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WAMJ

World Asian Medical Journal

Inspirational Asian Healthcare Leader

JAEWON RYU

President and Chief Executive Officer, Geisinger

BIOPHARMA REPORT I

Pepaxto's US Uptake to Stall in Multiple Myeloma Until FBA Provides Advice to Address Death Risk

BIOPHARMA REPORT II

Medicare's National Coverage Determination Could Boost Chances of Limited Aduhelm Coverage in Alzheimer's Disease Despite Current Backlash

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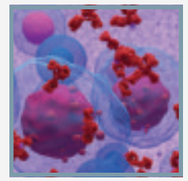

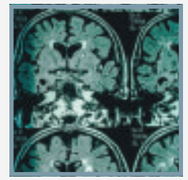

From the Publisher

In this issue of WAMJ, we interviewed Dr. Jaewon Ryu, an ER physician, an attorney and renowned health care system administrator who is the current president and chief executive officer of Geisinger Health System (GHS). Geisinger is a regional health care provider to Pennsylvania which services over three million patients in 45 counties. It has been widely recognized for delivering high-quality care at low cost through an integrated delivery system model of healthcare.

Dr. Jaewon Ryu became Geisinger's president and chief executive officer after serving as the executive vice president and chief medical officer since 2016. He oversees all aspects of patient care at Geisinger, working to improve the quality, affordability and experience of care delivered across the enterprise. During his tenure at Geisinger, Dr. Ryu has cultivated a spirit of innovation and transformation across the organization, engendering new approaches to some of healthcare's most complex problems which include initiatives like primary care redesign that brings healthcare services to patients in their homes. Dr. Ryu is committed to making health easier by improving outcomes, engagement, and affordability.

He said, "There is beauty in the simplicity of taking care of whoever comes in the door, for whatever they are there for, regardless of what insurance they have (or don't have) and what language they speak (or don't speak)."

In the era of pandemic, Dr. Ryu's philosophy serves as a paragon that the country's health care system needs to consider and adopt.

New trends and current issues of the bio-health industry are featured in our biopharmaceutical articles. In one of the articles titled "Medicare's National Coverage Determination could boost chances of limited Aduhelm coverage in Alzheimer's disease despite current backlash," the author explores how Medicare showed a willingness to provide limited coverage for Biogen's Aduhelm, which has been at the center of controversy for its little evidence of benefit for patients and how the CMS is likely to take an unprecedented route by covering the drug under CED in case of an outright coverage denial.

WAMJ has made major progress over the past few years and is celebrating the completion of our 24th edition. Thank you for your continued support. We will remain committed to our goal of always providing a quality journal for our readers. I hope that you enjoy our selection of articles and find them to be inspiring.

DoHyun Cho, PhD
Publisher
President & CEO of W Medical Strategy Group
Chairman of New York Health Forum

From the Editor-in-Chief

Having served the people of Pennsylvania for more than a century, Geisinger Health System has been nationally and internationally recognized for the breadth and quality of its services. The System evolved from a single, 63-bed hospital in 1913 into a healthcare colossus comprising a multi-specialty group practice with well over a thousand members, nine hospital campuses, two research centers, a 550,000-member health plan, and a medical school offering, among other things, a Primary Care Scholars Program that enables students graduate without tuition debt.

In this issue, the Journal is privileged to offer an interview with the renowned Jaewon Ryu, MD, JD, Geisinger's president and chief executive officer. His career is remarkable for its variety and scope, and for the innovation his leadership has fostered.

Dr. Ryu earned his BA degree from Yale and his MD and JD from Chicago. After college, he worked as an AmeriCorps member within an inner-city school, which allowed him to observe the impact of policy on vulnerable populations. He completed his residency training in emergency medicine at Harbor-UCLA Medical Center.

Later, Dr. Ryu held leadership roles at the University of Illinois Hospital & Health Sciences System; at Kaiser Permanente, where he continued his emergency medicine practice; and in government, at CMS, and as a White House Fellow at the Department of Veterans Affairs. Furthermore, Dr. Ryu served as president of integrated care delivery for Humana, where he assumed responsibility for Transcend, an MSO assisting affiliated practices to adopt population health under value-based reimbursement.

At Geisinger, Dr. Ryu has encouraged System-wide innovation. Among the initiatives he has nurtured are Geisinger at Home that brings healthcare to patients' homes; primary care redesign; and Geisinger 65 Forward, its senior-focused, concierge healthcare centers, where Geisinger offers not only diagnostic and therapeutic services but yoga lessons, for example, as well.

