used to evaluate the efficacy of Nuplazid 34 mg. Each item is scored on a scale of 0-5; therefore, the total score can range from 0 to 45 with higher scores reflecting greater severity of illness. A negative change in score indicates improvement. Primary efficacy was evaluated based on change from baseline to Week 6 in SAPS-PD total score. With statistical significance, Nuplazid was superior to placebo in decreasing the frequency and/or severity of hallucinations and delusions in patients with PD as measured by central, independent, and blinded raters using the SAPS-PD scale. Additionally, Nuplazid was not found to have an effect on motor function.

***Contraindications, Warnings, and Precautions.*** All atypical antipsychotics carry a black box warning from the Food and Drug Administration (FDA) for use in elderly patients, especially those with underlying dementia, due to increased risk of mortality and cerebrovascular events. Nuplazid is not approved for the treatment of patients with dementia-related psychosis unrelated to hallucinations or delusions. Nuplazid increases the QT interval and should be avoided in patients with existing QT prolongation, taking other medications that are known to increase the QT interval or in patients with risk factors for prolonged QT interval, such as hypokalemia and hypomagnesemia.

***Adverse Reactions.*** The most common adverse reactions observed in six-week, placebo-controlled trials include peripheral edema and confusional state. It is important to note the short study period of six weeks and, thus, the ability to assess for incidence for other adverse events that are commonly associated with atypical antipsychotics.

***Drug Interactions.*** Strong CYP3A4 inhibitors may reduce the metabolism of Nuplazid. It is recommended to reduce the dose of Nuplazid by half when taking with a strong CYP3A4 inhibitor such as itraconazole, ketoconazole, clarithromycin, and indinavir. Increased doses of Nuplazid may be required when taken concomitantly with a strong CYP3A4 inducer such as rifampin, carbamazepine, phenytoin, and St. John's wort.

***Administration, Dosing, and Availability.*** The recommended dose is 34 mg taken orally as two 17 mg tablets once daily. It may be taken with or without food. Each tablet contains 20 mg of pimavanserin tartrate, which is equivalent to 17 mg of pimavanserin free base. No dosage adjustments are required in patients with mild or moderate renal impairment. Use of Nuplazid is not recommended in patients with severe renal impairment or hepatic impairment.

## **Ixekizumab** (Taltz)

Ixekizumab is a humanized IgG4 monoclonal antibody that selectively binds with the interleukin-17A (IL-17A) cytokine and acts as an antagonist. It is indicated for the treatment of adults with moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy. IL-17A is a naturally occurring cytokine that is involved in normal inflammatory and immune responses. Ixekizumab inhibits the release of proinflammatory cytokines and chemokines.

***Plaque Psoriasis.*** Psoriasis is a chronic, immune-mediated, inflammatory disease characterized by recurrent exacerbations and remissions of thickened, erythematous, and scaling plaques. Plaque psoriasis, also called *psoriasis vulgaris*, is seen in 90 percent of psoriasis patients. Lesions are usually erythematous, red-violet in color, at least 0.5 cm in diameter, well demarcated, and covered with silver flaking scales. They may appear as single lesions in predisposed areas such as knees or elbows, or generalized over a large body surface area. Associated lesion pruritus may be severe, and lesions may cause physical debilitation or social isolation. Psoriatic arthritis (PsA) can be progressive and destructive involving both psoriatic lesions and inflammatory arthritis-like symptoms leading to impaired function and physical deformities. Psoriasis is classified as mild, moderate, or severe, and is based on affected body surface area and Psoriasis Area and Severity Index (PASI) measurements.

The pathophysiology of pso-

**Table 3**
**Patient counseling information for Taltz***

Inform patients and caregivers:
- to read the *Medication Guide* for Taltz;
- on proper subcutaneous injection technique, including aseptic technique, and how to use the autoinjector or prefilled syringe correctly;
- to store Taltz in the refrigerator; to remove the syringe from the refrigerator and allow it to reach room temperature prior to injection; to inject the full amount (1 mL) providing 80 mg of Taltz; and to rotate injection sites (upper arms, thighs, or any quadrant of abdomen);
- that if a dose is missed, it should be administered as soon as possible followed by resumption of dosing at regular scheduled time;
- that Taltz may lower the ability of their immune system to fight infections, to communicate any history of infections, and contact the healthcare provider if they develop any symptoms of infection; and
- to seek immediate medical attention if they experience any symptoms of serious hypersensitivity reactions.

