

Drug Pipeline MONTHLY UPDATE

Critical updates in an ever changing environment

DECEMBER 2021

NEW DRUG INFORMATION

- **Livtency™ (maribavir):** The U.S. Food and Drug Administration (FDA) has approved Takeda Pharmaceuticals' Livtency for the treatment of adults and pediatric patients 12 years of age and older and weighing at least 35kg with post-transplant cytomegalovirus (CMV) infection/disease that is refractory to treatment (with or without genotypic resistance) with ganciclovir, valganciclovir, cidofovir or foscarnet. Livtency was approved based on a Phase 3 clinical trial that demonstrated 55.7% of Livtency patients achieved confirmed CMV viremia clearance compared to 23.9% of patients taking the control.¹ According to FDA's briefing documents, Livtency proved safe across multiple studies and was statistically superior to investigator-assigned treatment (IAT) in the Phase 3 trial. FDA's concerns about discontinuations in the IAT arm of the trial also did not overshadow that statistical success.² The FDA stated Livtency "provides some advantages over currently available therapies, it appears to have a better safety profile, with taste disturbance being the most common adverse reaction associated with its use." Livtency is available as an oral tablet (similar to valganciclovir), providing ease of administration. Livtency has launched with a wholesale acquisition cost (WAC) of \$12,449.92 per month.
- **Xaciato® (clindamycin phosphate vaginal gel, 2%):** The FDA approved Daré Bioscience, Inc's Xaciato for the treatment of bacterial vaginosis (BV) in females 12 years of age and older. The product is administered via a user-filled disposable applicator delivering 5g of gel containing 100mg of clindamycin as a single dose. Xaciato's approval was supported by positive results from the DARE-BVFREE, a Phase 3 clinical trial that demonstrated Xaciato was statistically superior to placebo at the test of cure visit at day 21-30 in the intent-to-treat population, with 70.5% of patients clinically cured compared with 35.6% for placebo.³ Symbiomix Therapeutics' Solosec® (secnidazole) is FDA approved as an oral single-dose BV treatment. Both metronidazole and clindamycin, both available generically as oral or vaginal formulations, are also treatment options for BV. Xaciato is planning on launching in 2022 with pricing to follow.

- **Entadfi® (finasteride and tadalafil) capsule:** The FDA approved Veru Inc's Entadfi for the treatment of the signs and symptoms of benign prostatic hyperplasia (BPH) in men with an enlarged prostate for up to 26 weeks. Entadfi was approved via the 505(b)2 pathway using Eli Lilly's Cialis® (tadalafil) and Merck's Proscar® (finasteride) as its reference products.⁴ Entadfi is not recommended for more than 26 weeks because the incremental benefit of tadalafil decreases from 4 weeks until 26 weeks and the incremental benefit beyond 26 weeks is unknown. Entadfi is expected to launch early 2022 with pricing to follow.

GENERIC DRUG INFORMATION

- **Zortress®+ (everolimus tab):** Hikma launched their generic version of Novartis' Zortress for the prophylaxis of organ rejection in adult patients, specifically kidney transplant: at low-moderate immunologic risk in combination with basiliximab, cyclosporine (reduced doses) and corticosteroids and liver transplants no earlier than 30 days posttransplant in combination with tacrolimus (reduced doses) and corticosteroids. Zortress generated \$157 million in U.S. annual sales in 2020.
- **Arranon® (nelarabine inj 5mg/mL):** Zydus has launched their generic version of Novartis' Arranon for the treatment of patients with T-cell acute lymphoblastic leukemia and T-cell lymphoblastic lymphoma whose disease has not responded to or has relapsed following treatment with at least two chemotherapy regimens. This use is based on the induction of complete responses. Randomized trials demonstrating increased survival or other clinical benefit have not been conducted. Arranon generated \$39 million in U.S. annual sales in 2020.
- **Epiduo Forte gel® 0.3-2.5% (adapalene/benzoyl peroxide gel):** Teva launched their generic version of Galderma's Epiduo Forte gel as a combination of adapalene, a retinoid, and benzoyl peroxide, and is indicated for the topical treatment of acne vulgaris. Epiduo Forte gel generated \$315 million in U.S. annual sales in 2020.