Dr. Ryu was appointed to the Medicare Payment Advisory Commission, which advises Congress on payment and other policies governing health plans and providers serving Medicare beneficiaries. He has also served on the Board of Directors of the White House Fellows Foundation and Association, of My Health Direct Inc. (acquired by Experian), a provider of digital care coordination services, and of MCCI and JenCare, organizations focused on care financing and delivery.

In recognition of these and other accomplishments, Dr. Ryu was chosen as a member of the Council of Korean Americans and was selected as one of Modern Healthcare's 2020 Top 25 Minority Leaders. WAMJ is deeply honored to have the opportunity to speak with Dr. Ryu and to present our interview with him in this issue. We hope you enjoy it.

Joseph P. McMenamin, MD, JD, FCLM
Editor in Chief
EVP of W Medical Strategy Group

WAMJ Recap of the Last Issue

COVER STORY
Edison Liu, M.D., President and Chief Executive Officer, The Jackson Laboratory (JAX)

Dr. Edison Liu is the president and CEO of The Jackson Laboratory, an independent research institute focused on complex genetics and functional genomics with campuses in Maine, Connecticut, and California. Previously, he was the founding executive director of the Genome Institute of Singapore and the president of the Human Genome Organization (HUGO). He is an international expert in cancer biology, systems genomics, human genetics, molecular epidemiology, and translational medicine. His own scientific research has focused on the functional genomics of human cancers, particularly breast cancer, uncovering new oncogenes, and deciphering on a genomic scale the dynamics of gene regulation that modulate cancer biology. He has authored over 320 scientific papers and reviews and co-authored two books. To learn more about Dr. Liu and his career story, please refer to issue 23 of WAMJ.

SPECIAL REPORT
Medical Korea 2021 - Insight into Global Healthcare and Medical Tourism

Medical Korea 2021, the 11th Global Healthcare and Medical Tourism Conference organized by the Korea Health Industry Development Industry (KHIDI), was held virtually from March 18th – 24th. With the theme "Global Healthcare, Where Your Days Begin Again," the conference brought together academic and industry experts from around the world to analyze and share insights on the latest healthcare industry trends. The event provided opportunities for business networking among stakeholders in the global healthcare industries. To find more about Medical Korea, please read issue 23 of WAMJ.

BIOPHARMACEUTICAL REPORT I
New SARS-CoV-2 Variants Push Back COVID-19 Vaccine Long-Term Durability Questions

Long-term COVID-19 vaccine durability has become less of an endgame since it has become increasingly likely additional shots will be needed after initial vaccination to combat new SARS-CoV-2 variants. In response, Novavax is aiming to develop vaccines offering both durability and breadth of protection. With new variants, there may be a higher likelihood of a longer-term need for potential additional vaccine administrations and modified COVID-19 vaccines. On 4 February, the FDA stated it will utilize influenza experience to inform a path forward with the SARS-CoV-2 variants. To learn more about COVID-19 vaccine durability that still has many unknowns, please read issue 23 of WAMJ.

BIOPHARMACEUTICAL REPORT II
COVID-19 Long-Hauler Treatments Could Employ Repurposed Trial Endpoints to Prove Aptitude

COVID-19 long-hauler treatment trials will likely rely on established endpoints and trial design features used in other conditions and will be based on a specific group of symptoms to prove clinical utility. COVID-19 long-haulers are terms used to encompass patients experiencing long-term symptoms in the months after a SARS-CoV-2 infection. Because the symptoms are difficult to measure biologically, patient-assessed scales of cognitive function are best equipped to determine symptom improvement. However, concerns remain about these scales lacking the sensitivity to detect subtle changes seen in COVID-19 long-haulers. To learn more about COVID-19 long-hauler treatments, please read issue 23 of WAMJ.

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Dr. Ryu standing at Geisinger Medical Center (Credit: Geisinger)

Inspirational Asian Healthcare Leader

Jaewon Ryu, M.D., J.D.

President and Chief Executive Officer, Geisinger

Geisinger

COVER STORY

1. Dr. Jaewon Ryu, you are known for your accomplishments in the healthcare industry and as a physician. Can you share with our readers what motivated you to become a physician and to take a career path in healthcare? Did the environment you grew up in affect your decision to become a physician?

