2018* New Drugs

Jill Johnson, Pharm.D., BCPS

*some in 2017

UAMS College of Pharmacy

Disclosure:
I have no conflicts of interest.

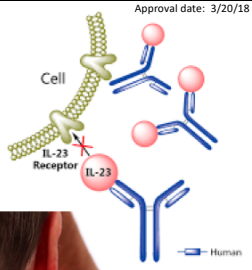
UAMS College of Pharmacy

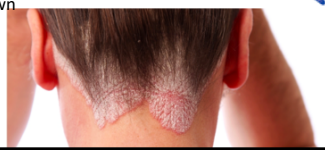
Plaque Psoriasis

Approval date: 3/20/18

Tildrakizumab (Ilumya®)

- Indication: treatment of moderate to severe plaque psoriasis
- MOA: monoclonal antibody to inhibit interleukin 23
- Dosing: SC 100mg W0, W4, then Q12W
- AWP Cost: Unknown





Tildrakizumab (Ilumya®)

- Evidence: 2 RCTs, phase 3
- Population: Mod to severe chronic plaque psoriasis

reSURFACE1 and reSURFACE2 Trials			
	Tildrakizumab 200mg N=308	Tildrakizumab 100mg N=309	Placebo N=154
PASI 75			
N(%)	192 (62%)	197 (64%)	9 (6%)
% difference from plac	56.6%	58.0%	NA
95% CI; p-value	44.8-58.5;P<0.0001	43.6-57.4;P<0.0001	
Clear or minimal PGA			
N (%)	109 (35%)	107 (35%)	4 (3%)
% difference from plac	32.9%	32.1%	NA
95%CI; p-value	26.8-38.8;p<0.0001	25.9-38.0;p<0.0001	

Reich, Kristian, et al. "Tildrakizumab versus placebo or etanercept for chronic plaque psoriasis (reSURFACE 1 and reSURFACE 2): results from two randomised controlled, phase 3 trials." *The Lancet* 390.10091 (2017): 276-288.

Tildrakizumab's place in therapy Mod-Sev Plaque Psoriasis*

Drug	PASI-75 (95%CI)	PGA/IGA 0/1
ustekinumab 90 mg	20.20 (13.82–29.54, p < .00001)	14.55 (10.42–20.31, p < .00001)
ixekizumab 80 mg q2w	19.83 (11.07–35.52, p < .00001)	20.41 (11.01–37.81, p < .00001)
ixekizumab 80 mg q4w	18.22 (10.63–31.23, p < .000001)	18.82 (10.36–34.16, p < .00001)
secukinumab 300 mg	17.65 (12.38–25.17, p < .00001)	26.13 (16.05–42.53, p < .00001)
secukinumab 150 mg	15.36 (10.76–21.94, p < .00001)	20.91 (12.82–34.13, p < .00001)
brodalumab 210 mg	14.79 (9.86–22.16, p < .00001)	21.93 (15.52–31.01, p < .00001)
ustekinumab 45 mg	13.75 (8.49–22.28, p < .00001)	9.81 (5.70–16.89, p < .00001)
guselkumab 100 mg	12.40 (8.87–17.34, p < .00001)	10.84 (7.91–14.85, p < .00001)
brodalumab 140 mg	11.55 (7.77–17.18, p < .00001)	16.59 (11.72–23.49, p < .00001)
tildrakizumab 200 mg	11.45 (7.45–17.58, p < .00001)	10.97 (6.44–18.69, p < .00001)
tildrakizumab 100 mg	11.02 (7.17–16.93, p < .00001)	10.03 (6.45–15.59, p < .00001)

*Risk ratios of achieving PASI-75 and PGA/IGA 0/1 relative to placebo in a NMA.

Bilal, Jawad, et al. "A systematic review and meta-analysis of the efficacy and safety of the interleukin (IL)-12/23 and IL-17 inhibitors ustekinumab, secukinumab, ixekizumab, brodalumab, guselkumab and tildrakizumab for the treatment of moderate to severe plaque psoriasis." *Journal of Dermatological Treatment* (2018): 1-10.

HIV

Approval date: 3/6/18

Ibalizumab-uiyk (Trogarzo®) IV injection

- Indication: Treatment of HIV-1 in combination w/ other antiretrovirals in heavily treatment-experienced adults with multidrug resistant HIV-1 infection failing their current regimen
- Dose: 2g single IV LD, then 800mg q2 weeks
- AWP Cost: LD=$10,240; MD/28d $8,192. Cost/y $108,550
- MOA: recombinant MAB, post-attachment inhibitor. It blocks HIV-1 from infecting CD4+ T cells by binding to domain 2 of CD4+ cell receptors leading to a conformational change that blocks gp120 and HIV co-receptors. Active against CCR5 and CXCR4 isolates. Blocks HIV entry without causing immunosuppression or depleting CD4+ cell counts.

Ibalizumab-uiyk (Trogarzo®) IV infusion

- Evidence:

Trial TMB-301 (from package insert)
Single arm, n=40 heavily treatment-experienced HIV-infected subjects with MDR HIV-1; viral load >1000 copies/mL and documented resistance to ≥1 ARV from each of 3 classes (NRTI, NNRTI, and PI)
Primary outcome: **Proportion of subjects achieving a ≥0.5 log10 decrease in VL from beginning to the end of the "Functional monotherapy period" as compared to the proportion achieving a ≥0.5 log 10 decrease from the beginning to the end of the "Control period".**

Ibalizumab-uiyk (Trogarzo®) Trial TMB 301 Results

Baseline median viral load and CD4+ T cell counts were 35,350 copies/ mL and 73 cells/mm³, respectively.

		Proportion achieving a >0.5 log_{10} Decrease in Viral Load	95% CI
End of Control Period		3%	(0.06%, 13%)
End of Functional Monotherapy Period		83%	(67%, 93%)
At week 25		% achieving <50 HIV-1 RNA copies/mL	% achieving <200 HIV-1 RNA copies/mL
CD4 Cell Counts	<50	18%	24%
	50-200	60%	70%
	>200	62%	69%
Viral Load	≤100,000	49%	58%
	>100,000	14%	14%
INSTI Resistance	With	41%	44%
	Without	46%	62%

Ibalizumab-uiyk (Trogarzo®)

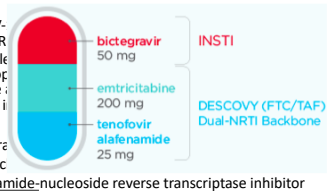
- Every 2 week IV infusion
  - Word is a SC dosage form is in the works
- Not meant to be used as monotherapy; should continue other ARV tx

NOW AVAILABLE BIKTARVY®

bictegravir 50mg/emtricitabine 200mg tenofovir alafenamide 25mg tablets

Approval date: 2/7/18

- Indication:
  - Treatment of HIV-
    initial therapy, OR
  - To replace a stable
    (viral load <50 cop
    treatment failure
    resistance to the i
- MOA:
  - Bictegravir-integra
  - Emtricitabine-nuc
  - Tenofovir alafenamide-nucleoside reverse transcriptase inhibitor
- AWP Cost: $3,535/30d; $43,006/y



Biktarvy® Evidence

Table 10 Virologic Outcomes of Randomized Treatment in Trials 1489 and 1490 at Week 48[a] in Subjects with No Antiretroviral Treatment Histo

