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PharmNOTES

Summary about new FDA-approved products,
new indications, first-time generics,
and WHAT IS IN THE PIPELINE.
From: MARCH 2019

Date: 4/9/2019

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Pharmacy Benefit Management
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NEWS……

Drug Issue	Date	News/Event
FDA takes action against marketer of unapproved products claiming to treat addiction, chronic pain and other serious conditions	03/19/2019	The FDA posted a warning letter to Nutra Pharma Corp. for illegally marketing unapproved products labeled as homeopathic with claims about their ability to treat addiction and chronic pain, including pain associated with cancer, diabetes, shingles, fibromyalgia and other serious conditions. The FDA issued a warning letter to Nutra Pharma for their products: “Nyloxin Oral Spray,” “Nyloxin Topical Gel,” “Nyloxin Topical Roll-On,” “Nyloxin Topical Roll-On ES,” “Nyloxin Professional Size Pump Topical Gel” and “Regular Strength Sample Pack.”. These products also may confuse consumers because its name is similar to FDA-approved drugs. The warning letter is available at: https://www.fda.gov/ICECI/EnforcementActions/WarningLetters/ucm633800.htm?utm_campaign=FDA%20takes%20action%20against%20marketer%20of%20unapproved%20products%20claiming%20to%20tre&utm_medium=email&utm_source=Eloqua
UPDATE on angiotensin II receptor blocker (ARB) recalls:	03/20/2019	To ensure patient access to losartan, FDA will not object to certain manufacturers temporarily distributing losartan containing N-Nitroso-N-methyl-4-aminobutyric acid (NMBA) above the interim acceptable intake limit of 0.96 parts per million (ppm) and below 9.82 ppm until the impurity can be eliminated. For more details regarding this issue, please visit: https://www.fda.gov/Drugs/DrugSafety/ucm613916.htm?utm_campaign=Update%20on%20ARB%20recall%3A%20FDA%20not%20objecting%20to%20losartan%20with%20NMBA%20below%209.82%20ppm&utm_medium=email&utm_source=Eloqua
Venclext™a (venetoclax): Risks Associated with the Investigational Use of Venclexta in Multiple Myeloma	03/22/2019	The FDA is alerting health care professionals, oncology clinical investigators and patients about the risks associated with the investigational use of Venclexta™ for the treatment of patients with multiple myeloma based on data from a clinical trial. Of note, Venclexta™ is not approved for the treatment of multiple myeloma. The FDA reviewed data from the BELLINI clinical trial evaluating the use of Venclexta™ combined with bortezomib, a proteasome inhibitor, and dexamethasone in patients with multiple myeloma. The interim trial results demonstrated an increased risk of death for patients receiving Venclexta™ as compared to the control group. On March 6, 2019, the FDA required no new patients be enrolled on the Bellini trial. Patients who are receiving clinical benefit can continue treatment in the trial after they reconsent. This statement does not apply to patients taking Venclexta™ for an approved indication**. Patients taking Venclexta™ for an approved indication should continue to take their medication as directed by their health care professional**. Venclexta™ is safe and effective for its approved uses.

New FDA Approved Products

Drug/ Manufacturer	Therapeutic Class	Indications	Date	Comments

Spravato™ (esketamine) Nasal Spray / Janssen Pharmaceuticals, Inc.	Central nervous system agent; Antidepressant; N-methyl D-aspartate (NMDA) receptor antagonist
	
	Note: CIII
		In conjunction with an oral antidepressant, for use in adults with treatment-resistant depression in adults
		
		Limitations of use
		Not approved as an anesthetic agent. The safety and effectiveness as an anesthetic agent have not been established.
		
		Black box warning
		Sedation; dissociation; abuse and misuse; and suicidal thoughts and behaviors.
			03/05/2019	**DOSAGE AND ADMINISTRATION**
				Induction phase
				• Weeks 1 to 4: Administer twice per week as follows:
				  • Day 1 starting dose: 56 mg
				  • Subsequent doses: 56 mg or 84 mg
				
				Maintenance phase
				• Weeks 5 to 8: Administer 56 mg or 84 mg once weekly
				• Weeks 9 and after: Administer 56 mg or 84 mg every 2 weeks or once weekly*
				
				*Dosing frequency should be individualized to the least frequent dosing to maintain remission/response.
				
				Administer intranasally under the supervision of a healthcare provider.
				
				Assess blood pressure prior to and after administration.
				
				Dosage adjustments should be made based on efficacy and tolerability.
				
				Evidence of therapeutic benefit should be evaluated at the end of the induction phase to determine need for continued treatment.
				
				DOSAGE FORMS AND STRENGTHS
				Nasal Spray: 28 mg of esketamine per device. Each nasal spray device delivers two sprays containing a total of 28 mg of esketamine.

New FDA Approved Products

Drug/ Manufacturer	Therapeutic Class	Indications	Date	Comments
Spravato™ (esketamine) Nasal Spray / Janssen Pharmaceuticals, Inc. (continuation)	Central nervous system agent; Antidepressant; N-methyl D-aspartate (NMDA) receptor antagonist Note: CIII	In conjunction with an oral antidepressant, for use in adults with treatment-resistant depression in adults **Limitations of use** Not approved as an anesthetic agent. The safety and effectiveness as an anesthetic agent have not been established. **Black box warning** Sedation; dissociation; abuse and misuse; and suicidal thoughts and behaviors.	03/05/2019	**CONTRAINDICATIONS** • Aneurysmal vascular disease (including thoracic and abdominal aorta, intracranial and peripheral arterial vessels) or arteriovenous malformation. • Intracerebral hemorrhage. • Hypersensitivity to esketamine, ketamine, or any of the excipients. **WARNINGS AND PRECAUTIONS** • **Increases in blood pressure:** Patients with cardiovascular and cerebrovascular conditions and risk factors may be at an increased risk of associated adverse effects. • **Cognitive impairment:** Spravato™ may impair attention, judgment, thinking, reaction speed and motor skills. • **Impaired ability to drive and operate machinery:** Do not drive or operate machinery until the next day after a restful sleep. • **Embryo-fetal toxicity:** May cause fetal harm. Consider pregnancy planning and prevention in females of reproductive potential. **ADVERSE REACTIONS** Most common adverse reactions: dissociation, dizziness, nausea, sedation, vertigo, hypoesthesia, anxiety, lethargy, blood pressure increased, vomiting, and feeling drunk. **DRUG INTERACTIONS** • **Central nervous system (CNS) depressants:** Concomitant use with CNS depressants (e.g. benzodiazepines, opioids, alcohol) may increase sedation. Closely monitor for sedation with concomitant use.