- I grew up with physicians in the family, so I was always familiar with and interested in getting into healthcare. Between college and medical school, I worked as an AmeriCorps member in a teaching and enrichment program for inner-city kids, where I saw firsthand the impact that policy has especially on the lives of vulnerable populations – that's when I became more interested in the policy side of things. And medical school was where these two interests came together, where I became active in community health programs and the same themes came to light – things like how upstream policies impacted people's downstream health and well-being.

It was this interest in the crossroads of healthcare and policy that attracted me to the idea of a joint MD/JD degree program. Whether working as an ER physician or in government, on the payer side or now with an integrated delivery system, that perspective of how all things upstream affect downstream health has helped shape so many decisions for me along the way.

2. You achieved educational degrees in both medicine (M.D.) and law (J.D.). Which of the two did you pursue first and what led you to pursue education in two different fields? How has your educational background affected your professional decisions? Did you ever practice both professions at the same time?

- To be honest, I can't say that my educational path was all that planned. My interests have always gravitated toward the intersection of policy, payment, and care delivery. I've always believed that when these factors come together, we can focus on care models and programs that keep people and communities healthy. The joint degree program just became a natural way to pursue these areas of interest. I started medical school first, took an extended leave of absence halfway through to attend law school and then spent time working as a corporate healthcare attorney. After going back and finishing medical school and then my residency training in emergency medicine, I started practicing as an ER physician and really enjoyed that work. In many ways, it has informed other stops along my journey. The ER truly is the crossroads of healthcare where so many components of the industry come together. So, while my path has been a bit of a choppy one, it has been fun and rewarding. And no, I never practiced both professions at the same time.

Dr. Ryu administering the COVID-19 vaccine to an RN at Geisinger Medical Center (Credit: Geisinger)

3. Geisinger is a regional healthcare provider serving more than 1 million people with more than half a million members enrolled in Geisinger health plan. It also has nine hospital campuses, two research centers, and the Geisinger Commonwealth School of Medicine. As the President and CEO of Geisinger with nearly 24,000 employees and more than 1,600 employed physicians, what do you think is most important in managing and growing such a large organization? What was your greatest achievement with Geisinger and what do you envision for its future?

- Geisinger is a decent size health system, yes, but more importantly it's one with more than 100 years of history in our communities. Because of that, everywhere you go,

you'll run into someone with a connection to Geisinger. It is a good reminder of how we are so tightly woven into the fabric of the community. And it's also why we are so focused on being a health partner that makes better health easier for our communities. We know we can make health easier when we meet people where they are, building clinical capabilities and moving them closer to where people live and work. Most of the time, that means things like bringing programs into the home, into the clinics, or even interacting with people remotely. I'm especially proud of the different teams here who make this a reality every day. It can be the fitness instructor teaching yoga at our 65 Forward clinics, or the Geisinger at Home nurse hanging IV medications in a living room, or even the Free2BMom counselor helping mothers battling opioid addiction to care for themselves and their babies.

Dr. Ryu at the ceremony for last beam placement of new Cancer Center expansion (Credit: Robb Malloy, Geisinger)

These and other programs illustrate how we're tackling not just the medical issues but also the social determinants of health – going beyond what's inside the hospital and working to impact societal factors for overall health and well-being like food insecurity, transportation and housing. When we develop programs like these and then combine that with easier access to top-notch clinical services closer to the home and communities, we know great things happen for folks.

> "It is a good reminder of how we are so tightly woven into the fabric of the community. And it's also why we are so focused on being a health partner that makes better health easier for our communities"

4. Prior to your tenure at Geisinger, you held various leadership roles in health systems including the University of Illinois Hospital & Health Sciences Systems, Centers for Medicare and Medicaid Services, and the Department of Veterans Affairs as a White House Fellow. What were your roles in these different health systems and what was the most memorable position? Did you face any difficulties in these roles?

- Each of these roles came with challenges but provided me with great opportunities to continue to develop in my career journey. But on top of all of them, I think the most memorable and impactful position I've held was as an ER physician. In the ER, you never know what's coming through the door next, which keeps you on your toes and gets you very comfortable with the unpredictable. The ER is also the setting where you see so many gaps in healthcare come to a head. When care isn't coordinated, or when patients can't access services, or when there isn't a focus on prevention and care isn't managed effectively between payors and providers, you see the consequences in the ER. And by the same token, it also provides a close glimpse into the solutions needed to chart a better course, and hopefully that's something we can model for the entire industry.