+Specialty medication

NEW MOLECULAR ENTITY APPROVALS IN THE PAST TWELVE MONTHS

GENERIC NAME	BRAND NAME	MANUFACTURER	INDICATION(S)	DATE APPROVED*
maribavir	Livtencity™	Takeda	Cytomegalovirus (CMV) infection	November 2021
difelikefalin	Korsuva®	Cara Therapeutics	Chronic kidney disease-associated pruritis (CKD-aP) in hemodialysis patients	August 2021
fexinidazole	N/A	Sanofi	<i>Trypanosoma brucei gambiense</i> form of sleeping sickness	July 2021
finerenone	Kerendia®	Bayer	Chronic kidney disease (CKD) and type 2 diabetes	July 2021
brincidofovir	Temboxa®	Chimerix	Smallpox	June 2021
ibrexafungerp	Brexafemme®	Scynexis	Antifungal	June 2021
olanzapine and samidorphan	Lybalvi®	Alkermes	Schizophrenia or bipolar I disorder	June 2021
estetrol and drospirenone (E4/DRSP)	Nextstellis™	Mayne Pharma, Mithra Pharmaceuticals	Pregnancy prevention	April 2021
viloxazine hydrochloride	Qelbree™	Supernus Pharmaceuticals	ADHD	April 2021
oritavancin	Kimyrza™	Melinta Therapeutics	Acute bacterial skin and skin structure infections (ABSSSI)	March 2021
serdexmethylphenidate and dexamethylphenidate	Azstarys™	KemPharm	ADHD	March 2021
cabotegravir	Vocabria™	VIIV Healthcare	HIV-1 infection	January 2021
cabotegravir and rilpivirine	Cabenuva™	VIIV Healthcare	HIV-1 infection	January 2021
vericiguat	Verquvo™	Merck	Heart failure	January 2021

* Date indicates FDA approval date only. The product launch and marketing dates are determined by the approved product's manufacturer.

OTHER NEW PRODUCT APPROVALS IN THE PAST TWELVE MONTHS

GENERIC NAME	BRAND NAME	MANUFACTURER	INDICATION(S)	DATE APPROVED*
tadalafil/finasteride	Entadfi™	Veru	Benign prostatic hyperplasia	December 2021
baclofen oral granules	Lyvispah®	Saol	Spasticity resulting from multiple sclerosis	December 2021
clindamycin 2% hydrogel	Xaciato®	Daré Bioscience	Bacterial vaginosis	December 2021
topiramate oral solution, 25mg/mL	Eprontia®	Azurity Pharmaceuticals	Seizures	November 2021
pilocarpine HCL ophthalmic solution 1.25%	Vuity®	Allergan	Presbyopia	October 2021
tramadol 44mg and celecoxib 56mg tablet	Seglantis®	Esteve Pharmaceuticals and Kowa Pharmaceuticals America	Pain	October 2021
varenicline nasal spray	Tyrvaya®	Oyster Point Pharma	Dry eye disease	October 2021
naloxone pre-filled syringe	Zimhi®	Adamas Pharma	Opioid overdose	October 2021
atogepant	Qulipta®	AbbVie	Preventive treatment of migraine	September 2021
paliperidone palmitate extended-release injectable suspension	Invega Hafyera®	Janssen Pharmaceuticals, Inc.	Schizophrenia	September 2021
dihydroergotamine mesylate, DHE	Trudhesa®	Impel Neuropharma	Migraine	September 2021
benzoyl peroxide and tretinoin	Twynéo®	Sol-Gel Technologies	Acne vulgaris	July 2021
torsemide	Soanz®	Sarfez Pharmaceuticals	Edema caused by heart failure	June 2021
cyclosporine ophthalmic emulsion	Verkazia™	Santen	Vernal keratoconjunctivitis	June 2021
ephedrine injection	Rezipres®	Eton Pharmaceuticals	Hypotension	June 2021
semaglutide	Wegovy™	Novo Nordisk	Chronic weight management	June 2021
relugolix, estradiol and norethindrone	Myfembree™	Myovant (Sumitomo Dainippon)	Heavy menstrual bleeding	June 2021
bupivacaine and meloxicam extended-release solution	Zynrelef™	Heron Therapeutics	Postoperative pain	May 2021
naloxone hydrochloride nasal spray	Kloxxado™	Hikma Pharmaceuticals	Emergency treatment of known or suspected opioid overdose	April 2021
mirabegron for extended-release oral suspension	Myrbetriq™ Granules	Astellas	Neurogenic detrusor overactivity (NDO)	March 2021
ezetimibe and rosuvastatin	Roszet™	Althera Pharmaceuticals	Hyperlipidemia	March 2021
dasiglucagon HypoPal Rescue Pen	Zegalogue™	Zealand Pharma	Hypoglycemia	March 2021
bupivacaine solution for infiltration	Posimir™	Durect Corporation	Post-surgical pain	February 2021