New FDA Approved Products

Drug/ Manufacturer	Therapeutic Class	Indications	Date	Comments
Spravato™ (esketamine) Nasal Spray / Janssen Pharmaceuticals, Inc. (continuation)	Central nervous system agent; Antidepressant; N-methyl D-aspartate (NMDA) receptor antagonist Note: CIII	In conjunction with an oral antidepressant, for use in adults with treatment-resistant depression in adults **Limitations of use** Not approved as an anesthetic agent. The safety and effectiveness as an anesthetic agent have not been established. **Black box warning** Sedation; dissociation; abuse and misuse; and suicidal thoughts and behaviors.	03/05/2019	**DRUG INTERACTIONS** (continuation) • **Psychostimulants:** Concomitant use with psychostimulants (e.g. amphetamines, methylphenidate, modafanil, armodafinil) may increase blood pressure. Closely monitor blood pressure with concomitant use. • **Monoamine Oxidase Inhibitors (MAOIs):** Concomitant use with MAOIs may increase blood pressure. Closely monitor blood pressure with concomitant use. **USE IN SPECIFIC POPULATIONS** • **Pregnancy:** Not recommended during pregnancy. • **Lactation:** Breastfeeding not recommended. • **Females and males of reproductive potential:** Consider pregnancy planning and prevention for females of reproductive potential during treatment. • **Pediatric use:** Safety and effectiveness in pediatric patients have not been established. • **Geriatric use:** No overall differences in the safety profile were observed between patients 65 years of age and older and patients younger than 65 years of age. • **Hepatic impairment:** The mean esketamine AUC and t1/2 values were higher in patients with moderate hepatic impairment compared to those with normal hepatic function. Patients with moderate hepatic impairment may need to be monitored for adverse reactions for a longer period of time. Spravato™ has not been studied in patients with severe hepatic impairment (Child-Pugh class C). Use in this population is not recommended.

New FDA Approved Products

Drug/ Manufacturer	Therapeutic Class	Indications	Date	Comments
Trazimera™ (trastuzumab-qyyp) for Injection, for intravenous use / Pfizer Inc.	Antineoplastic agent; HER2/neu receptor antagonist Note: Biosimilar to Herceptin™	Treatment of HER2-overexpressing breast cancer, and the treatment of HER2-overexpressing metastatic gastric or gastroesophageal junction adenocarcinoma **Black box warning** Cardiomyopathy, infusion reactions, embryo-fetal toxicity, and pulmonary toxicity	03/11/2019	**DOSAGE AND ADMINISTRATION** <u>Adjuvant Treatment of HER2-Overexpressing Breast Cancer</u> Administer at either: • Initial dose of 4 mg/kg over 90 minute IV infusion, then 2 mg/kg over 30 minute IV infusion weekly for 12 weeks (with paclitaxel or docetaxel) or 18 weeks (with docetaxel and carboplatin). One week after the last weekly dose of Trazimera™, administer 6 mg/kg as an IV infusion over 30 to 90 minutes every three weeks to complete a total of 52 weeks of therapy, or • Initial dose of 8 mg/kg over 90 minutes IV infusion, then 6 mg/kg over 30 to 90 minutes IV infusion every three weeks for 52 weeks. <u>Metastatic HER2-Overexpressing Breast Cancer</u> • Initial dose of 4 mg/kg as a 90 minute IV infusion followed by subsequent weekly doses of 2 mg/kg as 30 minute IV infusions. <u>Metastatic HER2-Overexpressing Gastric Cancer</u> • Initial dose of 8 mg/kg over 90 minutes IV infusion, followed by 6 mg/kg over 30 to 90 minutes IV infusion every 3 weeks. Select patients for therapy based on an FDA-approved companion diagnostic for a trastuzumab product. **DOSAGE FORMS AND STRENGTHS** For Injection: 420 mg lyophilized powder in a multiple-dose vial for reconstitution **CONTRAINDICATIONS** None.

New FDA Approved Products

Drug/ Manufacturer	Therapeutic Class	Indications	Date	Comments
Trazimera™ (trastuzumab-qyyp) for Injection, for intravenous use / Pfizer Inc. (continuation)	Antineoplastic agent; HER2/neu receptor antagonist Note: Biosimilar to Herceptin™	Treatment of HER2-overexpressing breast cancer, and the treatment of HER2-overexpressing metastatic gastric or gastroesophageal junction adenocarcinoma **Black box warning** Cardiomyopathy, infusion reactions, embryo-fetal toxicity, and pulmonary toxicity	03/11/2019	**WARNINGS AND PRECAUTIONS** • Exacerbation of Chemotherapy-Induced Neutropenia. **ADVERSE REACTIONS** Most common adverse reactions vary per patient diagnosis and may include: headache, diarrhea, nausea, fever, chills, infection, congestive heart failure, insomnia, cough, rash, neutropenia, and/or other adverse reactions. **DRUG INTERACTIONS** • **Anthracycline:** Patients who receive anthracycline after stopping trastuzumab products may be at increased risk of cardiac dysfunction because of trastuzumab's long washout period based on population PK analysis. If possible, physicians should avoid anthracycline-based therapy for up to 7 months after stopping trastuzumab products. If anthracyclines are used, the patient's cardiac function should be monitored carefully. **USE IN SPECIFIC POPULATIONS** • **Pregnancy:** Can cause fetal harm. • **Females and males of reproductive potential:** Verify the pregnancy status of females prior to initiation. Advise females of reproductive potential to use effective contraception during treatment and for 7 months following the last dose. • **Pediatric use:** Safety and effectiveness of trastuzumab products in pediatric patients have not been established.