5. Dr. Ryu, as a leader in the healthcare industry, what do you think are the major challenges that the current U.S. healthcare system faces and what approaches do you foresee to address these challenges in the next five to ten years?

- One big challenge that comes to mind is the affordability of healthcare. Especially as segments of our population age and hopefully continue to live longer, there is a greater need and as a result, a greater cost. At the same time, working-age populations and their employers see increases in healthcare costs as well. While these trends are sobering, they also present an opportunity to transform the way in which we deliver care and the way we pay for such care.

Shifting the focus of care delivery further upstream can spark prevention of more costly downstream health problems. Whether it is investing in food programs for food-insecure diabetic patients like our Fresh Food Farmacy or investing in care coordination and treatment in the home setting like our Geisinger at Home program, we have seen firsthand that these efforts end up decreasing the downstream need for ER visits or hospitalizations. We've also tried to make it easier to access primary and specialty services in the clinic environment, and as we've done that, we've seen the use of ERs decrease as accessing the right care at the right time in those other settings becomes easier.

(Left to right) Mary Casale, GWV Auxiliary; Sarah Ryu; Dr. Ryu, Geisinger's president and CEO; Brigitte Henry-Cooper, author; Bethany Moy, illustrator; Olivia Moy, illustrator; and Donna Connery, GWV Auxiliary (Credit: Geisinger)

But programs like these are turbo-boosted with the right payment model. As payment and delivery move closer in healthcare, the incentives align better to invest in such programs. As both public and private payers increase the adoption of value-based payment models, I believe the momentum will continue to build in creating an environment where providers can accordingly adapt care delivery models focused on value and upstream prevention.

Geisinger Medical Center

Dr. Ryu standing outside of Geisinger Medical Center in Danville, PA (Credit: Geisinger)

6. Your experience will be a true inspiration to our readers and many in the healthcare industry. Could you please share a message for future physicians and healthcare professionals that aspire to exceptional careers and accomplishments?

- One piece of advice that some mentors of mine have impressed upon me over the years has proven to be true, especially over the past year and a half with the pandemic. And that advice was to embrace change and uncertainty and to get comfortable rolling with the punches. Of course, during this pandemic, this has become a way of life for our team at Geisinger, as folks have tackled this pandemic head-on, pivoting when needed, shifting gears along the way, and remembering that flexibility is what will help us come out the other side of this. I've never been prouder to be a part of a team as our Geisinger team has just risen to this occasion in these ways. And even aside from a pandemic context, this has ended up being pretty good career advice as well, since being adaptable seems to open the doors of opportunity more often. W

Jaewon Ryu, M.D., J.D.

President and Chief Executive Officer, Geisinger

Jaewon Ryu, M.D., J.D., is a president and chief executive officer of Geisinger. He came to Geisinger as the executive vice president and chief medical officer in 2016. During his tenure at Geisinger, Dr. Ryu has cultivated a spirit of innovation and transformation across the organization, driving new approaches to some of healthcare's most complex problems. These include initiatives like primary care redesign; Geisinger at Home, which brings healthcare services to patients in their home; and Geisinger 65 Forward, senior-focused, concierge healthcare centers. This dedication to innovation for the health of communities earned Dr. Ryu a top 20 spot on Modern Healthcare's Most Influential Clinical Executives list for 2019. Previously at Humana, Dr. Ryu was president of integrated care delivery and responsible for Humana's owned and joint ventured care delivery assets. Prior to Humana, Dr. Ryu held various leadership roles at the University of Illinois Hospital & Health Sciences System; Kaiser Permanente (where he also practiced as an emergency medicine physician); and in government, at the Centers for Medicare and Medicaid Services, and as a White House Fellow at the Department of Veterans Affairs. He was also a practicing corporate healthcare attorney with the international firm McDermott, Will & Emery. Dr. Ryu was appointed to the Medicare Payment Advisory Commission, an independent body legislatively tasked with advising Congress on payment and other policies governing health plans and providers serving Medicare beneficiaries. Dr. Ryu earned his BA degree from Yale University and his MD and JD from The University of Chicago. He completed his residency training in emergency medicine at Harbor-UCLA Medical Center.

