# PERSPECTIVE ON THE RXPIPELINE

Understanding changes in the medication market and their impact on cost and care.

EnvisionRx continuously monitors the drug pipeline. As treatment options change, we evaluate and share our perspective on the clinical benefits, cost-effectiveness and overall impact to payers and patients. Our Perspective on the Rx Pipeline report provides ongoing actionable insights from our team of clinical experts and the steps we are taking to protect and improve plan performance.

## Included in this Edition

- Drug Costs Alone Are Not Always the Best Way To Evaluate HIV Therapy Options
- New Therapeutic Class Could Bring Relief to Migraine Sufferers, But At What Cost?



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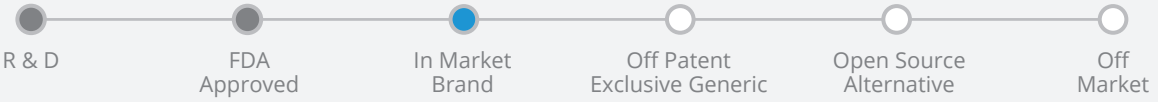
# HIV MANAGEMENT

## Drug Costs Alone Are Not Always the Best Way to Evaluate HIV Therapy Options

An analysis of HIV therapies.

**PIPELINE STAGE**




### TIMING

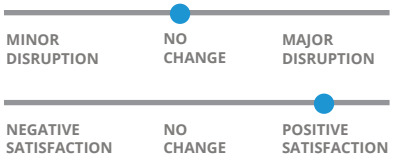
*When will payers be impacted?*


### CLINICAL EFFECTIVENESS

*Compared to available options, is this drug better for treatment?*


### PATIENT EXPERIENCE

*Will this positively or negatively impact members?*




### PAYER IMPACT

*How will this influence Rx spend?*


### Situation Summary

In 2014, there were an estimated 37,600 new HIV infections.[1] That number is down from 2008, however, there are still an estimated 1.1 million people in the United States living with HIV as of the end of 2015.[1]

Treatment with HIV medications is described as antiretroviral therapy (ART). There have been decades of advances in ART; however, there is still no cure for HIV, only virus suppression, which allows people with HIV to live longer and healthier lives. HIV has, therefore, become a chronic condition that can be costly to treat. The Centers for Disease Control and Prevention (CDC) estimated that the lifetime treatment cost for HIV was $379,688 in 2010.[1]

While current antiretroviral therapy is safe and effective, there is always room for improvement; with less pills per regimen, smaller pill sizes, less frequent dosing, fewer side effects and drug interactions, and stronger resistance profiles. Therefore, there are a number of HIV medications in the pipeline. There were two new, fixed-dose combination, single tablet regimens approved within the last quarter, and there are 12 compounds to treat HIV within phase II clinical trials. Some have novel mechanisms of action, and some are new combinations of previously approved drugs to help lower the pill burden.

Typically, with advances in treatment comes an increase in cost. While it's common to do a direct comparison of therapies using the drug cost alone, EnvisionRx examines all sides of the complex HIV therapy landscape in order to evaluate cost effectiveness and determine where spend control should or shouldn't be managed.

***Available HIV Therapies:*** Since 1987, the HIV pipeline has seen dramatic shifts as new classes were launched and innovations were made. There are currently 25 antiretroviral medications within roughly six classes based



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# HIV MANAGEMENT

on viral target, with a focus on safety and simplicity to promote medication adherence. Since 1990, when it was discovered that combining antiretroviral therapies led to a decrease in death from HIV/AIDS, there has only been a small availability of fixed-dose combinations. Original therapies for HIV/AIDS could have reached a pill burden of up to 15 tablets per day. Newly developed products reduce the pill burden, requiring the patient to take as few as one or two tablets daily. The first single pill regimen, approved in 2006, was Atripla®, which was followed shortly by Stribild®, Triumeq®, Genvoya®, Odefsey® and Complera®.

The most recent of these approvals includes Juluca (dolutegravir and rilpivirine), which is intended to be a complete regimen for those patients who are treatment experienced and are already virologically suppressed.[2] Juluca, approved in late 2017, provides the option to replace a patient's current regimen containing three or more agents with a single, fixed-dose combination of two agents, decreasing the pill burden and likelihood of potential side effects, without compromising the therapeutic effect.