	Trial 1489		Trial 1490	
	BIKTARVY (N=314)	ABC/DTG/3TC (N=315)	BIKTARVY (N=320)	DTG + FTC/TAF (N=325)
HIV-1 RNA < 50 copies/mL	92%	93%	89%	93%
Treatment Difference (95% CI) BIKTARVY vs. Comparator	-0.6% (-4.8% to 3.6%)		-3.5% (-7.9% to 1.0%)	
HIV-1 RNA ≥ 50 copies/mL[b]	1%	3%	4%	1%
No Virologic Data at Week 48 Window	7%	4%	6%	6%
Discontinued Study Drug Due to AE or Death[c]	0	1%	1%	1%
Discontinued Study Drug Due to Other Reasons and Last Available HIV-1 RNA <50 copies/mL[d]	5%	3%	3%	4%
Missing Data During Window but on Study Drug	2%	<1%	2%	1%

Table 11 Virologic Outcomes of Trials 1844 and 1878 at Week 48[a] in Virologically-Suppressed Subjects who Switched to BIKTARVY

	Trial 1844		Trial 1878	
	BIKTARVY (N=282)	ABC/DTG/3TC (N=281)	BIKTARVY (N=290)	ATV- or DRV-based regimen[b] (N=287)
HIV-1 RNA ≥ 50 copies/mL[c]	1%	<1%	2%	2%
Treatment Difference (95% CI)	0.7% (-1.0% to 2.8%)		0.0% (-2.5% to 2.5%)	
HIV-1 RNA < 50 copies/mL	94%	95%	92%	89%
No Virologic Data at Week 48 Window	5%	5%	6%	9%
Discontinued Study Drug Due to AE or Death and Last Available HIV-1 RNA < 50 copies/mL	2%	1%	1%	1%
Discontinued Study Drug Due to Other Reasons and Last Available HIV-1 RNA < 50 copies/mL[d]	2%	3%	3%	7%
Missing Data During Window but on Study Drug	2%	1%	2%	2%

Biktarvy®

- BBW:
  - Severe acute exacerbations of hepatitis B have been reported in patients coinfected with HIV-1 and HBV and have discontinued products containing emtricitabine (FTC) and/or tenofovir disoproxil fumarate (TDF), and may occur with discontinuation of BICTARVY. Closely monitor hepatic function in these patients. If appropriate, anti-hepatitis B therapy may be warranted.

Prostate Cancer

Approval date: 2/14/18

Apalutamide (Erleada®)

- Indication: Treatment of non-metastatic, castration-resistant prostate cancer (NM-CRPC)
- MOA: a nonsteroidal androgen receptor inhibitor. It binds directly to the androgen receptor ligand-binding domain to prevent androgen-receptor translocation, DNA binding, and receptor-mediated transcription, resulting in decreased proliferation of tumor cells and increased apoptosis, leading to decreased tumor volume.
- Dose is 4 tabs daily
- AWP Cost: $13,104/30 days

Apalutamide Evidence

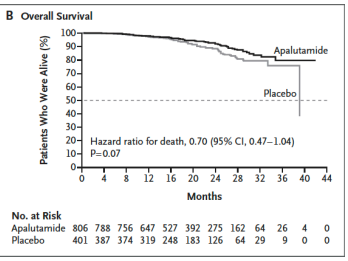
Erleada (apalutamide) 60 mg tablets

Study	Methods	Subjects	Endpoints	Results
SPARTAN[1]	240mg daily, continuous, randomized 2:1, DB, placebo controlled, multi-centered (Concomitant GnRH)	N=1207, high risk for disease progression Castration-resistant prostate adenocarcinoma, castrate levels of testosterone within 4 weeks, ≥4 wks since 1st generation anti-androgen AND increase in PSA, ≥ 4 weeks since use of 5-alpha RI's, estrogens, and any other anti-cancer, ≥4 weeks since surgery, ECOG Status 0 or 1	Metastasis-free survival (time to metastasis or death)	Apa: 40.5 mo Placebo: 16.2 mo HR: 0.28 (0.24,0.35) AE: rash in 23.8%
Bicalutamide v. APA in vitro[2]	APA is more potent than bicalutamide in blocking AR pathway			

[1] Smith, M. R., Saad, F., Chowdhury, S., Oudard, S., Hadaschik, B. A., Graff, J. N., ... & Lopez-Gitlitz, A. (2018). Apalutamide Treatment and Metastasis-free Survival in Prostate Cancer. *New England Journal of Medicine*.
[2]Koukourakis, M. I., Kakouratos, C., Kalamida, D., Mitrakas, A., Pouliliou, S., Xanthopoulou, E., ... & Giatromanolaki, A. (2018). Comparison of the effect of the antiandrogen apalutamide (ARN-509) versus bicalutamide on the androgen receptor pathway in prostate cancer cell lines. *Anti-cancer drugs*, *29*(4), 323-333.

OS Evidence with apalutamide

Erleada (apalutamide) 60 mg tablets

Study	
SPARTAN[1]	

AEs leading to WD from study	Apalutamide N=803	Placebo N=398
	10.6%	7.0%

No stats given.

[1] Smith, M. R., Saad, F., Chowdhury, S., Oudard, S., Hadaschik, B. A., Graff, J. N., ... & Lopez-Gitlitz, A. (2018). Apalutamide Treatment and Metastasis-free Survival in Prostate Cancer. *New England Journal of Medicine*.

Apalutamide's place in therapy Nonmetastatic CRPC

- Unknown; gathering options
- No head to head comparisons yet with enzalutamide or abiraterone.

	Agent:	Dosing	Unit Strengths	AWP Cost/30 Days
Erleada	Apalutamide	4 tabs QD	60mg tab	$13,104
†Xtandi	Enzalutamide	4 tabs QD	40mg cap	$13,086
†Zytiga	Abiraterone	4 tabs QD	250mg tab	$12,279
†Casodex	Bicalutamide	3 tabs QD	50mg tab	$2,077
†Generic			50mg tab	$1,651
†Flutamide(gen)	Flutamide	250mg TID	125mg cap	$376
†Nilandron	Nilutamide	300mg QD	150mg tab	$1,351

†Not indicated for nonmetastatic CRPC.

Cystic Fibrosis

symdeko™
(tezacaftor/ivacaftor and ivacaftor)
100 mg/150 mg and 150 mg tablets

Approval date: 2/13/18

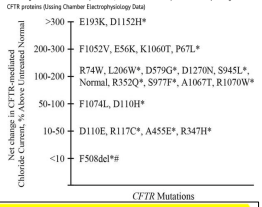
Tezacaftor/ivacaftor (Symdeko®)

- Indication: CF patients, age 12+ who are homozygous for F508del mutation OR who have at least one mutation in the CFTR gene that is responsive to tezacaftor/ivacaftor based on *in vitro* data and/or clinical evidence
- MOA:
  Tezacaftor: facilitates the cellular processing and trafficking of normal & select mutant forms of CFTR (including F508del-CFTR) to increase the amount of mature CFTR protein delivered to the cell surface.
  Ivacaftor: Potentiates CFTR; facilitates increased Cl transport by potentiating the channel gating of the CFTR protein at the cell surface.
- AWP Cost: $26,880/28 days

Tezacaftor/ivacaftor (Symdeko®) Evidence

*Figure 1: all mutations listed with * have associated CLINICAL data, all others are derived from in-vitro data.*

Figure 1: Net Change Over Baseline (% of untreated normal) in CFTR-Mediated Chloride Transport Following Addition of SYMDEKO (tezacaftor/ivacaftor combination) in FRT Cells Expressing Mutant CFTR proteins (Ussing Chamber Electrophysiology Data)



The minimum response threshold was designated as a net increase of at least 10% of untreated normal over baseline. The tezacaftor/ivacaftor incubation resulted in either similar or increased chloride transport compared to ivacaftor alone. In vitro data may not accurately predict added clinical benefit of SYMDEKO (tezacaftor/ivacaftor combination) over KALYDECO (ivacaftor) alone for individual mutations. In addition, the magnitude of the net change over baseline in CFTR-mediated chloride transport is not correlated with the magnitude of clinical response for individual mutations.