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Biopharma Report

BIOPHARMACEUTICAL REPORT I

PEPAXTO'S US UPTAKE TO STALL IN MULTIPLE MYELOMA UNTIL FDA PROVIDES ADVICE TO ADDRESS DEATH RISK

BIOPHARMACEUTICAL REPORT II

MEDICARE'S NATIONAL COVERAGE DETERMINATION COULD BOOST CHANCES OF LIMITED ADUHELM COVERAGE IN ALZHEIMER'S DISEASE DESPITE CURRENT BACKLASH

Pepaxto's US Uptake to Stall in Multiple Myeloma Until FDA Provides Advice to Address Death Risk

Blood cancer oncologists are likely to hold back for now on using **Oncopeptides'** (STO:ONCO) Pepaxto (melphalan flufenamide) in triple-class refractory multiple myeloma patients, experts said. Oncologists will be waiting on the FDA to provide further guidance on how to manage its increased death risk.

On 28 July, the FDA alerted oncologists that in the Phase III OCEAN trial (NCT03151811), Pepaxto led to an increased risk of death. Subsequently, the FDA encouraged them to review their patients' progress with Pepaxto. All ongoing Pepaxto trials have also been suspended. A public meeting will be staged to discuss additional OCEAN findings and explore continued marketing of the treatment.

Until the FDA decides on how it should address Pepaxto's OCEAN data, most US oncologists will likely be more reluctant to use the treatment, said OCEAN investigator Dr Fredrik Schjesvold, head, Oslo Myeloma Center, Norway. They will wait to hear from the FDA on any mitigation strategy to reduce risk before resuming use of Pepaxto, added Dr Thomas Martin, clinical professor of medicine, University of California San Francisco Medical Center.

Pepaxto garnered FDA accelerated approval in February 2021. And so, the treatment is not so established in US oncologists' practice for there to be a comfort level to keep using Pepaxto, said OCEAN investigator Dr Ulf-Henrik Mellqvist, professor, Department of Hematology and Coagulation, Sahlgrenska University Hospital, Gothenburg, Sweden. Upon accelerated approval, the therapy's overall efficacy data drew some pause for clinical benefit, which likely contributed to delayed uptake in the past five months, he added. Pepaxto's April net sales amounted to USD 3.3m, according to a 26 May media release.

The FDA advised oncologists to discuss the risks of continued Pepaxto administration with patients in context of other treatments. In patients who are yet to take any therapies in the triple-class refractory setting, there are two notable options available: **GlaxoSmithKline's** (LON:GSK) Blenrep (belantamab mafodotin) and **Karyopharm Therapeutics'** (NASDAQ:KPTI) Xpovio (selinexor), Martin said. However, both treatments have respective side-effect issues, he noted, adding it might come down to patient preference. Blenrep has a boxed warning on ocular toxicity; Xpovio has warnings on thrombocytopenia, neutropenia, gastrointestinal toxicity, among others.

An Oncopeptides spokesperson said it does not have any concerns that the new FDA warning would dramatically impact uptake in the US. Pepaxto's patient population has an unmet medical need with limited treatment options, he added. Perhaps Pepaxto can still be used in patients who have early progression from Blenrep and Xpovio, Martin noted.

According to the FDA guidance, in the confirmatory trial OCEAN, in the overall survival (OS) secondary endpoint, there were 117 deaths in the 246-patient Pepaxto arm (48%), compared with 108 deaths in 249 patients (43%) in the **Bristol Myers Squibb** (NYSE:BMY) Pomalyst (pomalidomide) active comparator arm. The median OS with Pepaxto is 19.7 months, versus 25 months with Pomalyst. The spokesperson said it will present OCEAN's complete data at a scientific congress later this fall.

Subgroup analysis a possible way to find ideal Pepaxto patients

The next step to understand Pepaxto's clinical value is to find patient subgroups who are best suited for the therapy, experts said. OCEAN recruited all comers and finding subpopulations may be paramount due to the trial comparing two therapies with different mechanisms, Schjesvold noted. OCEAN investigated the peptide-conjugated alkylating drug Pepaxto versus immunomodulatory imide drug Pomalyst. All patients are given low-dose dexamethasone.

