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New Drugs: Impavido, Myalept, Neuraceq, and Otezla

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Dr. Thomas A. Gossel has no relevant financial relationships to disclose.

Goal. The goal of this lesson is to provide information on apremilast (Otezla®), florbetaben F18 (Neuraceq™), metreleptin (Myalept™) and miltefosine (Impavido®).

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

1. identify the new drugs by generic name, trade name and chemical name when relevant;
2. select the indication(s), pharmacologic action(s) and clinical application(s) for each drug;
3. recognize important therapeutic uses for the drugs and their applications in specified pathologies; and
4. demonstrate an understanding of adverse effects and toxicity, significant drug-drug interactions, and patient counseling information for these drugs.

Three of the new-molecular entity drugs discussed in this lesson are indicated to treat a variety of pathologies, and the other to aid in the diagnosis of Alzheimer's Disease (Table 1). The lesson provides a brief introduction to the drugs, and is not intended to extend beyond an overview of the topic. The reader is, therefore, urged to consult the products' full prescribing information leaflet (package insert), *Medication Guide* when available, and other published sources for detailed descriptions.

Apremilast (Otezla)

Psoriatic arthritis (PsA) is a form of arthritis that affects some individuals who have psoriasis. Approved treatments for PsA before Otezla included corticosteroids; and blockers of tumor necrosis factor alpha (TNF_α), interleukin-12 (IL-12), IL-23, and other inflammatory cytokines. Cytokines include a broad category of small proteins that function in intercellular signaling. Much attention has been directed toward development of powerful biologicals. At the same time, new molecules that do not require the expensive production process of biological agents and that have a selective focus on a key step in the pathogenesis of psoriasis have been eagerly sought. Otezla provides that new treatment option for patients suffering from PsA.

Indication and Uses. Otezla is indicated for treatment of adult patients with active psoriatic arthritis.

Psoriatic Arthritis. PsA is a chronic inflammatory arthritis associated with psoriasis. Forty percent of patients with psoriasis are estimated to develop PsA, with prevalence in the general U.S. population between 0.3 to 1.0 percent. PsA is associated with poor health-related quality of life, including overall health, physical functioning, and bodily pain. In a survey sponsored by the National Psoriasis Foundation, 44 percent of patients with PsA who were unemployed reported that their work disability was partially or entirely due to PsA. Most affected individuals develop psoriasis first, and are later diagnosed with PsA. Joint pain, stiffness and swelling are the main signs and symptoms of PsA.

Immune system mechanisms can halt the immune response and avoid tissue damage from chronic inflammation. Of note, cyclic-adenosine monophosphate (cAMP) is one such intrinsic modulator of inflammatory responses that has generated much research interest over the past decade. The cAMP level in cells is regulated by phosphodiesterases (PDEs), enzymes responsible for its hydrolysis. PDE4 is a cAMP-specific PDE and the dominant PDE in inflammatory cells. Inhibition of PDE4 elevates intracellular cAMP levels, which in turn down-regulates the inflammatory response by the inflammatory cytokines.

Mechanism of Action. Apremilast is an oral small-molecule inhibitor of PDE4 specific for cAMP. PDE4 inhibition results in increased intracellular cAMP levels. The precise mechanism(s) by which apremilast exerts its therapeutic action in psoriatic arthritis patients is not well defined.

Efficacy and Safety. Safety and efficacy were evaluated in three multicenter, randomized, double-blind, placebo-controlled clinical trials involving 1,493

Table 1
Selected new drugs

Generic (Proprietary) Name	Distributor	Indication	Dose*	Dosage Form	Most Common Side Effects	Medication Guide±
Apremilast (Otezla)	Celgene Corp.	active psoriatic arthritis	titrate to 30 mg twice daily	10, 20, 30 mg tablets	(≥5%): diarrhea, nausea, and headache	No
Florbetaben F18 (Neuraceq)	Piramal Imaging, S.A.	diagnostic aid for Alzheimer's disease and other cognitive decline	see product prescribing information	30 mL multi-dose vials, 1.4-135 mCi/mL	injection site reactions: erythema (1.7 %), irritation (1.2%), and pain (3.9%)	No
Metreleptin (Myalept)	AstraZeneca Pharmaceuticals	complications of leptin deficiency in patients with congenital or acquired generalized lipodystrophy	see product prescribing information	lyophilized cake of 11.3 mg/vial to be reconstituted to 5 mg/mL	(≥10%): headache, hypoglycemia, decreased weight, abdominal pain	Yes
Miltefosine (Impavido)	Paladin Therapeutics, Inc.	visceral, cutaneous, and mucosal leishmaniasis infections	50 mg two to three times a day for 28 days	50 mg capsules	(≥2%): nausea, vomiting, diarrhea, headache, decreased appetite, dizziness, abdominal pain, pruritus, somnolence, elevated transaminases and creatinine	Yes

