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PharmNOTES

Summary of New FDA-Approved Products,
New Indications, First-Time Generics,
and WHAT'S IN THE PIPELINE
For: **APRIL 2022**

urac ACCREDITED
Pharmacy Benefit Management
Expires 12/01/2022

Date: 05/06/2022

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NEWS

- No drug safety alert published by the FDA in April.

NEW FDA-APPROVED DRUG PRODUCTS

NEW MOLECULAR ENTITIES, NEW ACTIVE INGREDIENTS

DRUG NAME	MANUFACTURER	APPROVAL DATE
VIVJOA™ (OTESECONAZOLE) CAPSULES	MYCOVIA PHARMACEUTICALS INC.	04/26/2022

THERAPEUTIC CLASS
Azole antifungal

FDA-APPROVED INDICATION(S)
To reduce the incidence of recurrent vulvovaginal candidiasis (RVVC) in females with a history of RVVC who are NOT of reproductive potential

DOSAGE AND ADMINISTRATION
There are two recommended dosage regimens.

Vivjoa™-only dosage regimen:
- **On Day 1**: Administer 600mg (as a single dose), then
- **On Day 2**: Administer Vivjoa™ 450mg (as a single dose), then
- **Beginning on Day 14**: Administer Vivjoa™ 150mg once a week for 11 weeks (Weeks 2 through 12).

Fluconazole/Vivjoa™ dosage regimen:
- **On Day 1**, **Day 4 and Day 7**: Administer fluconazole 150mg orally, then
- **On Days 14 through 20**: Administer Vivjoa™ 150mg once daily for 7 days, then
- **Beginning on Day 28**: Administer Vivjoa™ 150mg once a week for 11 weeks (Weeks 4 though 14)

DOSAGE FORMS AND STRENGTHS
Capsules: 150mg of oteseconazole

SAFETY PROFILE

CONTRAINDICATIONS
- Females of reproductive potential
- Pregnant and lactating women
- Hypersensitivity to oteseconazole

WARNINGS AND PRECAUTIONS
- Embryo-fetal toxicity: Based on animal studies, Vivjoa™ may cause fetal harm. The drug exposure window of approximately 690 days (based on 5 times the half-life of oteseconazole) precludes adequate mitigation of the embryo-fetal toxicity risks. Advise patients that Vivjoa™ is contraindicated in females of reproductive potential, and in pregnant and lactating women because of potential risks to a fetus or breastfed infant.

ADVERSE REACTIONS
- The most frequently reported adverse reactions (incidence > 2%) were headache and nausea.

DRUG INTERACTIONS
- Breast Cancer Resistance Proteins (BCRP) Substrates: Concomitant use of Vivjoa™ with BCRP substrates may increase the exposure of drugs that are BCRP substrates, which may increase the risk of adverse reactions associated with these drugs. Use the lowest possible starting dose of the BCRP substrate or consider reducing the dose of the substrate drugs and monitor for adverse reactions.

USE IN SPECIFIC POPULATIONS
- Pregnancy: Vivjoa™ is contraindicated in females of reproductive potential and in pregnant women. Based on animal studies, Vivjoa™ may cause fetal harm when administered to pregnant women.
- Pediatric use: The safety and effectiveness of Vivjoa™ have not been established in pre-menarchal pediatric females.
- Geriatric use: Clinical studies of Vivjoa™ did not include sufficient numbers of patients 65 years of age and older to determine whether they respond differently from younger adult patients.
- Renal impairment: No dosage adjustment of Vivjoa™ is recommended in patients with mild to moderate renal impairment. Clinical studies of Vivjoa™ did not include sufficient numbers of patients with severe renal impairment or end-stage renal disease (ESRD). Therefore, Vivjoa™ is not recommended for use in patients with severe renal impairment or ESRD.
- Hepatic impairment: No dosage adjustment of Vivjoa™ is recommended in patients with mild hepatic impairment. There is insufficient information to determine the safety of Vivjoa™ in patients with moderate or severe hepatic impairment (Child-Pugh B-C). Therefore, Vivjoa™ is not recommended for use in patients with moderate or severe hepatic impairment.