Tezacaftor/ivacaftor (Symdeko®) Evidence

EVOLVE trial—in CF HOMOZYGOUS for F508del

Endpoint	Placebo (n=256)	SYMDEKO (n=248)	Difference (95% CI)	Notes:
Absolute change from baseline in % of predicted FEV_1	-0.6 (-1.3 – 0.0)	3.4 (2.7 – 4.0)	4.0 (3.1 to 4.8) p<0.001	No MCID established in CF, although NICE states 5%
Relative Change in ppFEV1 from baseline through week 24 (%)	-0.5 (-1.7 – 0.6)	6.3 (5.1 – 7.4)	6.8 (5.3 – 8.3) p<0.001	No MCID established in CF
Number of Pulmonary Exacerbations from baseline through wk 24	122 (0.99)	78 (0.64)	0.65 (0.48 – 0.88) p< 0.0054	
Rate of Pulm. Exac. Leading to Hosp. (event rate/year)	0.54	0.29	0.25 (0.34 – 0.82)	
Absolute change in BMI from baseline at Wk 24 (kg/m2)	0.12 (0.03 - 0.22)	0.18 (0.08 – 0.28)	0.06 (-0.08 – 0.19)	Did not meet statistical significance. All results after are insignificant by hierarchical study design
Absolute change in CFQ-R Respiratory Domain Score from baseline through Wk 24 (points)	−0.1 (−1.6 to 1.4)	5.0 (3.5 to 6.5)	5.1 (3.2 to 7.0)	$MCID_{Stable}$: 4.0 $MCID_{Exacerbation}$: 8.5^

^Chest Vol.135, Issue 6, June 2009 1610 – 1618. MCID=minimal clinically important difference

Taylor-Cousar, Jennifer L., et al. "Tezacaftor–Ivacaftor in Patients with Cystic Fibrosis Homozygous for Phe508del." *N Eng J Med*. 377.21 (2017): 2013-2023.

Definition of "pulmonary exacerbation"

Per the EVOLVE Protocol: A pulmonary exacerbation was defined as a:

- new or change in antibiotic (IV, Inhaled, or oral) for **any 4 or more** of the following signs/s
  - change in sputum,
  - new or increased hemoptysis,
  - increased cough,
  - increased dyspnea,
  - malaise,
  - fatigue,
  - lethargy,
  - temp above 100.4F,
  - anorexia or wt loss,
  - sinus pain or tenderness,
  - change in sinus discharge,
  - change in physical exam of the chest,
  - decrease in pulm function by 10%,
  - CXR indicative of pulm infection.

Taylor-Cousar, Jennifer L., et al. "Tezacaftor–Ivacaftor in Patients with Cystic Fibrosis Homozygous for Phe508del." *N Eng J Med.* 377.21 (2017): 2013-2023. EVOLVE.

Tezacaftor/ivacaftor (Symdeko®) Evidence

EVOLVE trial—in CF HOMOZYGOUS for F508del

Endpoint	Placebo (n=256)	SYMDEKO (n=248)	Difference (95% CI)	Notes:
Number of Pulmonary Exacerbations from baseline through wk 24	122 (0.99)	78 (0.64)	0.65 (0.48 – 0.88) p< 0.0054	See note above describing criteria See calc. below
Rate of Pulm. Exac. Leading to Hosp. (event rate/year)	0.54	0.29	0.25 (0.34 – 0.82)	

Pharmacoeconomics of TEZ/IVA in EVOLVE:

Assumption: Each exacerbation corresponds to a separate patient encounter.

- Exac rate for placebo: $\frac{122\ Pulmonary\ Exacerbations}{256\ patients} = 0.47, or\ 47\%\ of\ patients\ had\ pulm\ exac\ at\ 24\ w$
- Exac rate for TEZ/IVA: $\frac{78\ Pulmonary\ Exacerbations}{248\ patients} = 0.31, \text{or } 31\%\ of\ patient\ had\ pulm\ exac\ at\ 24w$
- NNT for 24 weeks to prevent 1 Exac: $\frac{1}{0.47-0.31} = 6.25\ \approx 7\ Pts$

Cost to prevent 1 Exac in 24 wks: $24\ wks\ \left(\frac{7\ days}{1\ wk}\right)\left(\frac{\$960.00}{1\ day}\right)(7) = \mathbf{\$1,128,960.00}$,

Cost to prevent 1 Exac leading to Hosp (absolute numbers not given):

0.25 pt/year or 4 pts **for 1 year** = **$1,401,600.00**

ICER INSTITUTE FOR CLINICAL AND ECONOMIC REVIEW

5/2018:

- For G551D and R117H mutations, adequate evidence for a net health benefit with Kalydeco
- For homozygous F508del, adequate evidence for net health benefit for Orkambi or Symdeko, but not adequate to distinguish between them.
- For heterozygous F508del and a residual function mutation responsive to Symdeko, there is adequate evidence for a net health benefit.
- HOWEVER, considered LOW VALUE since the drug cost is so high. For value, compared to best supportive care, the ICER = $840,568 to $974,348 per QALY gained

Diagnostic

Approval date: 1/26/18

Lutetium Lu 177 dotatate (Lutathera®)

- Indication: the treatment of somatostatin receptor+ gastroenteropancreatic neuroendocrine tumors (NETs) including foregut, midgut, and hindgut NETs in adults
- MOA: It is a beta- and gamma-emitting radionuclide which binds to somatostatin receptors where the lutetium Lu 177 dotatate compound is internalized. The beta emission induces cellular damage by forming free radicals in somatostatin receptor+ and surrounding cells.

Intravenous infusion	Concentration into neuroendocrine tumor (NET) sites	LUTATHERA® binds to somatostatin receptors type 2 (SSTR2) overexpressed by NETs	LUTATHERA® is internalized in the NET cell	LUTATHERA® delivers radiation within the cancer cell	Radiation induces DNA strand breaks causing tumor cell death

Source: Google search, Novartis Investor Presentation.

Lutetium Lu 177 dotatate (Lutathera®)-NETTER-1 Trial Results

	Lutathera + LA Octreotide 30mg N=116	LA Octreotide 60mg N=113
PFS by IRC, Events (%)	27 (23%)	78 (69%)
Progressive disease, n (%)	15 (13%)	61 (54%)
Death, n (%)	12 (10%)	17 (15%)
Median in months (95% CI)	NR	8.5 (5.8, 9.1)
HR (95%CI)	0.21 (0.13, 0.32); p<0.0001	
OS (Updated)		
Deaths (%)	27 (23%)	43 (38%)
Median OS in months, (95%CI)	NR (31.0, NE)	27.4 (22.2, NE)
HR (95%CI	0.52 (0.32, 0.84)	

Question: For which CF population has Symdeko been shown to reduce pulmonary exacerbations?