New FDA Approved Products

Drug/ Manufacturer	Therapeutic Class	Indications	Date	Comments
Zulresso™ (brexanolone) Injection, for intravenous use / Sage Therapeutics	Central nervous system agent; Antidepressant; Gamma-aminobutyric acid A (GABA) receptor positive allosteric modulator Note: Controlled substance schedule pending	Treatment of postpartum depression (PPD) in adults **Black box warning** Excessive sedation and sudden loss of consciousness	03/19/2019	**DOSAGE AND ADMINISTRATION** Zulresso™ must be administered as a continuous intravenous infusion over 60 hours (2.5 days) as follows: • 0 to 4 hours: Initiate with a dosage of 30 mcg/kg/hour • 4 to 24 hours: Increase dosage to 60 mcg/kg/hour • 24 to 52 hours: Increase dosage to 90 mcg/kg/hour (alternatively consider a dosage of 60 mcg/kg/hour for those who do not tolerate 90 mcg/kg/hour) • 52 to 56 hours: Decrease dosage to 60 mcg/kg/hour • 56 to 60 hours: Decrease dosage to 30 mcg/kg/hour A healthcare provider must be available on site to continuously monitor the patient, and intervene as necessary, for the duration of the infusion. **DOSAGE FORMS AND STRENGTHS** Injection: 100 mg/20 mL (5 mg/mL) single-dose vial. **CONTRAINDICATIONS** None. **WARNINGS AND PRECAUTIONS** • **Suicidal thoughts and behaviors:** Consider changing the therapeutic regimen, including discontinuing, in patients whose PPD becomes worse or who experience emergent suicidal thoughts and behaviors. **ADVERSE REACTIONS** Most common adverse reactions: sedation/somnolence, dry mouth, loss of consciousness, and flushing/hot flush.

New FDA Approved Products

Drug/ Manufacturer	Therapeutic Class	Indications	Date	Comments
Zulresso™ (brexanolone) Injection, for intravenous use / Sage Therapeutics (continuation)	Central nervous system agent; Antidepressant; Gamma-aminobutyric acid A (GABA) receptor positive allosteric modulator Note: Controlled substance schedule pending	Treatment of postpartum depression (PPD) in adults **Black box warning** Excessive sedation and sudden loss of consciousness	03/19/2019	**DRUG INTERACTIONS** • **CNS depressants:** Concomitant use with CNS depressants (e.g. opioids, benzodiazepines) may increase the likelihood or severity of adverse reactions related to sedation. • **Antidepressants:** In placebo-controlled studies, a higher percentage of Zulresso™-treated patients who used concomitant antidepressants reported sedation-related events. **USE IN SPECIFIC POPULATIONS** • **Pregnancy:** May cause fetal harm. • **Pediatric use:** Safety and effectiveness in pediatric patients have not been established. • **Hepatic impairment:** Dosage adjustment in patients with hepatic impairment is not necessary. Modest increases in exposure to unbound brexanolone and modest decreases in exposure to total brexanolone were observed in patients with moderate to severe hepatic impairment with no associated change in tolerability. • **Renal impairment:** No dosage adjustment is recommended in patients with mild (eGFR 60 to 89 mL/minute/1.73 m2), moderate (eGFR 30 to 59 mL/minute/1.73 m2) or severe (eGFR 15 to 29 mL/minute/1.73 m2) renal impairment. Avoid use of Zulresso™ in patients with end stage renal disease (ESRD) with eGFR of < 15 mL/minute/1.73 m2 because of the potential accumulation of the solubilizing agent, betadex sulfobutyl ether sodium.

New FDA Approved Products

Drug/ Manufacturer	Therapeutic Class	Indications	Date	Comments
Sunosi™ (solriamfetol) Tablets, for oral use / Jazz Pharmaceuticals plc	Central nervous system agent; Central nervous system stimulant; Selective dopamine and norepinephrine reuptake inhibitor (DNRI) Note: Controlled substance schedule pending	Treatment of excessive sleepiness in adult patients with narcolepsy or obstructive sleep apnea (OSA) **Limitations of use** Not indicated to treat the underlying airway obstruction in OSA. Ensure that the underlying airway obstruction is treated (e.g. with continuous positive airway pressure (CPAP)) for at least one month prior to initiating Sunosi™ for excessive daytime sleepiness. Modalities to treat the underlying airway obstruction should be continued during treatment with Sunosi™. Sunosi™ is not a substitute for these modalities.	03/20/2019	**DOSAGE AND ADMINISTRATION** Sunosi™ is to be administered once daily upon awakening. • Starting dose for patients with narcolepsy: 75 mg once daily. • Starting dose for patients with OSA: 37.5 mg once daily. Dose may be increased at intervals of at least 3 days. The maximum dose is 150 mg once daily. Avoid administration within 9 hours of planned bedtime because of the potential to interfere with sleep. For patients with renal impairment: • Moderate impairment: Starting dose is 37.5 mg once daily. • May increase to 75 mg once daily after at least 7 days. • Severe impairment: Starting dose and maximum dose is 37.5 mg once daily. • End stage renal disease (ESRD): Not recommended. **DOSAGE FORMS AND STRENGTHS** Tablets: 75 mg (functionally scored) and 150 mg. **CONTRAINDICATIONS** • Concurrent treatment with a monoamine oxidase inhibitor (MAOI) or use of an MAOI within the preceding 14 days. **WARNINGS AND PRECAUTIONS** • **Blood pressure and heart rate increases:** Measure heart rate and blood pressure prior to initiating and periodically throughout treatment. Control hypertension before and during therapy. Avoid use in patients with unstable cardiovascular disease, serious heart arrhythmias, or other serious heart problems.