* Date indicates FDA approval date only. The product launch and marketing dates are determined by the approved product's manufacturer.

PIPELINE WATCH

GENERIC NAME	BRAND NAME	MANUFACTURER	INDICATION(S)	ANTICIPATED FDA DECISION DATE*
budesonide oral suspension	Eohilia™	Takeda	Localized esophageal inflammation	Delayed
benzoyl peroxide	Epsolay™	Sol-Gel Technologies	Rosacea	Delayed
ET-104 (zonisamide oral suspension)	N/A	Azurity Pharmaceuticals	Anticonvulsant	Delayed
AXS-05 (dextromethorphan and bupropion)	N/A	Axsome Therapeutics	Major depressive disorder	Delayed
reltecimod	N/A	Atox Bio	Necrotizing soft tissue infection	Delayed
testosterone undecanoate	Kyzatrex®	Marius Pharmaceuticals	Hypogonadism	Delayed
dapivirine vaginal ring	N/A	International Partnership for Microbicides and Johnson & Johnson	HIV-1	December 2021
dextroamphetamine transdermal system (ATS)	N/A	Noven Therapeutics	ADHD	December 2021
buprenorphine depot, formerly CAM2038	Brixadi™	Braeburn Pharmaceutical	Opioid use disorder	December 2021
diazepam buccal film	Libervant™	Aquestive Therapeutics	Seizures	December 2021
BXCL501 (dexmedetomidine orally dissolving film)	N/A	BioXcel Therapeutics	Schizophrenia and bipolar disorders	January 2022
daridorexant	N/A	Idorsia	Insomnia	January 2022
oteseconazole (VT-1161)	N/A	Mycovia Pharmaceuticals	Vulvovaginal candidiasis	January 2022
lenacapavir	N/A	Gilead Sciences	HIV	February 2022
letibotulinumtoxinA	N/A	Hugel America	Frown lines	March 2022
gefapixant	N/A	Merck	Chronic cough	March 2022
udenafil	N/A	Mezzion Pharma	Single ventricle heart disease (SVHD) who have undergone the Fontan operation	March 2022
donepezil, transdermal	AdIarity®	Corium	Alzheimer's disease	March 2022
meloxicam-rizatriptan	MoSEIC™	Axsome Therapeutics	Acute migraine	April 2022
paracetamol and ibuprofen solution for infusion	Maxigesic® IV	Hyloris Pharmaceuticals SA	Postoperative pain	September 2022
linzagolix	N/A	ObsEva	Uterine fibroids	September 2022