A. All types of CF populations
B. Only those heterozygous for G551D mutation
C. Those homozygous for the F508del mutation
D. Those homozygous for the mutation R117C

Question: For which CF population has Symdeko been shown to reduce pulmonary exacerbations?

A. All types of CF populations
B. Only those heterozygous for G551D mutation
C. Those homozygous for the F508del mutation
D. Those homozygous for the mutation R117C

Glaucoma

Approval date: 11/2/2017

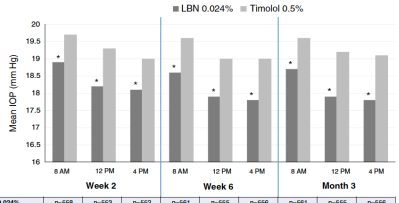
Latanoprostene bunod ophthalmic solution (Vyzulta®)

- Indication: to treat intraocular pressure in patients with open-angle glaucoma or ocular hypertension
- MOA: metabolized in the eye to latanoprost acid, an F_2 alpha prostaglandin analog, and to butanediol mononitrate. Latanoprost acid is thought to lower IOP by increasing outflow of aqueous humor through trabecular meshwork and uveoscleral routes.
- AWP Cost: $432/month (5mL vial)

Latanoprostene bunod ophthalmic solution (Vyzulta®) Evidence

Pooled analysis, 2 Phase 3 RCT (APOLLO and LUNAR)

Adults with OAG or OHT. N=523 in latanoprostene (LBN) 0.024% QD X3 months; N=251 in timolol 0.5% BID[1], then open label LBN for 3 –9 months



LBN 0.024% Mean IOP (mm Hg)	n=558 18.9	n=553 18.2	n=552 18.1	n=561 18.6	n=555 17.9	n=556 17.8	n=561 18.7	n=555 17.9	n=556 17.8
Timolol 0.5% Mean IOP (mm Hg)	n=268 19.7	n=266 19.3	N=266 19.0	n=269 19.6	n=267 19.0	n=267 19.0	n=269 19.6	n=267 19.2	n=267 19.1
LS mean diff (95% CI)	-0.8 (-0.3, -1.3)	-1.1 (-0.6, -1.6)	-0.9 (-0.5, -1.3)	-1.0 (-0.5, -1.4)	-1.1 (-0.6, -1.5)	-1.1 (-0.7, -1.6)	-1.0 (-0.5, -1.4)	-1.3 (-0.8, -1.7)	-1.3 (-0.9, -1.8)

[1]Weinreb, Robert N., et al. "Latanoprostene Bunod 0.024% in Subjects With Open-angle Glaucoma or Ocular Hypertension: Pooled Phase 3 Study Findings." *Journal of glaucoma* 27.1 (2018): 7-15.

Vyzulta's Comparative Cost

Generic (Brand)	Strength	Package size	AWP Cost/unit 1/9/18	Cost/mL Cost/mo**
Single Entity Prostaglandin Analog Products Dosing is 1 drop in affected eye daily for each product				
Latanoprostene (Vyzulta)	0.02%	5 mL(brand)	$432	$86 $432
Bimatoprost (Lumigan)	0.03%	5 mL (generic)	$269	$53.83 $269
Latanoprost (Xalatan)	0.005%	2.5 mL (generic)	$24	$9.75 $49
Tafluprost (Zioptan)	0.0015%	30 single use (brand)	$220	N/A $441
Travoprost (Travatan Z)	0.004%	2.5 mL	$196	$79 $393

1. Cost data come from Lexi-Comp.
2. El Hajj Moussa, Wissam Georges, et al. "Comparison of Efficacy and Ocular Surface Disease Index Score between Bimatoprost, Latanoprost, Travoprost, and Tafluprost in Glaucoma Patients." *Journal of ophthalmology*2018 (2018).

Approval date: 12/18/17

Netarsudil (Rhopressa®) Ophthalmic

ONCE-DAILY rhopressa (netarsudil ophthalmic solution) 0.02%

- Indication: reduces IOP in open angle glaucoma or ocular hypertension
- MOA: a rho kinase inhibitor. Mechanism is unknown but it may reduce IOP by increasing the outflow of aqueous humor through the trabecular meshwork route.
- Dosed once each evening.
- AWP cost (5/15/18): $274.80/2.5mL

Netarsudil (Rhopressa®) Evidence

Primary Endpoint for both ROCKET-1 and -2 was IOP at 8am, 10am, and 4pm at wks 2, 6, and month 3.

- ROCKET-1: did NOT meet it primary efficacy endpoint demonstrating non-inferiority of IOP lowering vs BID timolol. Follow up trial: ROCKET-4.
- ROCKET-2: Netarsudil, both QHS and BID DID MEET non-inferiority compared to BID timolol.
  - Baseline IOP 20-25
- ROCKET-4: DID MEET non-inferiority vs BID timolol

Netarsudil (Rhopressa®) Evidence-ROCKET-1

TABLE 4. ROCKET-1: Mean Intraocular Pressure (mm Hg) by Visit: Primary[a] and Post Hoc[b] Efficacy Populations

	< 27 mm Hg (Primary)						< 25 mm Hg (Post Hoc)					
	Netarsudil		Timolol		Netarsudil − Timolol		Netarsudil		Timolol		Netarsudil − Timolol	
	N	Mean IOP	N	Mean IOP	Mean Difference	95% CI	N	Mean IOP	N	Mean IOP	Mean Difference	95% CI
Baseline												
8:00 AM	182	23.42	188	23.37	0.06	(−0.29, 0.41)	113	22.39	124	22.50	−0.11	(−0.39, 0.18)
10:00 AM	182	22.28	188	21.92	0.36	(−0.07, 0.79)	113	21.28	124	21.07	0.21	(−0.21, 0.64)
4:00 PM	182	21.78	188	21.45	0.33	(−0.15, 0.82)	113	20.62	124	20.52	0.10	(−0.36, 0.56)
Week 2												
8:00 AM	177	18.68	187	18.33	0.35	(−0.27, 0.96)	108	17.34	123	17.78	−0.44	(−1.10, 0.22)
10:00 AM	176	17.29	186	17.55	−0.26	(−0.87, 0.36)	107	16.18	122	16.98	−0.81	(−1.44, −0.17)
4:00 PM	176	17.24	186	17.70	−0.45	(−1.08, 0.17)	107	16.22	122	17.14	−0.92	(−1.58, −0.26)
Week 6												
8:00 AM	170	19.35	184	18.24	1.11	(0.42, 1.80)	105	17.85	121	17.81	0.05	(−0.68, 0.77)
10:00 AM	170	18.14	184	17.44	0.70	(0.04, 1.36)	105	16.88	121	16.96	−0.08	(−0.74, 0.58)
4:00 PM	170	17.86	183	17.71	0.15	(−0.52, 0.83)	105	16.57	120	17.26	−0.69	(−1.40, 0.02)
Month 3												
8:00 AM	157	19.81	181	18.47	1.33	(0.64, 2.03)	99	18.22	119	17.91	0.31	(−0.40, 1.02)
10:00 AM	158	18.92	181	17.96	0.96	(0.26, 1.66)	99	17.34	119	17.43	−0.09	(−0.82, 0.63)
4:00 PM	158	18.48	181	17.74	0.74	(0.07, 1.42)	99	17.02	119	17.37	−0.35	(−1.03, 0.34)

CI = confidence interval; IOP = intraocular pressure.
Difference from timolol and 2-sided CIs and *P* values are based on 2-sample *t* tests comparing netarsudil vs timolol.
[a]Primary efficacy population: per-protocol subjects with baseline IOP < 27 mm Hg.
[b]Post hoc efficacy population: per-protocol subjects with baseline IOP < 25 mm Hg.