*Recommended dose for most patients

±Availability at the time of publication of this lesson

patients with active PsA. Patients treated with apremilast showed improvement in signs and symptoms of PsA, compared to placebo, including tender and swollen joints and physical function.

The most common adverse effects observed in patients treated with the drug were diarrhea, nausea, and headache. The majority of adverse reactions occurred within the first two weeks of treatment and tended to resolve over time with continued dosing. Treatment with apremilast was also associated with an increase in reports of depression compared to placebo. FDA is requesting a pregnancy exposure registry as a post-marketing requirement to assess the risks of Otezla in pregnant women.

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

• *Depression:* Advise patients, their caregivers, and families to be alert for the emergence or worsening of depression, suicidal thoughts or other mood changes, and if such changes occur to contact their healthcare provider. Carefully weigh risks and benefits of treatment with Otezla in patients with a history of depression and/or suicidal thoughts or behavior.

• *Weight Loss:* Monitor weight regularly. If unexplained or clinically significant weight loss occurs, evaluate the loss and consider discontinuation of Otezla.

• *Drug Interactions:* Use with strong cytochrome P450 enzyme inducers (e.g., rifampin, phenobarbital, carbamazepine, phenytoin) is not recommended because of decreased efficacy.

Known hypersensitivity to apremilast or any excipients in the formulation is the only **contraindication** listed.

Administration, Dosing, and Availability. It is recommended to titrate the drug over five days, starting with 10 mg on day 1 up to a maintenance dose of 30 mg twice daily, taken orally starting on day 6. The detailed titration dosing schedule can be found in the product's Prescribing Information. This titration is intended to reduce the gastrointestinal symptoms associated with initial therapy.

The dose should be reduced to 30 mg once daily in patients with severe renal impairment (creatinine clearance of less than 30 mL per minute). For initial dosage titration in this group, it is recommended that Otezla be titrated using only the morning schedule, omitting the evening doses.

Otezla is available in 10 mg, 20 mg, and 30 mg tablets.

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

Table 2
Patient information for Otezla*

Inform patients:
- with a history of depression and/or suicidal thoughts or behavior to be alert for the emergence or worsening of depression, suicidal thoughts or other mood changes and to notify their healthcare provider if these occur. Caregivers and family members should also be thus advised;
- to have their weight monitored regularly and the drug discontinued if unexplained or clinically significant weight loss occurs;
- to take the drug only as prescribed;
- to take the drug with or without food; but not to crush, split, or chew the tablets.

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

Florbetaben F18 (Neuraceq)

The prevalence of Alzheimer's Disease (AD) and cognitive impairment is increasing worldwide. Neuraceq is used to help diagnose these diseases.

Indication. Neuraceq is a radioactive diagnostic agent indicated for Positron Emission Tomography (PET) imaging of the brain to estimate ß-amyloid neuritic plaque density in adult patients who are being evaluated for AD and other causes of cognitive decline. A negative Neuraceq scan indicates sparse to no ß-amyloid neuritic plaques, and is inconsistent with a neuropathological diagnosis of AD at the time of image acquisition; a negative scan result reduces the likelihood that a patient's cognitive impairment is due to AD. A positive Neuraceq scan indicates moderate to frequent ß-amyloid neuritic plaques. Neuropathological examination has shown this amount of plaque is present in patients with AD, but may also be present in patients with other neurologic conditions, as well as older adults with normal cognition. Neuraceq is, therefore, an adjunct to other diagnostic evaluations.

Alzheimer's Disease. AD is an irreversible, progressive neurodegenerative disorder characterized by memory loss and other cognitive and functional decline. AD leads invariably to death, usually within seven to 10 years of diagnosis. Symptoms usually precede diagnosis by several years, and longitudinal studies in older populations have found a subtle decline in cognition up to 10 years before dementia is recognized.