Orphan status: N/A

NEW MOLECULAR ENTITIES, NEW ACTIVE INGREDIENTS

DRUG NAME	MANUFACTURER	APPROVAL DATE
CAMZYOS™ (MAVACAMTEN) CAPSULES	MYOKARDIA INC	04/28/2022

THERAPEUTIC CLASS
Cardiac myosin inhibitor

FDA-APPROVED INDICATION(S)
Treatment of adults with symptomatic New York Heart Association (NYHA) class II-III obstructive hypertrophic cardiomyopathy (HCM) to improve functional capacity and symptoms

DOSAGE AND ADMINISTRATION
Recommended starting dose is 5mg orally once daily; allowable subsequent doses with titration are 2.5mg, 5mg, 10mg or 15mg once daily.

DOSAGE FORMS AND STRENGTHS
Capsules: 2.5mg, 5mg, 10mg, 15mg

Orphan status: N/A

SAFETY PROFILE

CONTRAINDICATIONS
- Moderate to strong CYP2C19 inhibitors or strong CYP3A4 inhibitors
- Moderate to strong CYP2C19 inducers or moderate to strong CYP3A4 inducers

WARNINGS AND PRECAUTIONS
- **Black box warning**: Risk of heart failure
  - Camzyos™ reduces left ventricular ejection fraction (LVEF) and can cause heart failure due to systolic dysfunction.
  - Echocardiogram assessments of LVEF are required prior to and during treatment with Camzyos™. Initiation of Camzyos™ in patients with LVEF.
  - Concomitant use of Camzyos™ with certain cytochrome P450 inhibitors or discontinuation of certain cytochrome P450 inducers may increase the risk of heart failure due to systolic dysfunction.
  - Because of the risk of heart failure due to systolic dysfunction, Camzyos™ is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called CAMZYOS™ REMS PROGRAM.
- Heart failure: Consider interruption of Camzyos™ in patients with intercurrent illness.

WARNING AND PRECAUTIONS (cont.)
- Drug interactions leading to heart failure or loss of effectiveness: Advise patients of the potential for drug interactions including with over-the-counter medications.
- Embryo-fetal toxicity: May cause fetal harm. Advise females of reproductive potential to use effective contraception until 4 months after the last dose. Use a contraceptive not affected by CYP450 enzyme induction or add nonhormonal contraception.

ADVERSE REACTIONS
- Adverse reactions occurring in >5% of patients and more commonly on Camzyos™ than on placebo were dizziness (27%) and syncope (6%).

DRUG INTERACTIONS
- Weak CYP2C19 inhibitors and moderate CYP3A4 inhibitors: May increase risk of heart failure. If initiating an inhibitor, Camzyos™ dose reduction and additional monitoring are required.
- Negative inotropes: Close medical supervision and LVEF monitoring is recommended if a negative inotrope is initiated, or the dose of a negative inotrope is increased. Avoid certain combinations of negative inotropes.

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DOSAGE FORMS AND STRENGTHS
Capsules: 2.5mg, 5mg, 10mg, 15mg

Orphan status: N/A

SAFETY PROFILE

USE IN SPECIFIC POPULATIONS

- Pregnancy: Based on animal data, Camzyos™ may cause fetal harm when administered to a pregnant female. Advise pregnant females about the potential risk to the fetus with maternal exposure to Camzyos™ during pregnancy.
- Lactation: The presence of mavacamten in human or animal milk, the drug's effects on the breastfed infant, and the effects on milk production are unknown. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for Camzyos™ and any potential adverse effects on the breastfed child from Camzyos™ or from the underlying maternal condition.
- Females and males of reproductive potential: Based on animal data, Camzyos™ may cause fetal harm when administered to a pregnant female. Confirm absence of pregnancy in females of reproductive potential prior to initiation of Camzyos™. Advise females of reproductive potential to use effective contraception during treatment with Camzyos™ and for 4 months after the last dose. Use of Camzyos™ may reduce the effectiveness of combined hormonal contraceptives (CHCs). Advise patients using CHCs to use an alternative contraceptive method or add nonhormonal contraception.

USE IN SPECIFIC POPULATIONS (cont.)

- Pediatric use: The safety and effectiveness of Camzyos™ have not been established in pediatric patients.
- Geriatric use: Safety, effectiveness, and pharmacokinetics were similar between patients ≥65 years and younger patients.
- Hepatic impairment: No dosage adjustment is required in patients with mild to moderate hepatic impairment. Mavacamten exposure (AUC) increased up to 220% in patients with mild or moderate (Child-Pugh B) hepatic impairment compared to patients with normal hepatic function. However, no additional dose adjustment is required in patients with mild to moderate hepatic impairment with the recommended dose titration algorithm and monitoring plan. The effect of severe hepatic impairment is unknown.