Biktarvy® (bictegravir/emtricitabine/tenofovir alafenamide) was approved by the Food and Drug Administration (FDA) in February 2018. A combination of bictegravir (50mg) (BIC), a novel integrase strand transfer inhibitor (INSTI), and emtricitabine/tenofovir alafenamide (200/25mg) (FTC/TAF), Biktarvy can be a potential treatment of HIV-1 infection in treatment-naive adults.[3] This fixed-dose combination will provide patients with another option for simple, convenient dosing, which meets clinical guidelines for initial therapy in most HIV patients.

Trogarzo™ (ibalizumab), a humanized monoclonal antibody, approved by the FDA on March 6, 2018, is the first HIV therapy with a new mechanism of action in nearly ten years. This treatment will offer a new add-on option for those patients with multi-drug resistant HIV.[4] After the IV-infused loading dose, ibalizumab should be administered every two weeks, which offers the first infrequent adjunct therapy.

***Evaluation of the ART Landscape:*** While it seems intuitive to block the more expensive branded products and prefer the generic, multiple product regimens that are still effective, there is evidence against that managed care strategy. By following best practice guidelines, patients will typically need at least one brand, single-source drug to achieve viral suppression.[5] Additionally, use of generics within the antiretroviral space can increase a patient's pill burden by three to four times.

An increased pill burden can have a negative effect on adherence. While treatment adherence is considered important for any disease state, in HIV, non-adherence can negatively impact viral suppression, which can create an acute health condition for the

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# HIV MANAGEMENT

## PAYER ACTION PLAN

- **Review Plan**
  EnvisionRx recommends that plan sponsors review their coverage policies on HIV therapies to ensure the highest quality care while controlling costs. We recommend instituting prior authorizations and quantity limits in certain instances to decrease fraud and waste and ensure patients are receiving the appropriate therapy. We also recommend use of an HIV-specialized pharmacy to increase adherence, manage side effects, and provide education and support for members.

patient. In the U.S., the adherence rate shown in a meta-analysis was observed to be 55%.[6] Studies have found the standard goal for adherence in HIV patients ranges from 80% to 100%. In a study published in 2012 by Sax et al, a treatment adherence rate of 95% or higher was observed in approximately 47% of patients taking one pill a day, versus 41% in patients taking two pills a day, and 34% for patients taking three or more pills a day.[7] Hospitalization risk was also found to be lower in patients taking only one pill per day.

The generic pipeline is sparse at best, and represents only a small percentage of the current HIV market share, so the impact is expected to be minimal. Also, with HIV being a more complicated disease state to treat, there are other barriers that can reduce the cost-control opportunity. Clinical guidelines can change quickly so that when the generic is ready to launch, the drug may no longer be seen as an appropriate choice of therapy. In this class specifically, there are political and special interest pressures that can force regulations with mandates and managed care limits.

### Impact to the Pharmacy Care Experience

***Formulary:*** The EnvisionRx Standard Formulary has established both fixed-dose and brand HIV products in a non-preferred status. Quantity limits have been instituted for appropriate therapy levels and to deter potential fraud and waste from HIV patients sharing therapies. We have also implemented prior authorization limits for those HIV therapies in which patients must meet specific criteria to match the FDA-approved indication. By limiting prior authorization criteria to only those HIV therapies with potential for off-label use or safety concerns if used inappropriately, EnvisionRx can minimize disruption and still maintain cost controls around appropriate antiretroviral therapy.

***Pharmacy Network:*** EnvisionRx strongly encourages that HIV therapies are dispensed through an HIV-specialized pharmacy. HIV-specialized pharmacies can be found in a community pharmacy setting or a mail order/specialty pharmacy setting. These pharmacies have been found to be effective avenues for assisting patients to achieve a higher adherence rate with HIV regimens.[8] Clinical research has demonstrated the value of HIV-specialized pharmacies over traditional pharmacies; therefore, clients should consider implementing policies to encourage the use of such pharmacies for care of their HIV patients. While there are legal requirements at many state levels restricting the mandate of HIV therapies being filled at specific sites, we can work to encourage patients to understand why an HIV-specialized pharmacy would help meet their unique needs.

***Member Engagement:*** Members should work with their prescribers to continue on their current regimen or move to a

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# HIV MANAGEMENT

newer therapy with a lower pill burden or fewer side effects, which can potentially provide an increased quality of life. Members are also encouraged to work with specialty pharmacies that offer assistance with medication adherence and provide education on side effects.