Dementia is defined as cognitive impairment of sufficient severity that it prevents independent function in the patient's usual occupation or daily activities. Dementia is primarily caused by neurodegenerative disease. The most common neurodegenerative disease in older adults is AD, and this accounts for about 70 percent of cases of dementia. Metabolic problems such as hypothyroidism, severe vitamin B_{12} deficiency, chronic hypoxia, major organ failure, autoimmune encephalopathy, stroke, normal-pressure hydrocephalus, and subdural hematoma need to be excluded, but collectively account for fewer than 5 percent of patients presenting with progressive cognitive decline.

AD not only has devastating effects on patients and their families/caregivers, but also has significant socioeconomic impact on the health system, a burden that will only increase in the upcoming years as the population ages. The prevalence of AD is age-dependent, affecting 1 percent of the population at age 60 years and then doubling every five years, with the result that 25 percent of persons aged 85 years have the disease.

At this time there is no cure for AD, nor is there an effective means to slow the rate of neurodegeneration. Symptomatic treatment with an acetylcholinesterase inhibitor (donepezil [Aricept], galantamine [Razadyne], rivastigmine [Exelon]), or an N-methyl-D-asparate receptor antagonist (memantine [Namenda]) provides modest benefit, usually by temporary stabilization rather than noticeable improvement in memory function.

ß-amyloid plaques are present in moderate to frequent numbers in the cortical gray matter in all cases of AD, and develop many years before onset of dementia. ß-amyloid abnormalities have value for diagnosis of AD in that their presence strongly correlates with the extent of neurodegeneration.

Mechanism of Action. Florbetaben F18 is an F18-labeled stilbene derivative, which binds to ß-amyloid plaques in the brain. The F18 isotope produces a positron signal that is detected by a PET scanner.

Efficacy and Safety. FDA approval was based on safety data from 872 patients who participated in global clinical trials, and three studies that examined images from adults with a range of cognitive function. The studies included 205 end-of-life patients who had agreed to participate in a post-mortem brain donation program. Images were analyzed from 82 subjects with post-mortem confirmation of the presence or absence of ß-amyloid neuritic plaques. Correlation of the visual PET interpretation with histopathology in these 82 brains demonstrated that Neuraceq accurately detects moderate to frequent ß-amyloid neuritic plaques in the brain, and could be useful in estimating the density of these plaques.

The most frequently observed adverse drug reactions in subjects receiving Neuraceq were injection site reactions consisting of erythema, irritation, and pain. All adverse reactions were mild to moderate in severity and of short duration.

Warnings, Precautions and Contraindications. The following **warnings** and **precautions** are listed:
- *Image Interpretation Errors:* (especially false positives) have been observed.
- *Like all radiopharmaceuticals, Neuraceq contributes to a patient's long-term cumulative radiation exposure.* Long-term cumulative radiation exposure is associated with an increased risk of cancer. Ensure

safe handling to protect patients and healthcare workers from unintentional radiation exposure.

No **contraindications** are listed.

Drug Interactions. Drug-drug interaction studies have not been performed to establish the extent, if any, to which concomitant medications may alter Neuraceq image results.

Administration, Dosing, and Availability. The dose of Neuraceq is 300 MBq (8.1mCi). It should be administered as a single slow intravenous bolus (6 sec/mL) in a total volume of up to 10 mL. Neuraceq is supplied in 30 mL glass multi-dose vials, containing 50 to 5000 MBq/mL (1.4 to 135 mCi/mL). The vials are enclosed in a shielded container to minimize radiation exposure. The product does not contain a preservative.

Patient Counseling Information. Patients should inform their physician or healthcare provider if they are pregnant or breastfeeding. If breastfeeding, they should use alternate infant nutrition (e.g., stored breast milk or infant formula) for 24 hours after administration of the drug, or avoid use of the drug.

Metreleptin (Myalept)

Myalept (MAI-uh-lept) is an analog of the hormone leptin produced through recombinant DNA technology. It is the first approved therapy for treating complications of leptin deficiency, and provides a needed treatment option for patients with this orphan disease.

Indication and Uses. Myalept is used as an adjunct to diet as replacement therapy to treat the complications of leptin deficiency in patients with congenital or acquired generalized lipodystrophy. Its safety and effectiveness for treatment of complications of partial lipodystrophy, or for treatment of liver disease including nonalcoholic steatohepatitis (also called fatty liver disease), have not been established. The drug is not indicated for use in patients with HIV-related lipodystrophy, or in those with metabolic disease without concurrent evidence of generalized lipodystrophy.