New FDA Approved Products

Drug/ Manufacturer	Therapeutic Class	Indications	Date	Comments
Sunosi™ (solriamfetol) Tablets, for oral use / Jazz Pharmaceuticals plc (continuation)	Central nervous system agent; Central nervous system stimulant; Selective dopamine and norepinephrine reuptake inhibitor (DNRI) Note: Controlled substance schedule pending	Treatment of excessive sleepiness in adult patients with narcolepsy or obstructive sleep apnea (OSA) **Limitations of use** Not indicated to treat the underlying airway obstruction in OSA. Ensure that the underlying airway obstruction is treated (e.g. with continuous positive airway pressure (CPAP)) for at least one month prior to initiating Sunosi™ for excessive daytime sleepiness. Modalities to treat the underlying airway obstruction should be continued during treatment with Sunosi™. Sunosi™ is not a substitute for these modalities.	03/20/2019	**WARNINGS AND PRECAUTIONS** (continuation) • **Psychiatric symptoms:** Use caution in treating patients with a history of psychosis or bipolar disorders. Consider dose reduction or discontinuation of SUNOSI if psychiatric symptoms develop. **ADVERSE REACTIONS** Most common adverse reactions: headache, nausea, decreased appetite, insomnia, and anxiety. **DRUG INTERACTIONS** • **MAOIs:** Concomitant use of MAO inhibitors and noradrenergic drugs may increase the risk of a hypertensive reaction. Potential outcomes include death, stroke, myocardial infarction, aortic dissection, ophthalmological complications, eclampsia, pulmonary edema, and renal failure . • **Drugs that increase blood pressure and/or heart rate:** Concomitant use has not been evaluated, and such combinations should be used with caution. • **Dopaminergic drugs:** Dopaminergic drugs that increase levels of dopamine or that bind directly to dopamine receptors might result in pharmacodynamic interactions with Sunosi™. Interactions with dopaminergic drugs have not been evaluated. Use caution when concomitantly administering dopaminergic drugs. **USE IN SPECIFIC POPULATIONS** • **Pregnancy:** There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to Sunosi™ during pregnancy. Healthcare providers are encouraged to register pregnant patients, or pregnant women may enroll themselves.

New FDA Approved Products

Drug/ Manufacturer	Therapeutic Class	Indications	Date	Comments
Sunosi™ (solriamfetol) Tablets, for oral use / Jazz Pharmaceuticals plc (continuation)	Central nervous system agent; Central nervous system stimulant; Selective dopamine and norepinephrine reuptake inhibitor (DNRI) Note: Controlled substance schedule pending	Treatment of excessive sleepiness in adult patients with narcolepsy or obstructive sleep apnea (OSA) **Limitations of use** Not indicated to treat the underlying airway obstruction in OSA. Ensure that the underlying airway obstruction is treated (e.g. with continuous positive airway pressure (CPAP)) for at least one month prior to initiating Sunosi™ for excessive daytime sleepiness. Modalities to treat the underlying airway obstruction should be continued during treatment with Sunosi™. Sunosi™ is not a substitute for these modalities.	03/20/2019	**USE IN SPECIFIC POPULATIONS** (continuation) • **Pediatric use:** Safety and effectiveness in pediatric patients have not been established. • **Geriatric use:** No clinically meaningful differences in safety or effectiveness were observed between elderly and younger patients. • **Renal impairment:** Dosage adjustment is not required for patients with mild renal impairment (eGFR 60-89 mL/min/1.73 m2). Dosage adjustment is recommended for patients with moderate to severe renal impairment (eGFR 15-59 mL/min/1.73 m2). Sunosi™ is not recommended for patients with end stage renal disease (eGFR

New FDA Approved Products

Drug/ Manufacturer	Therapeutic Class	Indications	Date	Comments
Mayzent™ (siponimod) Tablets, for oral use / Novartis Pharmaceuticals Corporation	Immunological agent; Sphingosine-1-phosphate receptor modulator	Treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.	03/26/2019	**DOSAGE AND ADMINISTRATION** Specific assessment is required prior initiation of treatment. See Full Prescribing Information for details. Titration is required for treatment initiation and monitoring is recommended. See Full Prescribing Information for details. The recommended maintenance dosage is 2 mg. The recommended maintenance dosage in patients with a CYP2C9 *1/*3 or *2/*3 genotype is 1 mg. **DOSAGE FORMS AND STRENGTHS** Tablets: 0.25 mg and 2 mg. **CONTRAINDICATIONS** • Patients with a CYP2C9*3/*3 genotype . • In the last 6 months, experienced myocardial infarction, unstable angina, stroke, TIA, decompensated heart failure requiring hospitalization, or Class III/IV heart failure. • Presence of Mobitz type II second-degree, third-degree AV block, or sick sinus syndrome, unless patient has a functioning pacemaker. **WARNINGS AND PRECAUTIONS** • **Infections:** Mayzent™ may increase the risk. Obtain a complete blood count (CBC) before initiating treatment. Monitor for infection during treatment. Do not start in patients with active infection. • **Macular edema:** An ophthalmic evaluation is recommended before starting treatment and if there is any change in vision while taking Mayzent™. Diabetes mellitus and uveitis increase the risk.