FIRST GENERIC LAUNCHES OF TOP SELLING BRAND NAME DRUGS IN THE PAST TWELVE MONTHS

GENERIC NAME	BRAND NAME	BRAND MANUFACTURER	INDICATION(S)	APPROVAL DATE*
adapalene; benzoyl peroxide	Epiduo Forte®	Galderma	Acne	December 2021
zolmitriptan nasal spray, 5mg/sprav	Zomig® nasal sprav	AstraZeneca	Migraine headache	November 2021
everolimus+	Afinitor® (10mg)	Novartis	Kidney cancer	October 2021
everolimus+	Afinitor® Disperz	Novartis	Certain forms of cancer	October 2021
difluprednate ophth emulsion, 0.05%	Durezol®	Novartis	Endogenous Anterior Uveitis	September 2021
nebivolol	Bystolic®	Allergan	Hypertension	September 2021
sunitinib malate+	Sutent®	CPPI CV	Cancer	August 2021
ibuprofen/famotidine	Duexis®	Horizon Therapeutics USA	Rheumatoid arthritis (RA), osteoarthritis (OA), ulcers	August 2021
ferumoxytol	Feraheme®	AMAG Pharmaceuticals	Anemia	July 2021
formoterol fumarate	Perforomist®	Mylan	COPD	June 2021
arformoterol tartrate	Brovana®	Sunovion	COPD	June 2021
rufinamide	Banzel®	Eisai	Seizures associated with Lennox-Gastaut Syndrome	June 2021
isotretinoin	Absorica®	Ranbaxy	Acne	May 2021
brinzolamide	Azopt® ophth susp 1%	Novartis	Glaucoma or ocular hypertension	March 2021
droxidopa	Northera®	H. Lundbeck A/S	Parkinson's disease	February 2021
loteprednol ophth gel, 0.5%	Lotemax ophth gel® 0.5%	Bausch	Post-operative inflammation	February 2021
glucagon (rdna) for inj kit	Glucagon Emergency Kit®	Lilly	Hypoglycemia	January 2021

*Date usually indicates FDA approval date. The product's launch date is determined by the manufacturer. Generic approvals that do not come to market within three months of approval are listed and dated when they enter the market.

+Specialty medication

OTHER FIRST GENERIC LAUNCHES IN THE PAST TWELVE MONTHS

GENERIC NAME	BRAND NAME	BRAND MANUFACTURER	INDICATION(S)	APPROVAL DATE*
nelarabine inj, 5 mg/mL+	Arranon®	Novartis	Certain forms of T-cell acute lymphoblastic leukemia/T-cell lymphoblastic lymphoma	November 2021
everolimus tab, 1 mg	Zortress®	Novartis	Prophylaxis of organ rejection in certain transplantations	November 2021
enalapril oral soln, 1 mg/mL	Epaned®	Azurity Pharmaceuticals	Heart failure, hypertension	August 2021
buprenorphine buccal film	Belbuca®	BioDelivery Sciences	Pain management	August 2021
atropine prefilled syringe inj, 0.25 mg/5 mL (0.05 mg/mL)	N/A	Hospira	Temporary blockade of severe or life-threatening muscarinic effects	August 2021
argatroban	Argatroban®	Hikma	Heparin-induced thrombocytopenia (HIT)	July 2021
etravirine	Intelence®	Janssen	HIV	June 2021
lopinavir, ritonavir	Kaletra®	AbbVie	HIV	June 2021
bepotastine ophth soln, 1.5%	Bepreve®	Bausch Health	Allergic conjunctivitis	June 2021
tiopronin tab	Thiola®	Traverse Therapeutics	Prevention of cystine stone formation	May 2021
pregabalin	Lyrica CR®	Pfizer	Neurological pain	April 2021
hydrocodone bitartrate	Hysingla ER®	Purdue	Pain	March 2021
topiramate	Qudexy XR®	Upsher-Smith	Epilepsy	February 2021
foscarnet	Foscavir®	Novaplus/Hospira	CMV retinitis and mucocutaneous acyclovir resistant HSV infections	February 2021
imiquimod cream, 3.75%	Zyclara®	Bausch Health	Actinic keratosis and genital warts	February 2021
epoprostenol for inj+	Velettri®	Actelion Pharmaceuticals	Pulmonary arterial hypertension	January 2021
emtricitabine; tenofovir disoproxil fumarate	Truvada® (100 mg/150 mg, 133 mg/200 mg, 167 mg/250 mg)	Gilead	HIV	January 2021
levorphanol tab, 3 mg	Levorphanol®	Sentynl Therapeutics	Pain	January 2021
naproxen CR tab	Naprelan®	Almatica	Inflammation	January 2021