Generalized Lipodystrophy. Lipodystrophy has been reported in the medical literature for more than 100 years. Generalized lipodystrophy (also called lipoatrophy) is a rare condition associated with subcutaneous fat being almost completely or totally absent. Patients with congenital generalized lipodystrophy are born with little or no adipose (fat) tissue. Patients with acquired generalized lipodystrophy typically present in their late teens or early twenties. There is a female to male predilection of 3:1, and patients with acquired lipodystrophy generally lose fat tissue over weeks to years.

Because leptin is made by adipocytes, patients with generalized lipodystrophy have very low leptin levels. Native leptin, a protein of 167 amino acids, is secreted into the circulation and activates leptin receptors that are expressed throughout the body, with high expression in the hypothalamus. This leptin signals the CNS of the status of energy stores in the body. In patients with generalized lipodystrophy, leptin deficiency, resulting from the loss of adipose tissue, contributes to excess caloric intake (hyperphagia), which exacerbates the metabolic abnormalities as patients ingest large quantities of food, including fat. In patients with generalized lipodystrophy, the deficiency of adipose tissue leads to hypertriglyceridemia and ectopic deposition of fat in non-adipose tissues such as liver and muscle that contributes to metabolic abnormalities. This fat deposition in muscle increases insulin resistance, while in the liver, it can lead to nonalcoholic steatohepatitis, advanced liver fibrosis and even cirrhosis, sometimes requiring liver transplantation.

Mechanism of Action. Metreleptin binds to and activates leptin receptors. This supports the drug's use as a potential treatment for certain metabolic disorders (e.g., diabetes mellitus and hypertriglyceridemia) associated with lipodystrophy.

Efficacy and Safety. The drug's safety and effectiveness were evaluated in an open-label, single-arm clinical trial that included 48 patients with congenital or acquired generalized lipodystrophy who also had diabetes mellitus, hypertriglyceridemia, and/or elevated levels of fasting insulin. The trial showed reductions in glycosylated hemoglobin (HbA1c), fasting glucose, and triglycerides.

The trial also showed that anti-drug antibodies with neutralizing activity to leptin and/or metreleptin may develop, which could result in severe infections or loss of treatment effectiveness. T-cell lymphoma was reported in patients with acquired generalized lipodystrophy, both treated and not treated with metreleptin, so healthcare professionals should carefully consider the benefits and risks of treatment with metreleptin in patients with significant hematologic abnormalities and/or acquired generalized lipodystrophy.

In this and other clinical trials, the most common adverse effects observed at a level of ≥10 percent in patients treated with metreleptin were hypoglycemia, headache, decreased weight, and abdominal pain.

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

• *Anti-metreleptin Antibodies with Neutralizing Activity:* Their presence could inhibit endogenous leptin action and/or result in loss of Myalept efficacy. Test for neutralizing antibodies in patients with severe infections or loss of efficacy during Myalept treatment.

• *T-cell Lymphoma:* Carefully consider benefits and risks of treatment with Myalept in patients with significant hematologic abnormalities and/or acquired generalized lipodystrophy.

• *Hypoglycemia:* A dose adjustment, including possible large reductions, of insulin or insulin secretagogue may be necessary.

Closely monitor blood glucose in patients on concomitant insulin or insulin secretagogue therapy.

•*Autoimmunity:* Autoimmune disorder progression has been observed in patients treated with Myalept. Consider benefits and risks of Myalept treatment in patients with autoimmune disease.

•*Hypersensitivity:* Hypersensitivity reactions (e.g., urticaria or generalized rash) have been reported. Patients should promptly seek medical advice regarding suspected reactions.

•*Benzyl Alcohol Toxicity:* Preservative-free Sterile Water for Injection (WFI) contains no benzyl alcohol and is recommended for neonates and infants.

Two **contraindications** are noted: (1) general obesity not associated with congenital leptin deficiency, and (2) hypersensitivity to metreleptin.