New FDA Approved Products

Drug/ Manufacturer	Therapeutic Class	Indications	Date	Comments
Mayzent™ (siponimod) Tablets, for oral use / Novartis Pharmaceuticals Corporation (continuation)	Immunological agent; Sphingosine-1-phosphate receptor modulator	Treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.	03/26/2019	**WARNINGS AND PRECAUTIONS** (continuation) • **Bradyarrhythmia and atrioventricular conduction delays:** Mayzent™ may result in a transient decrease in heart rate; titration is required for treatment initiation. Consider resting heart rate with concomitant betablocker use; obtain cardiologist consultation before concomitant use with other drugs that decrease heart rate. • **Respiratory effects:** May cause a decline in pulmonary function. Assess pulmonary function (e.g. spirometry) if clinically indicated. • **Liver injury:** Obtain liver enzyme results before initiation. Closely monitor patients with severe hepatic impairment. Discontinue if significant liver injury occurs. • **Increased blood pressure (BP):** Monitor BP during treatment. • **Fetal risk:** Women of childbearing potential should use effective contraception during and for 10 days after stopping Mayzent™. **ADVERSE REACTIONS** Most common adverse reactions: headache, hypertension, and transaminase increases. **DRUG INTERACTIONS** • **Vaccines:** Avoid live attenuated vaccines during and for up to 4 weeks after treatment with Mayzent™. • **CYP2C9 and CYP3A4 inhibitors:** Increase in siponimod exposure; concomitant use of Mayzent™ with moderate CYP2C9 and moderate or strong CYP3A4 inhibitors is not recommended.

New FDA Approved Products

Drug/ Manufacturer	Therapeutic Class	Indications	Date	Comments
Mayzent™ (siponimod) Tablets, for oral use / Novartis Pharmaceuticals Corporation (continuation)	Immunological agent; Sphingosine-1-phosphate receptor modulator	Treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.	03/26/2019	**DRUG INTERACTIONS** (continuation) • **CYP2C9 and CYP3A4 inducers:** Decrease in siponimod exposure; concomitant use of Mayzent™ with moderate CYP2C9 and strong CYP3A4 inducers is not recommended. **USE IN SPECIFIC POPULATIONS** • **Pregnancy:** Based on animal data and its mechanism of action, Mayzent™ can cause fetal harm. • **Females and males of reproductive potential:** Before initiation of treatment, women of childbearing potential should be counselled on the potential for a serious risk to the fetus and the need for effective contraception during treatment. Since it takes approximately 10 days to eliminate the compound from the body after stopping treatment, the potential risk to the fetus may persist and women should use effective contraception during this period. • **Pediatric use:** Safety and effectiveness in pediatric patients have not been established. • **Geriatric use:** Clinical studies did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. • **CYP2C9 genotype:** Before initiation of treatment, test patients to determine CYP2C9 genotype. Mayzent™ is contraindicated in patients homozygous for CYP2C9*3 (e.g. CYP2C9*3/*3 genotype). Mayzent™ dosage adjustment is recommended in patients with CYP2C9 *1/*3 or *2/*3 genotype because of an increase in exposure to siponimod.

New FDA Approved Products

Drug/ Manufacturer	Therapeutic Class	Indications	Date	Comments
Mavenclad™ (cladribine) Tablets, for oral use / EMD Serono, Inc.	Purine antimetabolite	Treatment of relapsing forms of multiple sclerosis (MS), to include relapsing-remitting disease and active secondary progressive disease, in adults. Note: Because of its safety profile, use of Mavenclad™ is generally recommended for patients who have had an inadequate response to, or are unable to tolerate, an alternate drug indicated for the treatment of MS. **Limitations of use** Not recommended for use in patients with clinically isolated syndrome (CIS) because of its safety profile.	03/29/2019	**DOSAGE AND ADMINISTRATION** Specific assessment is required prior initiation of treatment. See Full Prescribing Information for details. **DOSAGE FORMS AND STRENGTHS** Tablets: 10 mg. **CONTRAINDICATIONS** • Patients with current malignancy. • Pregnant women, and women and men of reproductive potential who do not plan to use effective contraception during treatment and for 6 months after the last dose in each treatment course. • HIV infection. • Active chronic infections (e.g. hepatitis or tuberculosis). • History of hypersensitivity to cladribine. • Women intending to breastfeed on a MMavenclad™ treatment day and for 10 days after the last dose. **WARNINGS AND PRECAUTIONS** • **Lymphopenia:** Monitor lymphocyte counts before, during and after treatment. • **Infections:** Screen patients for latent infections; consider delaying treatment until infection is fully controlled. Vaccinate patients antibodynegative to varicella zoster virus prior to treatment. Administer anti-herpes prophylaxis in patients with lymphocyte counts less than 200 cells per microliter. Monitor for infections. • **Hematologic toxicity:** Monitor complete blood count before, during and after treatment.