NEW MOLECULAR ENTITIES, NEW ACTIVE INGREDIENTS

DRUG NAME	MANUFACTURER	APPROVAL DATE
CUVRIOR™ (TRIENTINE TETRAHYDROCHLORIDE) TABLETS	ORPHALAN SA	04/28/2022

THERAPEUTIC CLASS
Copper chelator

FDA-APPROVED INDICATION(S)
Treatment of adult patients with stable Wilson's disease who are de-coppered and tolerant to penicillamine

DOSAGE AND ADMINISTRATION
- Starting total daily dosage of Cuvrior™ In adults is 300mg up to 3,000mg orally in divided doses (2 times daily).
- Adjust the total daily dosage according to clinical assessment and laboratory monitoring of copper.
- If the number of tablets prescribed per day cannot be equally divided among doses, then divide total daily dosage such that the higher number of tablets is taken with the first daily dose.

DOSAGE FORMS AND STRENGTHS
Tablets: 300mg of trientine tetrahydrochloride, functionally scored.

Orphan status: Orphan

SAFETY PROFILE

CONTRAINDICATIONS
- Hypersensitivity to trientine or to any of the excipients in Cuvrior™.

WARNINGS AND PRECAUTIONS
- Potential for worsening of clinical symptoms at initiation of therapy: May include neurological deterioration. Adjust dosage or discontinue Cuvrior™ if clinical condition worsens.
- Cooper deficiency: Periodic monitoring is required.
- Iron deficiency: If iron deficiency develops, a short course of iron supplementation may be given.
- Hypersensitivity reactions: If rash or other hypersensitivity reaction occurs, consider discontinuing Cuvrior™.

ADVERSE REACTIONS
- Most common adverse reactions (>5%) are abdominal pain, change of bowel habits, rash, alopecia, and mood swings.

DRUG INTERACTIONS
- Mineral Supplements (e.g., iron, zinc, calcium, magnesium): Avoid concomitant use. If concomitant use is unavoidable:
  - Iron: Take Cuvrior™ at least 2 hours before or 2 hours after iron.
  - Other mineral supplements: Take Cuvrior™ at least 1 hour before or 2 hours after other mineral supplements.
- Other drugs for oral administration: Take Cuvrior™ at least 1 hour apart from any other oral drug.

USE IN SPECIFIC POPULATIONS
- Pregnancy: Available data from published literature and postmarketing experience over several decades with use of trientine for the treatment of Wilson's disease have not identified any drug-associated risks for major birth defects, miscarriages, or other adverse maternal or fetal outcomes.
- Lactation: The available published data are inconsistent regarding the detection of trientine in breastmilk.
- Pediatric use: The safety and effectiveness of Cuvrior™ in pediatric patients have not been established.
- Geriatric use: Clinical studies with trientine did not include sufficient numbers of patients aged 65 and over to determine whether they respond differently from younger adult patients.

NEW BIOSMILAR PRODUCTS

DRUG NAME / MANUFACTURER	THERAPEUTIC CLASS	INDICATION(S)	DATE	COMMENTS
ALYMSYS™ (BEVACIZUMAB-MALY) INJECTION / AMNEAL PHARMACEUTICALS LLC.	Antineoplastics and adjunctive therapies	[1] Treatment of metastatic colorectal cancer, in combination with intravenous fluorouracil-based chemotherapy for first- or second-line treatment; [2] treatment of metastatic colorectal cancer, in combination with fluoropyrimidine-irinotecan- or fluoropyrimidine-oxaliplatin-based chemotherapy for second-line treatment in patients who have progressed on a first-line bevacizumab product-containing regimen	4/13/2022	Alymsys™ represents the third bevacizumab biosimilar approved in the U.S. Availability is pending. Reference product: Avastin™ Orphan: N/A