Drug Interactions. No formal drug interaction studies have been conducted. Leptin is a cytokine and may have the potential to alter the formation of cytochrome P450 (CYP450) enzymes. This should be taken into account when taking concomitant drugs metabolized by CYP450 (e.g., oral contraceptives and drugs with a narrow therapeutic index). The effect of metreleptin on CYP450 enzymes may be clinically relevant for CYP450 substrates with a narrow therapeutic index, where the dose is individually adjusted. Upon initiation or discontinuation of Myalept, in patients being treated with these types of agents, therapeutic monitoring of effect (e.g., warfarin) or drug concentration (e.g., cyclosporine or theophylline) should be undertaken and the individual dose of the agent adjusted as needed.

Administration, Dosing, and Availability. Myalept is administered by subcutaneous injection once daily after the lyophilized cake is reconstituted. Dosage calculation is based on body weight and gender. The drug should be administered once daily at the same time every day. It can be given any time of day without regard to the timing of meals. If a dose is missed, it should be administered as soon as noticed, and the normal dosing schedule resumed the next day. Myalept is supplied as a lyophilized cake of 11.3 mg metreleptin per vial to deliver 5 mg per mL when reconstituted in 2.2 mL of diluent.

The product is available only through a restricted program called the MYALEPT REMS Program. Notable requirements of the Program include the following.

•Prescribers must be certified with the program by enrolling and completing training.

•Pharmacies must be certified with the program and only dispense Myalept after receipt of the MYALEPT REMS Prescription Authorization Form with each new prescription.

Patient Counseling Information. An FDA-approved *Medication Guide* must be dispensed with each prescription and refill for Myalept. Specific points for counseling are summarized in Table 3.

Table 3
Patient counseling information for Myalept*

Inform patients:
•to read the FDA-approved *Medication Guide* included with each prescription and/or refill;
•of the risk of developing neutralizing antibodies, lymphoma, hypoglycemia, autoimmune disease, and hypersensitivity reactions and symptoms of each condition;
•to immediately inform their physician if any of the symptoms of the conditions mentioned above appear;
•to prepare and inject Myalept following instructions given by the physician and/or pharmacist;
•to administer the drug only as instructed. If a dose is missed, administer the dose as soon as possible, then administer the next dose at the regularly scheduled time;
•to use Myalept during pregnancy only if the potential benefit justifies the potential risk to the fetus. For nursing mothers, breastfeeding is not recommended with Myalept use;
•to store the vials of powder in their carton in the refrigerator at 36°F to 46°F (2°C to 8°C) as soon as received. Do not freeze or use the product past the expiration date.

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

Miltefosine (Impavido)

Leishmaniasis is an infection caused by *Leishmania*, a parasite that is transmitted to humans through sandfly bites. The disease occurs primarily in individuals who live in tropical and subtropical climates, including southern United States. Most U.S. patients acquire leishmaniasis overseas. Impavido (im-PA-vee do) is the first FDA-approved drug to treat cutaneous or mucosal leishmaniasis.

FDA granted Impavido fast-track designation, priority review, and orphan product designation because the drug demonstrated the potential to fill an unmet medical need in a serious disease or condition, the potential to be a significant improvement in safety or effectiveness in treatment of a serious disease or condition, and is intended to treat a rare disease, respectively.

Indication and Uses. Impavido is an antileishmanial drug indicated in adults and adolescents ≥12 years of age weighing ≥30 kg (66 pounds) for treatment of visceral leishmaniasis (*Leishmania donovani*), cutaneous leishmaniasis (*L. braziliensis*, *L. guyanesis*, and *L. panamensis*), and mucosal leishmaniasis (*L. braziliensis*). *Leishmania* species evaluated in clinical trials were based on epidemiologic data. There may be geographic variation in the response of the same *Leishmania* species to miltefosine. The drug's efficacy in treatment of other *Leishmania* species has not been evaluated.

Leishmaniasis. Leishmaniasis is an intracellular protozoal infection in which tissue macrophages are targeted. It is transmitted by the bite of various *Leishmania* protozoa sandfly species. Fully expressed infection, caused by a diverse group of species, results in three basic clinical diseases:

cutaneous (CL), mucosal (ML), or visceral (VL) leishmaniasis. CL leishmaniasis presents with skin ulcers; ML with skin, nose and mouth ulcers; and VL with skin ulcers, fever, low red blood cells, and enlarged spleen and liver.

More than 90 percent of CL cases are found in only ten countries (Afghanistan, Iran, Iraq, Saudi Arabia, Algeria, Ethiopia, Sudan, Syria, Brazil, and Peru). More than 90 percent of VL is found in six countries: India, Bangladesh, Nepal, Sudan, Ethiopia, and Brazil. ML is primarily, but not exclusively, a disease of South America. After the diagnosis has been made, it is important to determine the extent of disease, region acquired, and infecting species (if possible) because this information may influence the choice of therapy, particularly in CL.