New FDA Approved Products

Drug/ Manufacturer	Therapeutic Class	Indications	Date	Comments
Mavenclad™ (cladribine) Tablets, for oral use / EMD Serono, Inc. (continuation)	Purine antimetabolite	Treatment of relapsing forms of multiple sclerosis (MS), to include relapsing-remitting disease and active secondary progressive disease, in adults. Note: Because of its safety profile, use of Mavenclad™ is generally recommended for patients who have had an inadequate response to, or are unable to tolerate, an alternate drug indicated for the treatment of MS. **Limitations of use** Not recommended for use in patients with clinically isolated syndrome (CIS) because of its safety profile.	03/29/2019	**WARNINGS AND PRECAUTIONS** (continuation) • **Graft-versus-host-disease with blood transfusion:** Irradiation of cellular blood components is recommended. • **Liver injury:** Obtain tests prior to treatment. Discontinue if clinically significant injury is suspected. **ADVERSE REACTIONS** Most common adverse reactions: upper respiratory tract infection, headache, and lymphopenia. **DRUG INTERACTIONS** • **Immunosuppressive drugs:** Consider overlapping effects on immune system, when used sequentially. Concomitant use not recommended. • **Hematotoxic drugs:** Monitor patients for additive effects on the hematological profile. • **Antiviral and antiretroviral drugs:** Avoid concomitant use. • **BCRP or ENT/CNT inhibitors:** May alter bioavailability of cladribine. Avoid concomitant use. **USE IN SPECIFIC POPULATIONS** • **Pregnancy:** Contraindicated in pregnant women. • **Lactation:** Contraindicated in breastfeeding women because of the potential for serious adverse reactions in breastfed infants. Advise women not to breastfeed during treatment and for 10 days after the last dose.

New FDA Approved Products

Drug/ Manufacturer	Therapeutic Class	Indications	Date	Comments
Mavenclad™ (cladribine) Tablets, for oral use / EMD Serono, Inc. (continuation)	Purine antimetabolite	Treatment of relapsing forms of multiple sclerosis (MS), to include relapsing-remitting disease and active secondary progressive disease, in adults. Note: Because of its safety profile, use of Mavenclad™ is generally recommended for patients who have had an inadequate response to, or are unable to tolerate, an alternate drug indicated for the treatment of MS. **Limitations of use** Not recommended for use in patients with clinically isolated syndrome (CIS) because of its safety profile.	03/29/2019	**USE IN SPECIFIC POPULATIONS** (continuation) • **Females and males of reproductive potential:** Contraindicated in females and males of reproductive potential who do not plan to use effective contraception. Pregnancy should be excluded before the initiation of each treatment course. Females of reproductive potential should prevent pregnancy by use of effective contraception during Matreatment and for at least 6 months after the last dose in each treatment course. Women using systemically acting hormonal contraceptives should add a barrier method during treatment and for at least 4 weeks after the last dose in each treatment course. Male patients of reproductive potential should take precautions to prevent pregnancy of their partner during treatment and for at least 6 months after the last dose in each treatment course. • **Pediatric use:** Safety and effectiveness in pediatric patients have not been established. • **Geriatric use:** Clinical studies did not include sufficient numbers of patients aged 65 and over to determine whether they respond differently from younger patients. • **Renal impairment:** The concentration of cladribine is predicted to increase in patients with renal impairment. No dosage adjustment is recommended in patients with mild renal impairment (CrCl 60 to 89 mL per minute). Mavenclad™ is not recommended in patients with moderate to severe renal impairment (CrCl below 60 mL per minute). • **Hepatic impairment:** The effect of hepatic impairment on the pharmacokinetics of cladribine is unknown. No dosage adjustment is recommended in patients with mild hepatic impairment. Mavenclad™ is not recommended in patients with moderate to severe hepatic impairment.

New FDA Approved Indications

Drug/ Manufacturer	Therapeutic class	Indications	Date	Comments
Tecentriq™ (atezolizumab) Injection / Genentech, Inc.	Antineoplastic agent; Programmed death-ligand 1 (PD-L1) blocking antibody	**Previous indication(s):** Treatment of advanced urothelial carcinoma; the treatment of metastatic non-small cell lung cancer (NSCLC); extensive-stage small cell lung cancer **New indication:** For use in combination with Abraxane for the treatment of metastatic triple-negative breast cancer	03/08/2019	The FDA has granted accelerated approval to Tecentriq™ plus chemotherapy (Abraxane [paclitaxel protein-bound particles for injectable suspension (albumin-bound); nab-paclitaxel]) for the treatment of adults with unresectable locally advanced or metastatic triple-negative breast cancer (TNBC) in people whose tumors express PD-L1, as determined by an FDA-approved test. The accelerated approval was based on progression-free survival (PFS). Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s). Data from a Phase III study demonstrated that Tecentriq™ plus nab-paclitaxel significantly reduced the risk of PFS) by 40% compared with nab- paclitaxel alone (median PFS=7.4 vs. 4.8 months; HR=0.60, 95% CI: 0.48-0.77, p<0.0001) in PD-L1-positive patients with unresectable locally advanced or metastatic TNBC who had not received prior chemotherapy for metastatic disease. Overall survival (OS) results were immature with 43% of events in all randomized patients (intent-to-treat; ITT), and further data will be shared with the FDA and presented at an upcoming medical meeting.
Dupixent™ (dupilumab) Injection / Sanofi and Regeneron Pharmaceuticals, Inc.	Antiasthma and dermatological agent; Monoclonal antibody; Interleukin-4 receptor alpha antagonist	**Previous indication(s):** Treatment of moderate-to-severe eczema (atopic dermatitis) in adults; Add-on maintenance treatment for moderate-to-severe asthma **Patient population altered:** To include the treatment of adolescent patients 12 to 17 years of age with moderate-to-severe atopic dermatitis	03/11/2019	Currently, Dupixent™ is the only IL-4/IL-13 inhibitor therapy on the market, both interleukins are thought to play a key underlying role in atopic dermatitis. Phase 3 trials demonstrated improved severity of disease, decreased itching, and resulted in clearer skin. Trials for atopic dermatitis treatment in children ages 6-11 are currently underway with a target completion date by the end of the 2019.