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

riasis involves cutaneous inflammatory T-cell-mediated activation by surface proteins and antigen-presenting cells. Activated T-cells migrate from lymph nodes and the bloodstream into skin, and secrete cytokines such as interferon-gamma and interleukin-2 that result in pathologic changes. Local keratinoctyes and neutrophils produce other cytokines such as tumor necrosis factor-alpha (TNF-alpha) and interleukin-8. T-cell production and activation result in keratinocyte proliferation. Research has revealed a significant genetic component to the disease.

Goals of treatment include minimizing or eliminating skin lesions, alleviating pruritus, reducing flare-ups, treating co-morbid conditions, and avoiding adverse effects. Based on disease severity and treatment response, treatment algorithms begin with topical steroids and moisturizers, and may lead to combination phototherapy and/or systemic therapy. Systemic therapy with biologic response modifiers (BRMs) is considered in moderate-to-severe psoriasis when other systemic therapies are inadequate or contraindicated. Prior to the approval of Taltz (tol[t]s) which targets IL-17, available BRMs included adalimumab, a monoclonal TNF-alpha antibody; etanercept, a fusion protein that binds to TNF-alpha; infliximab, a chimeric monoclonal antibody directed to TNF-alpha; alefacept, a fusion protein that binds to CD2 on T cells; and ustekinumab, an IL-12/23 monoclonal antibody.

The cytokine IL-17A promotes joint inflammation and damage by triggering the activation of immune cells, inducing proinflammatory cytokines and chemokines. Increased numbers of IL-17A-producing cells are present in the peripheral blood, synovial tissue and fluid, and skin plaques of patients with PsA. Ixekizumab, the first IL-17A antagonist, represents an emerging targeted approach to plaque psoriasis.

***Efficacy and Safety.*** Three multicenter, randomized, double-blind, placebo-controlled trials enrolled over 3800 subjects 18 years of age and older with plaque psoriasis who met criteria for disease severity and were candidates for phototherapy or systemic therapy. In all three trials, subjects were randomized to either placebo or Taltz at a dose of 80 mg every two weeks for 12 weeks, following a 160 mg initial dose. In two of the three trials, an active comparator arm was included in which subjects were also randomized to receive etanercept 50 mg twice weekly (U.S. approved dose) for 12 weeks. The coprimary efficacy endpoints were proportion of patients achieving a static Physician Global Assessment (sPGA) score of 0 or 1 (clear or minimal) and 75 percent or greater improvement in PASI score at week 12. An integrated analysis of the U.S. sites in the two active comparator studies using etanercept resulted in Taltz demonstrating superiority to etanercept 50 mg twice weekly on sPGA and PASI scores during the 12-week treatment period. Patients who were responders at week 12 in Trial 1 and Trial 2 were then randomized to receive an additional 48 weeks of an 80 mg every four weeks maintenance dose of Taltz or placebo to evaluate the maintenance and durability of response.

***Contraindications, Warnings, and Precautions.*** Taltz is contraindicated in patients with a previous serious hypersensitivity reaction, such as anaphylaxis, to ixekizumab or to any of the excipients. Serious hypersensitivity reactions have occurred with use, including angioedema and urticaria. Taltz may increase the risk of infection. In clinical trials, upper respiratory tract infections, oral candidiasis, conjunctivitis, and tinea infections occurred more frequently in the Taltz group than in the placebo group. All patients should be evaluated prior to initiating Taltz therapy and should not receive Taltz if he/she has an active TB infection or untreated latent TB infection. Crohn's disease and ulcerative colitis, including exacerbations, also occurred at a greater frequency in the Taltz group compared to placebo. It is also recommended that patients complete all age-appropriate immunizations prior to treatment with Taltz.

***Adverse Reactions.*** Adverse reactions, that occurred at a rate of at least 1 percent and at a higher rate in the Taltz group than in the placebo group during the 12-week study period of pooled clinical trials, include injection site reactions, upper respiratory tract infections, nausea, and tinea infections. Adverse reactions that occurred at rates less than 1 percent in the Taltz group and more frequently than in the placebo group during the 12-week induction period included rhinitis, oral candidiasis, urticaria, influenza, conjunctivitis, inflammatory bowel disease and angioedema.

***Drug Interactions.*** The use of live vaccinations should be avoided in patients being treated with

Taltz. The formation of CYP450 enzymes can be altered by increased levels of certain cytokines during chronic inflammation. Therefore, as Taltz antagonizes IL-17A, it may result in normalized levels of CYP450 enzymes. It is recommended that upon initiation or discontinuation of Taltz in patients receiving concomitant drugs which are CYP450 substrates, to increase monitoring, especially in medications with a narrow therapeutic index.