***Clinical Support:*** EnvisionSpecialty offers an HIV clinical program where pharmacists provide drug utilization reviews and intervention protocols for any patient who reports side effects, missed doses, or any other complications from the disease or treatment. The pharmacist-led HIV clinical assessment contains items such as:

- Missed dose tracking and adherence education
- Quality of life evaluation
- Patient support systems at home
- Impact on daily living
- Side effect evaluation, education and management
- Dose optimization and administration
- HIV disease education (e.g., symptoms, transmission, monitoring, complications, treatment, drug resistance, PrEP and PEP discussions)
- Linking with drug manufacturers and support websites

## *Sources*

[1] Cdc.gov. (2018). Basic Statistics | HIV Basics | HIV/AIDS | CDC. [online] Available at: https://www.cdc.gov/hiv/basics/statistics.html [Accessed 7 Mar. 2018].

[2] Juluca [package insert]. Research Triangle Park, NC: GlaxoSmithKline.; 12/2017.

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[5] Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV. Department of Health and Human Services. Available at http://www.aidsinfo.nih.gov/ContentFiles/AdultandAdolescentGL.pdf. [Accessed 7 Mar. 2018].

[6] Schaecher, Kenneth L. MD, FACP, CPC (2013).The Importance of treatment adherence in HIV. Am J Manag Care. 2013;19(12 suppl):S231-S237.

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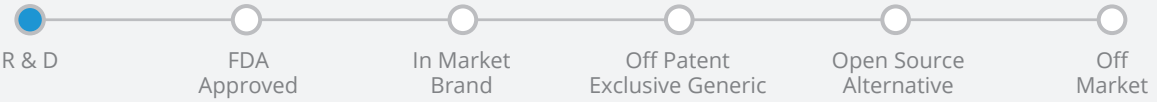
[8] Hirsch, J., Gonzales, M., Rosenquist, A., Miller, T., Gilmer, T. and Best, B. (2011). Antiretroviral Therapy Adherence, Medication Use, and Health Care Costs During 3 Years of a Community Pharmacy Medication Therapy Management Program for Medi-Cal Beneficiaries with HIV/AIDS. Journal of Managed Care Pharmacy, 17(3), pp.213-223.

# CALCITONIN GENE-RELATED PEPTIDE (CGRP) INHIBITORS

## New Therapeutic Class Could Bring Relief to Migraine Sufferers, But At What Cost?

The pros and cons of the calcitonin gene-related peptide (CGRP) inhibitors class.

**PIPELINE STAGE**

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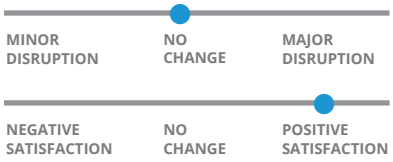


### PAYER IMPACT

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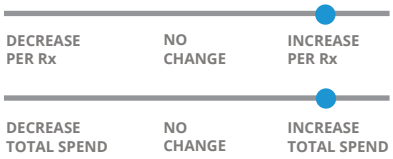


### Situation Summary

Migraines are a common disorder that can be debilitating and have a severe negative impact on a patient's quality of life and productivity. A 2015 article by the American Headache Society (AHS) reported that migraines and severe headaches affect about 14% of adults in the United States.[1] The same article also referenced that headaches were the fourth leading cause of emergency department visits in 2009-2010.[1]

Another recent study concluded that migraine treatment contributes over $9 billion a year to healthcare expenditures.[2] However, preventative medications for chronic migraine have remained an unmet need. This is because none of the commonly used treatments were researched and developed specifically for migraines, consisting of beta blockers (e.g., metoprolol and propranolol), antidepressants (e.g., amitriptyline and venlafaxine), and anti-seizure medications (e.g., valproate and topiramate). These can be effective at preventing migraine attacks, with 50% of patients experiencing a 50% reduction in migraine episodes; however, the high doses required often lead to intolerable adverse events requiring the medication to be discontinued.[3]

Migraine therapy is about to change though, with a new class of medications being developed known as calcitonin gene-related peptide (CGRP) inhibitors. Inhibiting the calcitonin gene-related peptide pathway represents a novel and targeted approach to chronic migraine prevention. Early clinical trial data has shown some promise in decreasing the amount of migraine days a patient may experience and is cause for cautious anticipation.