NEW FORMULATIONS, COMBINATION PRODUCTS, LINE EXTENSIONS

DRUG NAME / MANUFACTURER	THERAPEUTIC CLASS	INDICATION(S)	DATE	COMMENTS
IGALMI™ (DEXMEDETOMIDINE) SUBLINGUAL FILM / BIOXCEL THERAPEUTICS INC.	Hypnotics/sedatives/sleep disorder agents	Acute treatment of agitation associated with schizophrenia or bipolar I or II disorder in adult patients	4/5/2022	Igalmi™ is the first acute treatment for schizophrenia or bipolar disorder-associated agitation. It can be self-administered by the patient under the supervision of a healthcare provider. Orphan: N/A
VIJOICE™ (ALPELISIB) TABLETS / NOVARTIS PHARMACEUTICALS CORP.	PIK3CA-related overgrowth spectrum (PROS) agents	Treatment of adult and pediatric patients 2 years of age and older with severe manifestations of PROS who require systemic therapy	4/5/2022	Vijoice™ is the first approved treatment to specifically address the root cause of PROS conditions. Orphan: Yes
EPSOLAY™ (BENZOYL PEROXIDE) CREAM / SOL-GEL TECHNOLOGIES LTD.	Dermatologicals	Treatment of inflammatory lesions of rosacea in adults	4/22/2022	The benzoyl peroxide in Epsolay™ is encapsulated within silica-based patented microcapsules and it is designed to slowly release benzoyl peroxide over time to provide a favorable efficacy and safety profile. Orphan: N/A
CAPLYTA™ (LUMATEPERONE) CAPSULES / INTRA-CELLULAR THERAPIES, INC.	Antipsychotics/antimanic agents	[1] Treatment of schizophrenia; [2] treatment of depressive episodes associated with bipolar I or II disorder (bipolar depression) in adults, as monotherapy and as adjunctive therapy with lithium or valproate	4/25/2022	The FDA has approved two new dosage strengths of Caplyta™, 10.5mg and 21mg capsules, to provide dosage recommendations for patients concomitantly taking strong or moderate CYP3A4 inhibitors, and 21mg for patients with moderate or severe hepatic impairment (Child-Pugh class B or C). Orphan: N/A

NEW FIRST-TIME GENERIC APPROVALS

DRUG NAME / MANUFACTURER	THERAPEUTIC CLASS	INDICATION(S)	GENERIC FOR:	DATE
BRIMONIDINE TARTRATE AND TIMOLOL MALEATE OPHTHALMIC SOLUTION 0.2-0.5% / SANDOZ INC.	Ophthalmic agents	Glaucoma	Combigan™	4/4/2022
LACOSAMIDE INJECTION 200MG/20ML / INDOCO REMEDIES LIMITED	Anticonvulsants	Seizures	Vimpat™	4/7/2022
CYSTEINE HYDROCHLORIDE INJECTION 500MG/10ML / ETON PHARMACEUTICALS, INC.	Nutrients	Total parenteral nutrition	Elcys™	4/8/2022
REGADENOSON INTRVENOUS SOLUTION 0.4MG/5ML / ACCORD HEALTHCARE INC; APOTEX INC; HONG KONG KING-FRIEND INDUSTRIAL CO. LTD.; DR. REDDY'S LABORATORIES LTD.	Diagnostic products	Myocardial perfusion imaging	Lexiscan™	4/11/2022