New FDA Approved Indications

Drug/ Manufacturer	Therapeutic class	Indications	Date	Comments
Avycaz™ (avibactam and ceftazidime) Injection / Actavis Pharma, Inc.	Anti-infective agent; A next generation, non-β lactam β-lactamase inhibitor and third-generation, antipseudomonal cephalosporin antibiotic combination	**Previous indication(s):** Treatment of complicated intra-abdominal infections (cIAI), complicated urinary tract infections (cUTI), hospital-acquired bacterial pneumonia, and ventilator-associated bacterial pneumonia **Patient population altered:** To include pediatric patients 3 months and older for the treatment of cIAI in combination with metronidazole and cUTI	03/14/2019	This is the first FDA approval of a pediatric indication for cUTI and cIAI in more than a decade.
Tecentriq™ (atezolizumab) Injection / Genentech, Inc.	Antineoplastic agent; Programmed death-ligand 1 (PD-L1) blocking antibody	**Previous indication(s):** Treatment of advanced urothelial carcinoma; the treatment of metastatic non-small cell lung cancer (NSCLC); extensive-stage small cell lung cancer; in combination with Abraxane for the treatment of metastatic triple-negative breast cancer **New indication:** For the initial (first-line) treatment of adults with extensive-stage small cell lung cancer (ES-SCLC)	03/18/2019	This approval is based on results from a Phase III study that showed that Tecentriq™ in combination with chemotherapy helped people live significantly longer compared to chemotherapy alone (median overall survival [OS] = 12.3 versus 10.3 months; hazard ratio [HR] = 0.70, 95% CI: 0.54-0.91; p=0.0069) in the intention-to-treat (ITT) population. The Tecentriq™-based combination also significantly reduced the risk of Progression-free survival (PFS) compared to chemotherapy alone (PFS=5.2 versus 4.3 months; HR=0.77; 95% CI: 0.62-0.96; p=0.017). Safety for the Tecentriq™ and chemotherapy combination appeared consistent with the known safety profile of Tecentriq™.

New FDA Approved Indications

Drug/ Manufacturer	Therapeutic class	Indications	Date	Comments
Cimzia™ (certolizumab pegol) Injection / UCB, Inc.	Immunological agent; Anti-TNF	**Previous indication(s):** Treatment of Crohn's disease, rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, plaque psoriasis **New indication:** Treatment for non-radiographic axial spondyloarthritis (nr-axSpA)	03/28/2019	This approval makes Cimzia™ the first and only FDA-approved treatment for nr-axSpA.
Zelnorm (tegaserod) Tablets / US WorldMeds, LLC	Serotonin-4 (5-HT4) receptor agonist	**Indication:** Treatment of adult women less than 65 years of age with irritable bowel syndrome with constipation (IBS-C)	03/29/2019	Zelnorm™ was originally approved by the FDA in 2002 for the treatment of IBS-C in women. It was voluntarily withdrawn from the market in March 2007 because a safety analysis found a higher chance of heart attack, stroke, and unstable angina in patients treated with Zelnorm™ compared with treatment with a placebo. In July 2007, the FDA announced that it was permitting the restricted use of Zelnorm™ under a treatment investigational new drug (IND) protocol, which is a mechanism for providing eligible patients with investigational drugs for the treatment of serious and life-threatening illnesses for which there are no satisfactory alternative treatments. In March 2019, the FDA approved the reintroduction of Zelnorm™ for the treatment for IBS-C in women under 65. Approval came after a complete safety review by the FDA and the Gastrointestinal Drugs Advisory Committee (GIDAC). The review focused on the evaluation of clinical data from 29 placebo-controlled trials and newly-available sources of treatment outcome data. A positive GIDAC vote and FDA review both supported the reintroduction of Zelnorm™ for appropriate IBS-C patients.

New FDA Approved Formulations, Dosage Forms, Combination Products and Other Differences

Drug/ Manufacturer	Therapeutic class	Indications	Date	Comments
Rocklatan™ (netarsudil and latanoprost) Ophthalmic Solution / Aerie Pharmaceuticals, Inc.	Ophthalmologic agent; Antiglaucoma; Combination of the Rho kinase inhibitor netarsudil (Rhopressa™) and the prostaglandin F2α analogue latanoprost (Xalatan™)	To reduce elevated intraocular pressure (IOP) in patients with open-angle glaucoma or ocular hypertension	03/12/2019	Rocklatan™ is a once-daily eye drop that is a fixed-dose combination of latanoprost, a prostaglandin analog (PGA) widely-prescribed, and netarsudil, the active ingredient in Rhopressa™ (netarsudil ophthalmic solution) 0.02%, a first-in-class Rho kinase (ROCK) inhibitor specifically designed to target the trabecular meshwork (the eye's principal drainage pathway) that was approved by the FDA on December 2017.
Jatenzo™ (testosterone undecanoate) Capsules / Clarus Therapeutics, Inc.	Testosterone replacement therapy	Treatment of low testosterone in hypogonadal men	03/27/2019	Jatenzo™ is a new dosage form of testosterone undecanoate: oral capsule. The oral route of administration provides an new alternative to current available treatment options, which up until now where most commonly applied to the skin or injected. Sepcifically, testosterone undecanoate was already available in the market as an injectable solution for intramuscular use, under the brand name Aveed™. Oral testosterone was already available in the market as a buccal patch, under the brand name Striant™. It s of important note that this drug should not be used to treat older men with age-related hypogonadism. Note: CIII

New FDA Approved Formulations, Dosage Forms, Combination Products and Other Differences