***Administration, Dosing, and Availability.*** Taltz is available as an 80 mg/mL single-dose autoinjector or a pre-filled syringe, and is packaged with detailed instructions on how to prepare and administer either product. Patients may self-administer the injection after receiving training. Taltz is administered by subcutaneous injection at the recommended dose of 160 mg (two 80 mg injections) at initiation (week 0), followed by 80 mg at weeks 2, 4, 6, 8, 10, and 12; then 80 mg every four weeks. Patient counseling information for ixekizumab may be found in Table 3.

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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. Disclosure. The OPF trustees and other individuals responsible for planning OPF continuing pharmacy education activities have no relevant financial relationships to disclose.

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# continuing education quiz

## New Drugs: Briviact, Cinqair, Nuplazid, Taltz

1. Brivaracetam is indicated for which of the following types of seizures?
   a. Absence
   b. Generalized
   c. Partial-onset
   d. All of the above

2. Brivaracetam is structurally similar to which of the following antiepileptic drugs?
   a. Carbamazepine
   b. Valproic acid
   c. Levetiracetam

3. The maximum dose of brivaracetam is 75 mg twice daily in the patients with:
   a. hepatic impairment.
   b. renal impairment.
   c. concomitant rifampin use.

4. Reslizumab is indicated for:
   a. focal seizures.
   b. Parkinson's disease psychosis.
   c. severe asthma with allergic (IgE) phenotype.
   d. severe asthma with eosinophilic phenotype.

5. Patients taking reslizumab should be counseled on which of the following safety concerns?
   a. Risk of malignancy
   b. Fatigue and potential for inability to drive
   c. Reduced ability to fight infection

6. The most common adverse reaction observed in placebo-controlled clinical trials with reslizumab was:
   a. anaphylaxis.
   b. URI.
   c. oropharyngeal pain.
   d. parasitic infections.

7. After the initial dose, reslizumab may be given by intravenous push.
   a. True
   b. False

Completely fill in the lettered box corresponding to your answer.

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

❑ **I am enclosing $5 for this month's quiz made payable to: Ohio Pharmacists Association.**

1. Rate this lesson: (Excellent) 5 4 3 2 1 (Poor)
2. Did it meet each of its objectives? ❑ yes ❑ no
   If no, list any unmet_____
3. Was the content balanced and without commercial bias?
   ❑ yes ❑ no If no, why?_____
4. Did the program meet your educational/practice needs?
   ❑ yes ❑ no
5. How long did it take you to read this lesson and complete the quiz? _____
6. Comments/future topics welcome.

Please print.

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**Return quiz and payment (check or money order) to Correspondence Course, OPA, 2674 Federated Blvd, Columbus, OH 43235-4990**

8. Pimavanserin is indicated in patients with Parkinson's disease with which of the following?
   a. Dementia
   b. Hallucinations
   c. Confusion
   d. Cognitive impairment

9. Parkinson's disease is characterized by loss of neurons secreting which of the following?
   a. Dopamine
   b. Serotonin
   c. Norepinephrine

10. Pimavanserin's unique mechanism of action is due to its selectivity for which of the following receptors?
   a. Muscarinic
   b. Histaminic
   c. Adrenergic
   d. Serotonin 5-$HT_{2A}$

11. The most common adverse reactions in placebo-controlled clinical trials with pimavanserin included:
   a. fatigue and dizziness.
   b. peripheral edema and confusional state.
   c. increased infections and malignancies.

12. Ixekizumab treats plaque psoriasis by antagonizing which of the following cytokines?
   a. Interleukin-17A
   b. TNF-alpha
   c. Interleukin-12/23
   d. Interleukin-5

13. In clinical trials, ixekizumab increased risk of all of the following EXCEPT:
   a. tinea infections.
   b. Crohn's disease.
   c. ulcerative colitis.
   d. malignancies.

14. Patients taking ixekizumab should be counseled on all of the following EXCEPT:
   a. rotate injection sites (upper arms, thighs, abdomen).
   b. store at room temperature.
   c. administer the full amount 80 mg/mL.
   d. administer missed doses as soon as possible.

15. The most common adverse reactions in placebo-controlled clinical trials with ixekizumab included:
   a. fatigue and dizziness.
   b. peripheral edema and confusional state.
   c. injection site reactions and upper respiratory tract infections.

To receive CPE credit, your quiz must be received no later than January 15, 2020. A passing grade of 80% must be attained. CPE credit for successfully completed quizzes will be uploaded to the CPE Monitor. CPE statements of credit can be printed from the CPE Monitor website. Send inquiries to opa@ohiopharmacists.org.