Due to the ineffectiveness of existing migraine preventative therapies and the number of patients affected by chronic migraines, there is potential for high utilization of CGRP inhibitors. While not priced astronomically high



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# CALCITONIN GENE-RELATED PEPTIDE (CGRP) INHIBITORS

(estimated at $8,000–$14,000 per year), as compared to recent approved therapies for other diseases, the new treatment could attract a large number of migraine sufferers, and plan sponsors could see a significant financial impact. Alternatively, preventing migraines from occurring can greatly improve quality of life and may decrease overall expenditures on other healthcare costs (e.g., emergency room visits, primary care visits and medications prescribed to treat a migraine attack).

***Efficacy and Dosing of CGRP Inhibitors:*** Phase II clinical trials have demonstrated that the CGRP inhibitors can decrease the number of days that a patient experiences a migraine by one to two days versus placebo. The CGRP inhibitors have shown that 50% of patients responded to therapy with a 50% reduction in migraine days per month, while only 30% of patients responded in the placebo group. A recently released analysis of a phase II clinical trial for erenumab concluded that the efficacy in patients who have failed two or more previous therapies may be enhanced.[4] In phase III clinical trials (not published to date), early data suggests that some patients are achieving 75% and 100% reduction in migraine episodes.

### CGRP Inhibitors in the Pipeline

| Generic Name | Manufacturer | Administration | Status |
|---|---|---|---|
| **Erenumab** | Amgen Novartis | Subcutaneous | Under FDA Review Q2 2018 |
| **Fremanezumab** | Teva | Subcutaneous | Under FDA Review Q2 2018 |
| **Galcanezumab** | Eli Lilly | Subcutaneous | Under FDA Review Q3 2018 |
| **Eptinezumab** | Alder Bio | Intravenous | Phase III |
| **Atogepant** | Allergan | Oral | Phase III |
| **Ubrogepant** | Allergan | Oral | Phase III |
| **Rimegepant** | Biohaven<br>Bristol-Myers Squibb | Oral | Phase III |

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# CALCITONIN GENE-RELATED PEPTIDE (CGRP) INHIBITORS

## PAYER ACTION PLAN

- **Stay Informed**
  As CGRP inhibitors have not yet been approved by the FDA, there is no immediate action for plan sponsors. However, with the number of migraine sufferers and the potentially positive impact this class of medications could bring, payers should stay informed to determine the best course of action for plan management.

Overall, the available data suggests that CGRP inhibitors are well tolerated, safe and have a low incidence of serious adverse events. Nasopharyngitis (nasal swelling), respiratory tract infections, nausea and fatigue were reported as the most common side effects in phase II clinical trials.

There will potentially be various dosage forms available for this class of medications. The products scheduled to be reviewed by the FDA first are subcutaneous and intravenous injections. These formulations are dosed once a month with the possibility of every three month dosing for one of the products; however, this is still being investigated. Oral formulations of CGRP inhibitors may also be available in the future, but are currently in earlier stages of development.

### Impact to the Pharmacy Care Experience

The impact of the CGRP inhibitors on the migraine prevention landscape is yet to be determined. The need for medications that safely and effectively prevent or reduce the number of migraine episodes and the subsequent negative impact to quality of life, is great. Early clinical trial data suggests that medications that target the CGRP pathway may play an important role in the future of chronic migraine management.

As these products have yet to be approved by the FDA, EnvisionRx will continue to monitor the research pipeline and, as data becomes available, will provide more insight to the clinical management of these potentially impactful medications.

*Sources*

[1] Burch, R. C., Loder, S., Loder, E. and Smitherman, T. A. (2015). The Prevalence and Burden of Migraine and Severe Headache in the United States: Updated Statistics From Government Health Surveillance Studies. Headache: The Journal of Head and Face Pain, 55: 21–34. doi:10.1111/head.12482.

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## Our Clinical Steering Committee

The Envision Clinical Steering Committee brings together leaders from across our national pharmacy care company to monitor the drug landscape, provide recommendations on how to address changes, and to ensure our clients and patients are prepared—in advance.

With any new development, we partner with our Pharmacy & Therapeutics (P&T) Committee and consult with our best-in-class specialty pharmacy, to provide a balanced perspective on the clinical effectiveness of all available options, the cost impact to our plan sponsors and patients, and the impact on the overall patient experience.

**Kel Riley, MD**
*Chief Medical Officer*

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EnvisionRx is a Pharmacy Benefit Manager (PBM), providing affordable and effective prescription drug coverage for employers and health plans. Using its proprietary EnvisionCare model, EnvisionRx optimizes all aspects of the pharmacy care experience to consistently achieve better patient and plan outcomes.

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