Netarsudil (Rhopressa®) Evidence-ROCKET-2

TABLE 3. ROCKET-2: Mean Intraocular Pressure (mm Hg) by Visit: Primary Efficacy Population[a]

	Netarsudil q.d.		Netarsudil b.i.d.		Timolol		Netarsudil q.d. – Timolol		Netarsudil b.i.d – Timolol	
Day and Time	N	Mean IOP	N	Mean IOP	N	Mean IOP	Mean Difference	95% CI	Mean Difference	95% CI
Baseline										
8:00 AM	129	22.54	132	22.55	142	22.54	0.00	(−0.25, 0.25)	0.01	(−0.24, 0.26)
10:00 AM	129	21.29	132	21.27	142	21.27	0.02	(−0.37, 0.41)	−0.01	(−0.40, 0.38)
4:00 PM	129	20.43	132	20.56	142	20.71	−0.28	(−0.71, 0.14)	−0.15	(−0.58, 0.29)
Week 2										
8:00 AM	127	18.07	122	17.21	142	17.69	0.37	(−0.25, 0.99)	−0.48	(−1.19, 0.22)
10:00 AM	126	16.72	120	16.35	141	16.93	−0.21	(−0.82, 0.41)	−0.57	(−1.24, 0.09)
4:00 PM	126	16.68	118	15.65	141	16.83	−0.15	(−0.75, 0.46)	−1.18	(−1.82, −0.54)
Week 6										
8:00 AM	122	17.95	111	17.64	141	17.46	0.49	(−0.13, 1.12)	0.17	(−0.51, 0.86)
10:00 AM	120	16.95	106	16.28	141	16.63	0.32	(−0.31, 0.95)	−0.34	(−1.02, 0.33)
4:00 PM	120	17.00	106	15.75	141	16.60	0.40	(−0.22, 1.02)	−0.85	(−1.53, −0.17)
Month 3										
8:00 AM	116	18.24	91	17.58	140	17.47	0.77	(0.03, 1.50)	0.11	(−0.64, 0.86)
10:00 AM	114	17.03	88	16.94	140	16.92	0.10	(−0.59, 0.80)	0.02	(−0.72, 0.77)
4:00 PM	114	17.13	88	16.51	139	16.95	0.18	(−0.55, 0.91)	−0.44	(−1.16, 0.27)

CI = confidence interval; IOP = intraocular pressure.
Difference from timolol and 2-sided CIs and *P* values are based on 2-sample *t* tests comparing netarsudil vs timolol.
[a]Primary efficacy population: per-protocol subjects with baseline IOP < 25 mm Hg.

Breast Cancer

Approval date: 9/27/17

Abemaciclib (Verzenio®) 50, 100, 150, 200mg tablets

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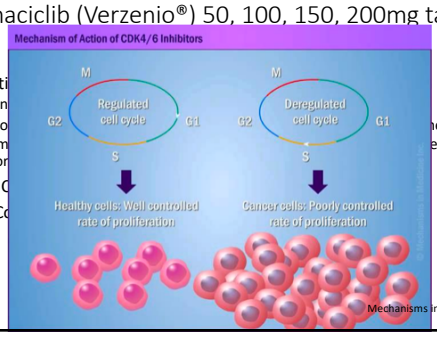
- MOA: C
- AWP Co



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Mechanisms in Medicine, 2014.

Abemaciclib (Verzenio) Evidence				
Key Trials	**Characteristics**	**Treatment**	**Comparator**	**Harms:D/C 2º AEs**
MONARCH-1 Phase II, **single arm**, open label	Median age: 58 ECOG=1 : 44.7% Median lines of ST: 3 (Disease progression on HT; also had received ≤2 prior CT for advanced or metastatic disease)	ABE (n=132) Median f/u: 18 m	None	7.6%
		PFS: 6.0 m; Median OS: 22.3 m		
		ORR: 19.7%	None	
MONARCH-2 **DB, RCT** **Phase III**	Median age: 59, ECOG=1: 39.5% Prior CT: 59.9%, Prior HT: 70.9% (Disease progression on HT)	ABE + FUL (n=446) Median f/u: 16.4 m	Placebo+FUL (n=223) Median f/u: 16.4 m	15.9% SAEs: 22.4% Tx-related deaths: 3 (0.7%)
		PFS HR: 0.553 (95% CI 0.449-0.681, p<0.001)		
		Median OS: Not yet mature Median PFS:16.4 m ORR: 72.2%	**Median OS: Not yet mature** Median PFS: 9.3 m ORR: 56.1%	
MONARCH-3 **DB, RCT** **Phase III**	Median age: 63, ECOG=1: 41.5% Prior CT: 38.1%, Prior HT: 45.7% (No prior therapy for advanced or metastatic disease)	ABE + AI (n=328) ORR 59% Median f/u: 17.8 m **Median PFS not reached**	Placebo + AI (n=165) ORR 44% P=0.004 Median f/u: 17.8 m **Median PFS=14.7m**	19.6% Tx-related deaths: 8
		PFS HR: 0.54 (95% CI, 0.41-0.72, p=0.000021)		
		Median OS: Not yet mature Median PFS: not reached ORR: 48.2%	**Median OS: Not yet mature** Median PFS: 14.7 m ORR: 34.5%	

Mantle Cell Lymphoma

Approval date: 10/31/2017

Acalabrutinib (Calquence®)

CALQUENCE (acalabrutinib) 100 mg capsules

- Indication: Treatment of mantle cell lymphoma (MCL) in patients who received ≥1 prior therapy
- MOA: a selective and irreversible 2nd generation Bruton's tyrosine kinase (BTK) inhibitor
- AWP Cost: $16,877/month; treat to dz progression or toxicity

Ibrutinib (Imbruvica®) is the other drug in the class of BTK inhibitors.

Acalabrutinib (Calquence®) Evidence

Trials	Patients	Tx Arms	Efficacy
Trial LY-004 **Phase 2** **ECOG 0-2** **Single-arm**	N=124 pts with MCL w/ prior tx (52% CHOP-based, 34% ARA-C based) 93% ECOG 0-1. 18% prior SCT. Prior BTK inhibitor excluded	acalabrutinib 100 mg BID until progression or unacceptable tox.	ORR* - 81% CR - 40% PR – 40% Duration of response NR

*ORR per 2014 Lugano Classification.
ORR=overall response rate, CR=complete response, PR=partial response

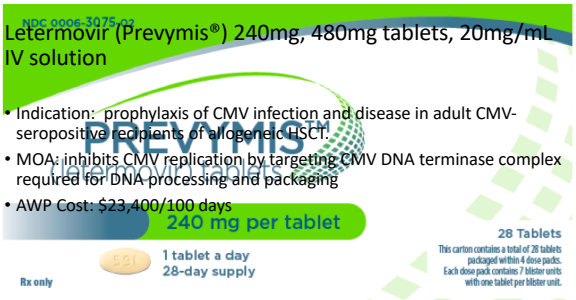
Current FDA-approval is based on overall response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

Misc. Infectious Disease

Approval date: November 2017

Letermovir (Prevymis®) 240mg, 480mg tablets, 20mg/mL IV solution

- Indication: prophylaxis of CMV infection and disease in adult CMV-seropositive recipients of allogeneic HSCT.
- MOA: inhibits CMV replication by targeting CMV DNA terminase complex required for DNA processing and packaging
- AWP Cost: $23,400/100 days



Letermovir Evidence

PREVYMIS® (letermovir)
240 mg, 480 mg tablets
Injection 20 mg/mL

Study	Pt population	Endpoints; CMV criteria	Methods	Results (tx v. placebo)

Letermovir
 	
Phase 3
	CMV sero+, undetectable level of CMV at baseline, allogeneic HSCT N=570	1': % of pts w/ clinically sig CMV infection, d/c trial or missing data through 24w after transplant.
		