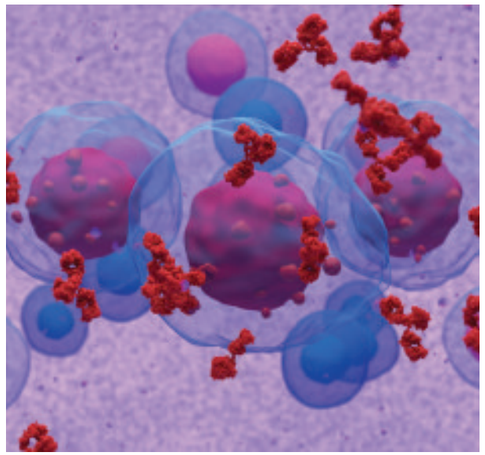
> "The next step to understand Pepaxto's clinical value is to find patient subgroups who are best suited for the therapy"

What treatment the patient has taken previously can help find Pepaxto's ideal subgroup, Schjesvold said. Triple-class refractory patients are ones resistant to all three classes of standard myeloma therapies: proteasome inhibitors, immunomodulatory agents, and monoclonal antibodies. Perhaps patients who have previously progressed from an alkylating agent may not benefit from Pepaxto, Schjesvold noted. In OCEAN, there are patients who have previously received an alkylating agent and some have not, he added.

Since the concerning discrepancy is related to Pepaxto's OS data, results may have been affected by what therapies OCEAN patients have taken after progressing from Pepaxto or Pomalyst, Mellqvist said. For example, if a Pomalyst patient in OCEAN progressed earlier than another patient on Pepaxto, the Pomalyst patient would have received subsequent therapies sooner, he noted, adding this could bolster the Pomalyst patient's OS result.

It is also possible that these subsequent therapies would be more effective if the patients have failed either Pomalyst or Pepaxto, further muddying OS data, Mellqvist added. Nevertheless, data collection of OCEAN patients' subsequent therapies is opportunity to find subgroups that experience the most OS benefit, he said. However, subsequent therapies can differ between countries, he noted.

The spokesperson said its analysis indicates there are patients that may benefit with Pepaxto, as well as patients that should have Pomalyst. How these hypothesis-generating data should be interpreted, and its clinical implications, are in an ongoing analysis, he added. Patients best suited for Pomalyst may be hard to pinpoint in OCEAN because all patients have progressed from an immunomodulatory imide drug, even if to various degrees, Schjesvold noted.



Prophylactic antibiotics may be a valuable tool to extend survival

Another possible way to help increase Pepaxto's OS data is to use prophylactic antibiotics, Martin said. Triple-class refractory multiple myeloma patients are already fragile, having gone through many prior lines of therapy on top of having low bone marrow reserves, he explained. And Pepaxto can further negatively impact these reserves, increasing risk of infection, he added. And so, preventive antibiotics might be able to help.

Apart from prophylactic antibiotics, another way is to increase these patients' leukocyte count, especially neutrophils, to be able to combat infections, Mellqvist added. Pepaxto's FDA label warns of thrombocytopenia, neutropenia, anemia and infections, among others. Patients who end up with neutropenia become highly sensitive to infections, and severe cases can be fatal, Martin explained.

But the spokesperson noted OCEAN did allow for antibiotics as prophylaxis and was recommended in both arms. While prophylactic antibiotics might be helpful, Schjesvold said that the number of infections in OCEAN between arms is not dramatically different. Pomalyst had slightly more infection events than Pepaxto in OCEAN, according to a 26 May company presentation.

OCEAN efficacy data still worth digging into

While it was judicious for the FDA to pause ongoing Pepaxto trials on the back of new OS data, there is still potential for the treatment to be used in its present setting where there are currently limited options, experts said. In OCEAN's primary endpoint, progression-free survival (PFS), final analysis shows Pepaxto was superior to Pomalyst (p=0.0311).

In OCEAN, while the OS data might favor Pomalyst, the confidence interval of the hazard ratio shows it may not be a definitive finding, Schjesvold added. The hazard ratio for OS of Pepaxto versus Pomalyst was 1.104, with a 95% confidence interval range of 0.846 and 1.441.

> "While it was judicious for the FDA to pause ongoing Pepaxto trials on the back of new OS data, there is still potential for the treatment to be used in its present setting where there are currently limited options"

However, based on available data so far, it might be challenging for Pepaxto to demonstrate dramatic superiority over Pomalyst in the OS endpoint, Schjesvold said. Pomalyst is a high bar, in contrast to Pomalyst's registrational trial which only compared it to steroids, Mellqvist noted. Pomalyst was FDA approved in multiple myeloma in 2013.

Oncopeptides has a SEK 3.08bn (USD 358.1m) market cap.