ML and VL are seldom encountered in the United States, but are always treated. Treatment is not normally required in CL in all instances, but in practice, most patients in the United States receive some type of drug therapy. Irrespective of the treatment, patients with any form of leishmaniasis should be made aware of two possible outcomes: first, that the initial response to treatment may prove unsatisfactory, requiring retreatment; and second, that despite a satisfactory clinical response, relapse may still occur within the first six to 12 post-treatment months.

Mechanism of Action. The specific mode of action of miltefosine against *Leishmania* species is unknown. The mechanism is likely to involve interaction with lipids (phospholipids and sterols), including membrane lipids, inhibition of cytochrome c oxidase (mitochondrial function), and apoptosis-like cell death.

Efficacy and Safety. Safety and efficacy were evaluated in four clinical trials. A total of 547 patients received Impavido and 183 patients received either a comparator drug or placebo. Results from these trials demonstrated that Impavido is safe and effective in treating visceral, cutaneous, and mucosal leishmaniasis.

The most common adverse effects were nausea, vomiting, diarrhea, headache, decreased appetite, dizziness, abdominal pain, itching, drowsiness, and elevated liver enzymes (transaminases) and creatinine. The labeling for Impavido includes a Boxed Warning to alert patients and healthcare professionals that the drug can cause fetal harm and, therefore, should not be given to pregnant women. Healthcare professionals should advise women to use effective contraception during, and for five months after, Impavido therapy.

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

- *Embryo-fetal Toxicity:* Do not use in pregnant women. Obtain a urine or serum pregnancy test prior to initiation of therapy. Advise use of effective contraception in females of reproductive potential.
- *Reproductive Effects.* Miltefosine caused testicular atrophy and impaired fertility in male and female rats. Advise patients of reproductive toxicities in animal studies and that the potential effects on human fertility have not been adequately evaluated.
- *Renal Effects:* Monitor serum creatinine during therapy and for four weeks after the end of therapy.
- *Hepatic Effects:* Monitor transaminases and bilirubin during therapy.
- *Gastrointestinal Effects:* Encourage fluid intake to avoid volume depletion.
- *Thrombocytopenia:* Monitor platelet count during therapy for visceral leishmaniasis.
- *Absorption of Oral Contraceptives:* Advise use of alternative method of contraception if vomiting and/or diarrhea occur.
- *Stevens-Johnson Syndrome:* Discontinue Impavido.

Contraindications to the drug include: (1) pregnancy, (2) Sjögren-Larsson Syndrome, and (3) hypersensitivity to miltefosine or any of its excipients.

Table 4
Patient counseling information for Impavido*

Inform patients:
- to read the FDA-approved *Medication Guide* included with each prescription and/or refill;
- to take Impavido with food to help eliminate gastrointestinal adverse effects;
- to swallow the capsule whole and not to chew it or break it apart, and complete the full course of therapy;
- that abdominal pain, nausea, vomiting, and diarrhea are common adverse effects of therapy. Instruct the patient to inform their healthcare provider if these gastrointestinal effects are severe or persistent. They should drink sufficient fluids to avoid dehydration and, consequently, the risk of kidney injury;
- that female patients of reproductive potential should use effective contraception during therapy and for five months after therapy ends. If vomiting and/or diarrhea occurs during therapy, women who use oral contraceptives should use additional non-hormonal or alternative method(s) of effective contraception;
- that nursing mothers should not breastfeed during therapy and for five months after therapy is completed;
- that the drug has caused infertility in male rats, impaired fertility in female rats, and caused atresia (absence or closure of an anatomical part) in ovarian follicles in female dogs. The potential for impaired fertility in humans has not been adequately evaluated.

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

Drug Interactions. *In vitro* and animal metabolism studies showed that miltefosine did not markedly induce or inhibit the activity of the major human cytochrome P450 enzymes. The potential of miltefosine to interact with drug transporters has not been evaluated.

Administration, Dosing, and Availability. Impavido is admin-

istered with food to ameliorate gastrointestinal adverse reactions. For patients weighing 30 to 44 kg, the dose is 50 mg twice daily; and for patients weighing 45 kg or greater, 50 mg three times daily. Treatment duration is 28 consecutive days.