		Clinically significant – initiation of preemptive tx or CMV disease
			480mg or 240mg QD (if on concomitant cyclosporine) vs. placebo x14wks
			
			Letermovir group n=325 placebo n=170
				• 1' at 24w: 37.5% vs 60.6% (p<0.001) sig in both high and low risk categories.
				• Clinically significant CMV infection:
				  • 17.5% vs 41.8%
				  • (1.5% vs 1.8% w/ CMV disease)
				• Mortality at wk24 postTx:
				  • 10.2% vs 15.9%
				  (95%CI 6.8 to 13.6)
				• Mortality at week 48:
				  • 20.9% vs 25.5%
				  (non sig)

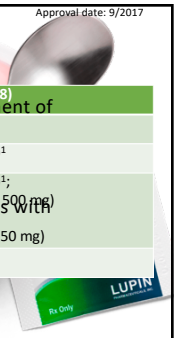
Marty, Francisco M., et al. "Letermovir prophylaxis for CMV in hematopoietic-cell transplantation." *NEJM.* 377.25 (2017): 2433-2444.

Secnidazole (Solosec®)

Approval date: 9/2017

- Indication: as a single packet dose for the treatment of bacterial vaginosis in women.
- MOA: a 5-nitroimidazole antibiotic that interferes with bacterial DNA systhesis of susceptible isolates.

	Regimen	AWP Cost (2/2018)
Secnidazole	2 gram packet	$324 per packet
Metronidazole tab	500 mg BID x 7 days	$9.68 (14 tablets)[1]
Metronidazole tab	750 mg QD x 7 days	$5.45 (14 tablets)[1]; **$4.84 (7 tab @ 500 mg) & $0.61 (7 tabs @ 250 mg)
Metronidazole**	2 g single dose (4 tablets)	$2.77[1]



**This treatment regimen is not in Lexicomp but is in package insert.
1. Lexicomp "Metronidazole AWP Pricing: US" (accessed February 16, 2018)

Secnidazole (Solosec®) Evidence

Study	Methods	Dosing	Subjects	Endpoints	Results
Schwebke et al.[1] Trial 2 PI	Phase 3 MC, P, RCT, DB	2g secnidazole vs placebo	189 BV pts	Clinical Outcome Responders (Cure*)	Overall: 2g secnidazole= 53.3% vs placebo 19.3%, (P<0.001) Black race: 2g secnidazole = 45.8% vs placebo 20.7% (P value =0.025) All others: 2g secnidazole = 62.5% vs placebo 17.9% (P<0.001)
Bohbot, et al.[2] (NI trial)	National, MC, P, RCT, DB, DD, NI trial	2g secnidazole vs metronidazole 500 mg BID x 7 days	577 BV pts secnidazole vs metronidazole	Clinical Cure (Cure*)	2 g secnidazole is at least as effective with a 10% noninferiority margin as metronidazole. (D14 cure = -0.097, D28 cure = -0.082)

Overall therapeutic success-D28	ITT	mITT	PP
Sec	58.3%	60.1%	63.4%
Met	57.8%	59.5%	62.9%
95%CI	-0.076 to 0.085	-0.082 to 0.094	-0.087 to 0.098

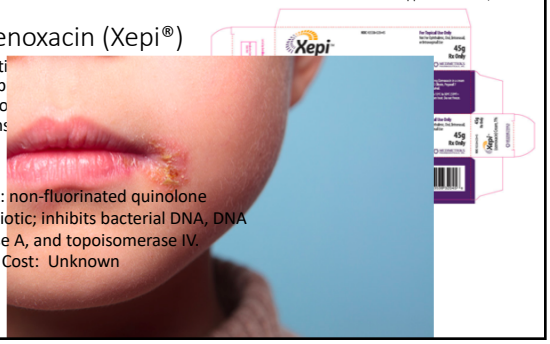
Study	Methods	Dosing	Subjects	Endpoints	Results
Thulkar, et al.[3]	P, RCT	2g single dose of metronidazole, secnidazole, tinidazole, or 1.5g ornidazole	N=344 BV pts	Amsel's Criteria**	

Drug	Cure rate @ w4:	P value vs metron.
Metronidazole	77.9%	
Tinidazole	97.7%	P<0.001
Secnidazole	80.2%	P=0.71
Ornidazole	97.7%	P<0.001

1. Schwebke, J. R., Morgan, F. G., Koltun, W., & Nyirjesy, P. (2017). A phase-3, double-blind, placebo-controlled study of the effectiveness and safety of single oral doses of secnidazole 2 g for the treatment of women with bacterial vaginosis. *American Journal of Obstetrics and Gynecology*, 277(6), 678.e1-678.e9. https://doi.org/10.1016/j.ajog.2017.08.017
2. Bohbot, J.-M., Vicaut, E., Fagnen, D., & Brauman, M. (2010). Treatment of Bacterial Vaginosis: A Multicenter, Double-Blind, Double-Dummy, Randomised Phase III Study Comparing Secnidazole and Metronidazole [Research article]. https://doi.org/10.1155/2010/705902
3. Thulkar, Jyoti, Alka Kriplani, and Nutan Agarwal. "A comparative study of oral single dose of metronidazole, tinidazole, secnidazole and ornidazole in bacterial vaginosis." *Indian journal of obstetrics* 44.2 (2012).

Approval date: 12/2017

Ozenoxacin (Xepi®)



- Indicati
  to Stap
  Strepto
  months
- MOA: non-fluorinated quinolone antibiotic; inhibits bacterial DNA, DNA gyrase A, and topoisomerase IV.
- AWP Cost: Unknown

Ozenoxacin (Xepi®) Evidence

- 2 trials, n=723 total, age 2m and older
- Xepi or placebo BID X5d
- Overall clinical success=no need for additional antimicrobial therapy and absence/reduction in clinical signs and symptoms at day 6-7

	Trial 1		Trial 2	
	XEPI	Placebo	Xepi	Placebo
	N=155 N (%)	N=156 N (%)	N=206 N (%)	N=206 N (%)
Clinical success	54 (34.8)	30 (19.2)	112 (54.4)	78 (37.9)
	P=0.002		P=0.001	
Clinical failure	98 (63.2)	120 (76.9)	91 (44.2)	121 (58.7)
Unable to determine	3 (1.9)	6 (3.8)	3 (1.5)	7 (3.4)

Per Dailymed.nlm.nih.gov. Searchterm: ozenoxacin.
Gropper, Savion, et al. "Ozenoxacin 1% cream in the treatment of impetigo: a multicenter, randomized, placebo-and retapamulin-controlled clinical trial." *Future microbiology* 9.9 (2014): 1013-1023.