NEW
FDA-APPROVED INDICATIONS
FOR EXISTING DRUGS

NEW FDA-APPROVED INDICATIONS FOR EXISTING DRUGS

DRUG NAME / MANUFACTURER	THERAPEUTIC CLASS	PREVIOUS INDICATION(S)	NEW INDICATION(S)	DATE
YESCARTA™ (AXICABTAGENE CILOLEUCEL) SUSPENSION / KITE, A GILEAD COMPANY	Antineoplastics and adjunctive therapies	Treatment of adult patients with relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy, including diffuse large B-cell lymphoma (DLBCL) not otherwise specified, primary mediastinal large B-cell lymphoma, high grade B-cell lymphoma, and DLBCL arising from follicular lymphoma	Treatment of adult patients with large B-cell lymphoma that is refractory to first-line chemoimmunotherapy or that relapses within 12 months of first-line chemoimmunotherapy	4/1/2022
VEKLURY™ (REMDESIVIR) INJECTION / GILEAD SCIENCES INC.	Antivirals	Treatment of coronavirus disease 2019 (COVID-19) in adults and pediatric patients (12 years of age and older and weighing at least 40kg) with positive results of direct severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) viral testing, who are: • Hospitalized • Not hospitalized and have mild-to-moderate COVID-19 and are at high risk for progression to severe COVID-19, including hospitalization or death.	Treatment of coronavirus disease 2019 (COVID-19) in adults and pediatric patients (28 days of age and older and weighing at least 3kg) with positive results of direct severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) viral testing, who are: • Hospitalized • Not hospitalized and have mild-to-moderate COVID-19 and are at high risk for progression to severe COVID-19, including hospitalization or death.	4/25/2022
ULTOMIRIS™ (RAVULIZUMAB-CWVZ) INJECTION / ALEXION PHARM	Hematological agents – Complement inhibitors	[1] Treatment of adult and pediatric patients one month of age and older with paroxysmal nocturnal hemoglobinuria (PNH); [2] treatment of adult and pediatric patients one month of age and older with atypical hemolytic uremic syndrome (aHUS) to inhibit completement-mediated thrombotic microangiopathy (TMA)	Treatment of adult patients with generalized myasthenia gravis (gMG) who are anti-acetylcholine receptor (AChR) antibody-positive	4/27/2022

NEW FDA-APPROVED INDICATIONS FOR EXISTING DRUGS

DRUG NAME / MANUFACTURER	THERAPEUTIC CLASS	PREVIOUS INDICATION(S)	NEW INDICATION(S)	DATE
RINVOQ™ (UPADACTINIB) EXTENDED-RELEASE TABLETS / ABBVIE	Analgesics – anti-inflammatory	[1] Treatment of adults with moderately to severely active rheumatoid arthritis who have had an inadequate response or intolerance to one or more TNF blockers; [2] treatment of adults with active psoriatic arthritis who have had an inadequate response or intolerance to one or more TNF blockers; [3] treatment of adults and pediatric patients 12 years of age with refractory, moderate to severe atopic dermatitis whose disease is not adequately controlled with other systemic drug products, including biologics, or when use of those therapies are inadvisable; [4] treatment of adults with moderately to severely active ulcerative colitis who have had an inadequate response or intolerance to one or more TNF blockers	Treatment of adults with active ankylosing spondylitis who have had an inadequate response or intolerance to one or more TNF blockers	4/29/2022
QELBREE™ (VILOXAZINE HYDROCHLORIDE) EXTENDED-RELEASE CAPSULES / SUPERNUS PHARMACEUTICALS INC.	ADHD/anti-narcolepsy/anti-obesity/anorexiants	Treatment of Attention Deficit Hyperactivity Disorder (ADHD) in pediatric patients 6 to 17 years of age	Treatment of Attention Deficit Hyperactivity Disorder (ADHD) in pediatric patients 6 years and older	4/29/2022

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DRUG NAME / MANUFACTURER	DATE	INDICATION(S)	COMMENTS	IMPACT
FUROSCIX™ (FUROSEMIDE INJECTION) / scPHARMACEUTICALS INC.	4/11/2022	Treatment of congestion due to fluid overload in adult patients with New York Heart Association (NYHA) Class II and Class III chronic heart failure who display reduced responsiveness to oral diuretics and who do not require hospitalization	Furoscix™ is an investigational, proprietary furosemide solution designed to allow for subcutaneous infusion via a wearable, pre-programmed on-body drug delivery system, for outpatient self-administration. NDA resubmitted.	Moderate
PEGZILARGINASE / AEGLEA BIOTHERAPEUTICS INC.	4/12/2022	Treatment of Arginase 1 deficiency (ARG1-D)	Pegzilarginase is a novel, recombinant human arginase 1 enzyme that has shown to normalize the elevated levels of the amino acid arginine in patients with ARG1-D, a rare, progressive disease characterized by high levels of arginine. Aeglea BioTherapeutics Inc. has requested FDA Priority Review. BLA submitted.	High
DAPRODUSTAT / GLAXOSMITHKLINE INC.	4/19/2022	Treatment of patients with anemia of chronic kidney disease	Daprodustat is an oral hypoxia-inducible factor prolyl hydroxylase inhibitor. The regulatory submission is based on the ASCEND phase III clinical trial program, consisting of five trials that all met their primary efficacy and safety endpoint in non-dialysis and dialysis patients. NDA accepted.	Moderate

REFERENCES

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