	Therapeutic class	Indications	Date	Comments
Maveclad™ (cladribine) / Emd Serono Inc.	Purine antimetabolite	Treatment of relapsing forms of multiple sclerosis (MS), to include relapsing-remitting disease and active secondary progressive disease, in adults. Note: Because of its safety profile, use of Mavenclad™ is generally recommended for patients who have had an inadequate response to, or are unable to tolerate, an alternate drug indicated for the treatment of MS.	03/29/2019	Maveclad™ is a new dosage form of cladribine: oral tablet. Cladribine was already available in the market as an injectable solution for intravenous (IV) use. However, this IV formulation is FDA-approved only for the treatment of Hairy Cell Leukemia. Maveclad™ comes to be the first and only short-course oral treatment for relapsing-remitting and active secondary progressive multiple sclerosis. The efficacy of Mavenclad™ was shown in a clinical trial in 1,326 patients with relapsing forms of MS who had least one relapse in the previous 12 months. Mavenclad™ significantly decreased the number of relapses experienced by these patients compared to placebo. Mavenclad™ also reduced the progression of disability compared to placebo.
Avaclyr™ (acyclovir) Ophthalmic Ointment / Fera Pharmaceuticals	Herpes simplex virus nucleoside analog DNA polymerase inhibitor indicate	Treatment of acute herpetic keratitis (dendritic ulcers) in patients with herpes simplex (HSV-1 and HSV-2) virus	03/29/2019	Avaclyr™ is a new dosage form of acyclovir: ophthalmic ointment. This ophthalmic formulation of acyclovir was granted Orphan Drug exclusivity by the FDA.
Duaklir Pressair™ (aclidinium bromide and formoterol fumarate) Inhalation Powder / Circassia Pharmaceuticals plc	long-acting muscarinic antagonist (LAMA) and long-acting beta2 agonist (LABA) fixed dose combination	Treatment of COPD	03/29/2019	Duaklir Pressair™ is a new fixed-dose combination of the LAMA aclidinium bromide (400 mcg) and LABA formoterol fumarate (12 mcg).

New First Time Generic Drug Approval

Drug/Manufacturer	Therapeutic Class	Date	Comments
Fulvestrant Injection 50mg/mL / Amneal Pharmaceuticals LLC	Antineoplastic agent; Antiestrogen	03/04/2019	Generic for: Faslodex
Bepotastine Besilate Ophthalmic Drops 1.5 % / Apotex Corporation	Ophthalmologic agent; Antihistamine	03/05/2019	Generic for: Bepreve
Pyridostigmine Bromide Syrup 60 mg/5 mL / Novitium Pharma LLC	Cholinergic agent	03/08/2019	Generic for: Mestinon Syrup
Naftifine Hydrochloride Topical Gel 1% / Tolmar Inc.	Dermatological agent; Antifungal	03/20/2019	Generic for: Naftin Gel 1%
Aliskiren Hemifumarate Tablets 150 mg (base) and 300 mg (base) / Anchen Pharmaceuticals, Inc.	Antihypertensive	03/22/2019	Generic for: Tekturna
Ambrisentan Tablets 5 mg and 10 mg / Watson Laboratories, Inc.; Mylan Pharmaceuticals Inc.; Zydus Pharmaceuticals (USA) Inc.; Sun Pharmaceutical Industries, Inc.	Antihypertensive; Endothelin receptor antagonist	03/28/2019	Generic for: Letairis

Source: https://www.drugs.com/generic-approvals.html

PIPELINE…….

Drug/Manufacturer	Date	Indications	Comments	Impact
Rexista (oxycodone hydrochloride) Extended-Release Tablets / Intellipharmaceutics International Inc.	03/04/2019	Treatment for: Pain	Rexista (oxycodone hydrochloride extended release) is an abuse and alcohol-deterrent controlled-release formulation of oxycodone hydrochloride in development for the relief of moderate to severe pain. Intellipharmaceutics announces resubmission of NDA for its Oxycodone ER.	Moderate
Fedratinib / Celgene Corporation	03/05/2019	Treatment for: Myelofibrosis	Fedratinib is a highly selective JAK2 inhibitor in development for the treatment of patients with myelofibrosis, which represent the first potential new treatment option after many years. The FDA granted priority review for fedratinib NDA in myelofibrosis.	High
FMX101 (minocycline) Foam / oamix Pharmaceuticals	03/07/2019	Treatment for: Acne	FMX101 (minocycline) is a topical foam formulation of minocycline in development for the treatment of moderate-to-severe acne vulgaris. Foamix Pharmaceuticals Ltd. announced that the FDA has accepted for review the NDA for FMX101.	Moderate
Ubrogepant / Allergan plc	03/11/2019	Treatment for: Migraine	Ubrogepant is a potent, orally-administered CGRP receptor antagonist in development for the acute treatment of migraine. Allergan announced FDA acceptance of NDA for ubrogepant for the acute treatment of migraine.	High

Source: https://www.drugs.com/new-drug-applications.html

PIPELINE…….

Drug/Manufacturer	Date	Indications	Comments	Impact
Lemborexant / Eisai Co., Ltd.	03/12/2019	Treatment for: Insomnia	Lemborexant is dual orexin receptor antagonist (DORA) in development for the treatment of insomnia. Eisai and Imbrium Therapeutics announced FDA filing acceptance of NDA for lemborexant.	Moderate
Ozanimod / Celgene Corporation	03/25/2019	Treatment for: Multiple Sclerosis, Ulcerative Colitis	Ozanimod is an investigational selective sphingosine 1-phosphate (S1P) 1 and 5 receptor modulator in development for the treatment of patients with relapsing multiple sclerosis, and ulcerative colitis. Celgene submitted an NDA for ozanimod.	Moderate

Source: https://www.drugs.com/new-drug-applications.html

References:

- Drugs.com (www.drugs.com)
- Food and Drug Administration (www.fda.gov)
- IBM Micromedex® (www.micromedexsolutions.com)
- Pharmacist Letter (www.pharmacistletter.com)
- P&T Community (www.ptcommunity.com)