Question: Which new drug effectively prevents CMV in allogeneic stem cell transplant?

A. Prevymis
B. Biktarvy
C. Xepi
D. Trogarzo
E. Solosec

Question: Which new drug effectively prevents CMV in allogeneic stem cell transplant?

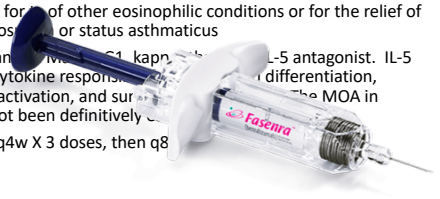
A. Prevymis
B. Biktarvy
C. Xepi
D. Trogarzo
E. Solosec

Eosinophilic Asthma

Approval date: 11/14/17

Benralizumab (Fasenra®) 30mg/mL SC inj.

- Indication: in asthma as add-on maintenance treatment of severe asthma in adults and children 12+ with an eosinophilic phenotype
- Not indicated for [illegible] of other eosinophilic conditions or for the relief of acute bronchos[illegible] or status asthmaticus
- MOA: a human[illegible]G1 kapp[illegible]L-5 antagonist. IL-5 is the major cytokine respons[illegible] differentiation, recruitment, activation, and sur[illegible]The MOA in asthma has not been definitively [illegible]
- Dose: 30mg q4w X 3 doses, then q8



Benralizumab (Fasenra®)

Brand	Generic	MOA	FDA approval	Dose	Route	Frequency	AWP cost 5/14/18	1 year AWP
Fasenra	Benralizumab	IL-5 antag	• Add-on maintenance for severe asthma age ≥12 with eosinophilic phenotype	30mg	SC	q4w X 3 doses, then q8w	$5702/ dose	$45,620
Nucala	Mepolizumab	IL-5 antag	• Add-on maintenance for severe asthma age ≥12 with eosinophilic phenotype	100 mg-asthma	SC	Q4w	$3442/ dose	$41304
			• Eosinophilic granulomatosis	300mg q4w-EG			$10327/ dose	$123924
Xolair	Omalizumab	IgE antag on mast cells	• Mod-sev persistent asthma, age ≥6 w/ + skin test or in vitro reactivity to a perennial aeroallergen & sxs not controlled w/ ICS • Chronic idiopathic urticuria age 12+ w/ symptoms despite H1 antihistamines.	Depends	SC	Q2W or Q4W	$1301/ 150mg (1)	$67652 dosed 300mg q2w. $15,612 dosed 150mg q4w

Sly Syndrome

Approval date: 11/2017

Vestronidase alfa-vjbk (Mepsevii®) IV injection

- Indication: treatment of mucopolysaccharidosis VII (MPS VII, Sly syndrome)
- MOA: recombinant human beta-glucuronidase; replaces missing enzyme by IV injection every two weeks.

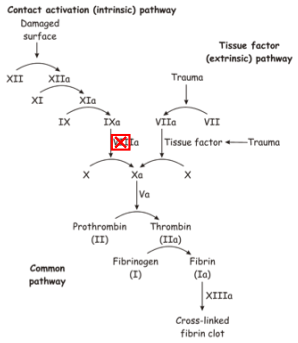
Drug	AWP cost (5/15/18) $507.60 per mL 10mg/5mL	AWP cost q2w (10kg child) dose 4mg/kg	AWP cost q2w (50kg teen) Dose 4mg/kg
Vestronidase Alfa-VJBK	Vial=$2538	40mg; $10,152/dose (infusion)	200mg/dose; $50760 (infusion)
Cost/year		$263,952	$1,319,760

Mepsevii™
(vestronidase alfa-vjbk)
injection, for intravenous use

- Boxed warning: Anaphylaxis, as early as the 1st dose. Observe patient during and for 60 minutes after infusion.

Evidence from Package Insert:
Trial 301:
Only 10 of 12 patients were evaluable for the outcome of 6MWT.
3 patients improved. The PI did not state the trial was blinded. Because of the small numbers, no stats were given.
Liver and spleen volumes were measured; did not change with treatment.

Hemophilia A w/ Inhibitors



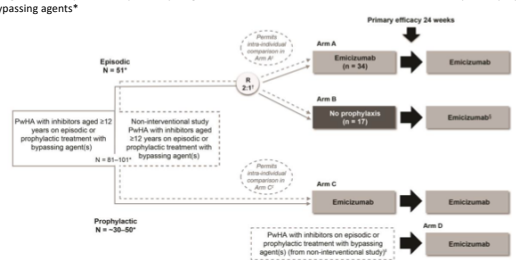
Approval date: 11/2017

Emicizumab-kxwh (Hemlibra®)

- Indication: Hemophilia A, prophylaxis to prevent or reduce the frequency of bleeding episodes in congenital factor VIII deficiency with factor VIII inhibitors
- MOA: a humanized monoclonal modified immunoglobulin G4 (IgG4) antibody with a bispecific factor IXa- and factor X-directed Ab, that bridges activated factor IX & X to restore the function of missing activated factor VIII that is needed for hemostasis.
- Dose: Given 3mg/kg QW X 4w, then 1.5mg/kg QW thereafter.

Emicizumab-kxwh (Hemlibra®)-HAVEN-1

Congenital hemophilia A (any severity), high factor VIII inhibitor titer (≥5 Bethesda units/mL), on episodic prophylactic bypassing agents*



*Bypassing agents are blood products that bypass inhibited factors. Two are available: activated Prothrombin Complex Concentrate (FEIBA), recombinant Factor VIIa (NovoSeven).

Oldenburg, Johannes, et al. "Emicizumab prophylaxis in hemophilia A with inhibitors." *New England Journal of Medicine* 377.9 (2017): 809-818.

Emicizumab-kxwh (Hemlibra®)-HAVEN-1

HAVEN-1 Results	Population	Annualized Bleeding Rates # events (95%CI)
Randomized:		
Arm A	Prior episodic BPA treatment	2.9 (1.7, 5.9); 63% had no events/24w
Arm B	Prior episodic BPA treatment	23.3 (12.3, 43.9); 6% had no events/24w
Nonrandomized:		
Arm C	Prior prophylactic BPA	5.1 (2.28, 11.22); 69.4% w/ no events/24w
Arm D	Prior BPA proph or treatment	Data not available

HAVEN-2 (pediatric population) results not yet published.

*Bypassing agents (BPA) are blood products that bypass inhibited factors. Two are available: activated Prothrombin Complex Concentrate (FEIBA), recombinant Factor VIIa (NovoSeven).

Emicizumab-kxwh (Hemlibra®)-Cost

Dosing:	Strength	Cost (AWP)	Cost Per Yr for 75 kg pt. ($199.04/mg emicizumab)
3 mg/kg SubQ QW X 4w, then 1.5 mg/kg QW	30 mg/mL 60 mg/0.4 mL 105 mg/0.7 mL 150 mg/mL	$3,571.28 - $17,856.43	1st year - $1,253,952.00 2nd year - $1,164,384

Cost effective? Yes. Because of fewer bleeds needing costly treatment with FEIBA and NovoSeven, an estimated annual savings of $706 million per year in people 12+ and $146million per year for kids under 12.