Impavido is available as 50 mg capsules. The capsules are supplied in a folded peel/push-through blister card, each card containing 14 capsules. Each carton contains two blister cards. The drug should be dispensed only in its original carton.

Patient Counseling Information. An FDA-approved *Medication Guide* must be dispensed with each prescription and refill for Impavido. Specific points for counseling are summarized in Table 4.

Overview and Summary.

The new drugs are indicated to treat a wide variety of pathologies or aid in the diagnosis of a major disease. In each case, the drugs have been shown to be effective and safe when used as directed. Each offers advantages over earlier treatments.

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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 CE activity and is targeted to pharmacists in all practice settings.

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CE Hours: 1.5 (0.15 CEU)

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continuing education quiz

New Drugs: Impavido, Myalept, Neuraceq, and Otezla

1. All of the following are true about psoriatic arthritis (PsA) EXCEPT:
   a. 40 percent of patients with psoriasis are estimated to develop PsA.
   b. its prevalence in the U.S. general population is about 10 percent.
   c. it is associated with poor health-related quality of life.
   d. most affected individuals develop psoriasis first.

2. Apremilast inhibits:
   a. PDE4.
   b. PDE10.
   c. cAMP.
   d. ATP.

3. All of the following statements about adverse events with apremilast are true EXCEPT:
   a. the most common is hypoglycemia.
   b. most occurred within the first two weeks of treatment.
   c. they tended to resolve over time with continued dosing.

4. A contraindication for Otezla is:
   a. use with strong cytochrome P450 enzyme inducers.
   b. creatinine clearance of less than 30 mL/minute.
   c. general obesity not associated with leptin deficiency.
   d. known hypersensitivity to apremilast.

5. The most common neurodegenerative disease in older adults is:
   a. mucosal leishmaniasis.
   b. Sjögren-Larsson Syndrome.
   c. Alzheimer's Disease.
   d. Parkinson's Disease.

6. Florbetaben F18 binds with which of the following substances in the brain?
   a. Alpha-methyltyrosine
   b. Dopamine beta-hydroxylase
   c. Gamma-aminobutyric acid
   d. Beta-amyloid

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]		8.	[a]	[b]	[c]	[d]	13.	[a]	[b]	[c]	[d]
4.	[a]	[b]	[c]	[d]	9.	[a]	[b]	[c]	[d]	14.	[a]	[b]	[c]	[d]
5.	[a]	[b]	[c]	[d]	10.	[a]	[b]	[c]	[d]	15.	[a]	[b]	[c]	[d]

❑ **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
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   ❑ yes ❑ no
5. How long did it take you to read this lesson and complete the quiz? _____
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7. Myaleft is FDA-approved to treat complications of leptin deficiency in patients with:
   a. general obesity.
   b. Sjögren-Larsson Syndrome.
   c. acquired generalized lipodystrophy.
   d. nonalcoholic steatohepatitis.

8. All of the following are warnings or precautions associated with Myalept therapy EXCEPT:
   a. thrombocytopenia.
   b. hypoglycemia.
   c. hypersensitivity.
   d. autoimmunity.

9. Myalept is administered once daily:
   a. orally.
   b. subcutaneously.
   c. intravenously.
   d. sublingually.

10. Impavido is indicated to treat all of the following forms of leishmaniasis EXCEPT:
   a. cardiac leishmaniasis.
   b. mucosal leishmaniasis.
   c. visceral leishmaniasis.
   d. cutaneous leishmaniasis.

11. Duration of treatment for Impavido is:
   a. 7 days.
   b. 14 days.
   c. 21 days.
   d. 28 days.

12. The mechanism of action of miltefosine is likely to involve interaction with which of the following substances?
   a. Protein
   b. Lipids
   c. Carbohydrates
   d. Amyloid

13. All of the following are patient counseling advice for Myalept EXCEPT:
   a. read the *Medication Guide* with each prescription.
   b. breastfeeding is not recommended.
   c. administer a missed dose as soon as possible.
   d. store the vials in the freezer until use.

14. The labeling for the following drug includes a box warning for fetal harm.
   a. Otezla
   b. Neuraceq
   c. Myalept
   d. Impavido

15. Pharmacies may dispense the following drug only after receiving a REMS Prescription Authorization Form.
   a. Impavido
   b. Myalept
   c. Neuraceq
   d. Otezla

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