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+Specialty medication

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GENERIC NAME	BRAND NAME	BRAND MANUFACTURER	INDICATION(S)	TO MARKET DATE*
aztreonam+	Cayston®	Gilead	Cystic fibrosis	12/20/2021
carglumic acid+	Carbaglu®	Orphan Europe Recordati	Metabolic disorders	4Q 2021
cabazitaxel+	Jevtana Kit®	Sanofi	Prostate cancer	2H 2021
vasopressin	Vasostriect®	Par Endo Pharmaceuticals	Hypotension	2H 2021
exenatide synthetic	Byetta®	AstraZeneca	Diabetes mellitus	2022
glycopyrrolate	Cuvposa®	Merz Pharma	Cerebral palsy	2022
roflumilast	Daliresp®	AstraZeneca	COPD	2022
aprepitant	<u>Emend® (for oral suspension)</u>	Merck & Co	Nausea and vomiting	2022
teriparatide recombinant human+	Forteo®	Eli Lilly	Osteoporosis	2022
ritonavir	<u>Norvir® (capsules)</u>	AbbVie	HIV	2022
posaconazole	<u>Noxafil® (oral suspension)</u>	Merck & Co	Fungal infection	2022
unoprostone isopropyl	Rescula®	Sucampo R-Tech Ueno	Glaucoma	2022
octreotide acetate+	Sandostatin LAR®	Novartis	Endocrine disorders	2022
fesoterodine fumarate	Toviaz®	Pfizer	Overactive bladder	2022
benzyl alcohol	Ulesfia®	Concordia Shionogi	Head lice	2022
oxycodone hydrochloride	Oxaydo®	Egalet Acura Pharmaceuticals Zyla	Pain	01/01/2022
brimonidine tartrate; timolol maleate	Combigan®	Allergan AbbVie	Glaucoma	2022
formoterol fumarate; mometasone furoate	Dulera®	Merck & Co Organon	Asthma	2022
fluticasone propionate	Flovent® HFA	GSK	Asthma	2022
lenalidomide+	Revlimid® (2.5, 20 mg)	Celgene Bristol-Myers Squibb	Myelodysplastic syndromes	2022
tafluprost	Zioptan®	Akorn	Glaucoma	2022

ethinyl estradiol; levonorgestrel	Balcoltra®	Avion Pharmaceuticals	Contraception	2022
enalapril maleate	Epaned® KIT	Silvergate	Heart failure	2022
naloxone hydrochloride	Narcan® (nasal spray)	Adapt Pharma	Opioid overdose	2022
rotigotine	Neupro®	UCB	Parkinson's disease	2022

* Expected to market dates are predictions made by Prime Therapeutics based on industry information.

+Specialty medication

REFERENCES

1. <https://www.biospace.com/article/releases/fda-approves-takeda-s-livtencity-maribavir-first-treatment-approved-for-post-transplant-cytomegalovirus-cmv-infection-resistant-to-other-drugs/>
2. <https://www.fda.gov/media/152715/download>
3. <https://www.empr.com/home/news/xaciato-vaginal-gel-approved-for-bacterial-vaginosis/>
4. <https://verupharma.com/pipeline/entadfi/#:~:text=Tadalafil%205mg%20daily%20has%20been,to%20prevent%20progression%20of%20BPH>