ICER. https://icer-review.org/wp-content/uploads/2017/08/ICER_Hemo_RAAG_041618.pdf

Diabetes

Approval date: 12/5/17

Semaglutide (Ozempic®)

OZEMPIC®
semaglutide injection

- Indication: T2DM as adjunct to diet and exercise to improve glycemic control in adults with T2DM
- MOA: a glucagon-like peptide-1 receptor agonist (GLP-1 agonist); it increases glucose-dependent insulin secretion, decreases inappropriate glucagon secretion, and slows gastric emptying. Increases first- and second-phase insulin secretion.

Summary of FDA approved DM drugs

Approved to lower HbA1c		FDA-Approved to REDUCE CV risk	
Insulin & analogs	Multiple products		
Biguanides	Metformin		
Sulfonylureas	Chlorpropamide, Glipizide Glimepiride, glyburide		
Thiazolidinediones	Rosi-, pioglitazone		
Meglitinides	Repaglinide, Nateglinide		
Alpha glucosidase inhibitors	Acarbose, Miglitol		
DPP4 inhibitors	Sita-, saxa-, alo-, lina-gliptin		
GLP1 agonists	Exenatide Liraglutide Albiglutide Dulaglutide Lixisenatide Semaglutide	Liraglutide	Lower rate of 1st composite: CV death, NFMI, NF stroke
SGLT2 inh.	Canagliflozin Dapagliflozin Empagliflozin	Empagliflozin	Lower rate of composite: CV death, NFMI, NF stroke
Amylin analogs	Pramlintide		

Semaglutide (Ozempic®)-Evidence

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Semaglutide (Ozempic®)-Evidence-SUSTAIN-6

Primary Analysis of MACE-Number of events—Post Hoc analysis; P-values not adjusted for multiplicity

	Semaglutide N=1648 Person-years = 3408.2	Placebo N=1649 Person-years = 3401.1	Hazard Ratio (95%CI)
MACE (FAS)	108 [3.2]	146 [4.3]	0.74 (0.58, 0.95)
Cardiovascular death	44	46	0.98 (0.65, 1.48)
Non-fatal MI	47	64	0.74 (0.51, 1.08)
Non-fatal Stroke	27 [0.79]	44 [1.3]	0.61 (0.38, 0.99)

[ ] indicates incidence rate per 100 person-years

Source: https://www.accessdata.fda.gov, accessed 5/21/18.

Semaglutide (Ozempic®)-Harms-SUSTAIN-6

Diabetic retinopathy complications

	Semaglutide N=1648 Person-years = 3408.2	Placebo N=1649 Person-years = 3401.1	Hazard Ratio (95%CI)
Diabetic Retinopathy	50	29	1.76 (1.11, 2.78)
Need for retinal photocoagulation	38	20	
Vitreous Hemorrhage	16	7	
Need for intravitreal agents	16	13	
Onset of diabetes-related blindness	5	1	
By Retinopathy at baseline			
Yes (n=969; 29%	42/501 (8.2%)	24/459 (5.2%)	
No/unknown (N=2328; 71%)	8/1138 (0.7%)	5/1190 (0.4%)	

Source: https://www.accessdata.fda.gov, accessed 5/21/18.

Ertugliflozin (Steglatro®)

Approval date: 12/2017

- Indication: Adjunct therapy to diet and exercise to improve glycemic control in T2DM
- MOA: SGLT2 inhibitor
- AWP Cost: $628.20/30 days

Ertugliflozin (Steglatro®) Evidence

Key Trials	Primary endpoint- Mean HbA1C reduction vs comparator, W26
VERTIS Mono	
5mg	0.99%, p<0.001
15mg	1.16%, p<0.001
Placebo	---
VERTIS Factorial	
Ertug 5mg, 15mg	1%, 1.1%
Sitagliptin	1.1%
Combo	1.5%

Key Trials	Primary endpoint- Mean HbA1C reduction vs comparator, W26
VERTIS SITA2	
Ertug 5mg	0.69%
Ertug 15mg	0.76%
Plac	---, p<0.001 vs either
VERTIS MET	
Ertug 5mg +Met	0.7%
Ertug 15mg+Met	0.9%
Plac	0%
	P<0.001

Across 7 Phase 3 clinical trials with STEGLATRO, non-traumatic lower limb amputations were reported in 1 (0.1%) patient in the comparator group, 3 (0.2%) patients in the STEGLATRO 5 mg group, and 8 (0.5%) patients in the STEGLATRO 15 mg group. A causal association between STEGLATRO (ertugliflozin) and lower limb amputation has not been definitively established.

Question: Which drug used to treat T2DM has the FDA approval for reducing CV risk?

A. Metformin
B. Empagliflozin
C. Semaglutide
D. Insulin

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Shock

Approval date: 12/21/17

Angiotensin II (Giapreza®)

- Indication: To increase BP in adults with septic or other distributive shock
- MOA: It stimulates the RAAS that causes vasoconstriction and increases aldosterone release, which raises BP.
- Dosed: Continuous IV infusion with intensive monitoring. 20-80 ng/kg/min
- AWP cost $1800/vial

Angiotensin II (Giapreza®) Evidence-ATHOS-3

N=321 with shock and who remained hypotensive despite fluid and vasopressors.
Targeted MAP of >75mmHg during first 3 hours, then targeted MAP 65-70 mmHg to 48 hours.

Arms	1` endpoint: % of patients who achieved MAP>75mmHg or a >10MMHg increase in MAP without increase in vasopressors at 3 hours	P-value
Angiotensin II	70%	P<0.0001
Placebo	23%	

AEs: thromboembolic events 12.9% vs 5.1%

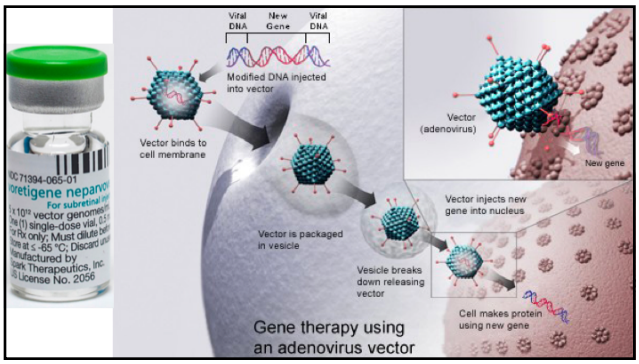
Giapreza PI, accessed 5/18/18.

Gene therapy

FDA-approved: 1/12/2018

Voretigene naparovec (Luxturna®)

- Indication: an adeno-associated virus vector-based gene therapy indicated for the treatment of patients with confirmed biallelic RPE65 mutation-associated retinal dystrophy
- AWP Cost: $425,000 per eye; $850,000 both eyes.



Voretigene neparvovec-rzyl (Luxturna®) Evidence

Study	Methods	Dosing	Subjects	Endpoints	Results
Efficacy and safety of voretigene neparvovec in patients with RPE65-mediated IRD ClinicalTrials.gov #NCT00999609	R, C, OL, P3 trial	Bilateral, subretinal injection of 0.3mL	31 subjects Intervention (n=21) Control (n=10)	1-year change in MLMT performance	At 1 year, mean bilateral MLMT change score was 1.8 (SD 1.1) light levels in the intervention group versus 0.2 (1.0) in the control group (difference of 1.6, 95% CI 0.72–2.41, p=0·0013).

Questions?

UAMS College of Pharmacy