Reynald Castaneda
Reporter, London

Reynald Castaneda, prior to moving to London, was a journalist for healthcare newspaper New Zealand Doctor, covering primary care health politics and medical research. He has a BSc in Biological Sciences from the University of Auckland and a postgraduate diploma in journalism from AUT University. Prior to venturing into journalism, Reynald worked as a laboratory technician for Massey University's Institute of Molecular Biosciences.

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Jane's Journey: The Rare Disease Landscape From a Mother's Perspective

When Jane discovered that her 15-month-old son had the autoimmune disorder Histiocytosis, suddenly she was forced to navigate the complex and unfamiliar terrain of what she called "rare disease land."

She began her journey with questions. The answers were not straightforward. Jane needed compassionate experts to translate the complex clinical language and guide her family through the steps. Fortunately, she connected with doctors who didn't define her son by his disease, as well as with advocates who provided resources for understanding and navigating the clinical landscape.

Over time, Jane became part of the support network, and now serves as a board member of the Histiocytosis Association, helping others who seek guidance for their own journeys.

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Medicare's National Coverage Determination Could Boost Chances of Limited Aduhelm Coverage in Alzheimer's Disease Despite Current Backlash

By opening a National Coverage Determination (NCD) on **Biogen's** (NASDAQ:BIIB) Aduhelm (aducanumab) for Alzheimer's disease, Medicare has signaled a willingness to provide some level of coverage in the US without outright denying its use.

Typically, the Center for Medicare & Medicaid Services (CMS) makes coverage decisions through Local Coverage Determinations (LCDs), which largely remain unnoticed. NCDs are normally employed for controversial medical technologies.

However, in the case of Aduhelm, a former CMS official said an NCD is a promising sign for Biogen. Since the drug has faced uniquely intense public scrutiny, most LCDs would have denied coverage to avoid controversy. However, an NCD signals the CMS' openness to significantly restricting the drug without completely denying coverage.

Given the thorough, transparent process of an NCD, the CMS could confidently stand behind a decision to provide limited coverage in the face of political pressures, a healthcare regulatory consultant explained. The CMS' best tool for narrowing coverage—the rarely used Coverage with Evidence Determination (CED) process—is only available via an NCD, a bioethicist added. A CED would only provide Aduhelm coverage to patients in open-label studies or enrolled in future studies and planned clinical trials, subject to the population coverage restrictions applied by the CMS.

Nevertheless, there has been a trend toward more stringent NCDs and increased pressure to avoid the same kind of controversy as the FDA faced following its Aduhelm approval, adding uncertainty to the process.

On 29 July, the expected nine-month NCD process began with an open public comment period. Biogen did not respond to a request for comment.

National determination could be a positive sign

Under an NCD, all Medicare Administrative Contractors (MACs)—which normally make Medicare coverage decisions on the regional level—are bound to follow the NCD outcome. Historically, NCDs are extremely rare for drugs, with almost all NCDs taking place for medical devices, said James Chambers, PhD, researcher, Center for the Evaluation of Value and Risk in Health, Tufts Medical Center, Medford, Massachusetts. Chambers, who has researched trends in NCDs, noted NCDs, have almost always provided coverage for FDA-approved therapies but occasionally deny coverage for devices.

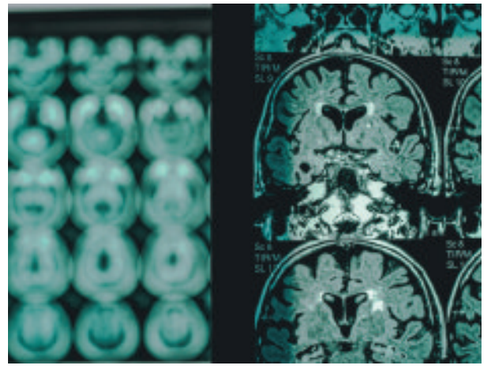
Given the unprecedented backlash against Aduhelm, the safest and most likely decision from MACs would be to deny Aduhelm coverage because its evidence does not meet Medicare coverage requirements, the former CMS official, now a regulatory consultant, said. As a result, the decision to pursue an NCD is likely a positive sign for Biogen, he explained. By pursuing this route, the CMS has signaled the tools available in an NCD are more useful for granting some Aduhelm coverage than if the issue were left to regional MACs, he said.

Nevertheless, LCDs give the manufacturer multiple opportunities to gain regional coverage without the risk of national noncoverage as a result of one NCD, Chambers noted. However, the CMS normally strongly considers the impact of any debilitating condition on patients and their families in its coverage decisions, the former official noted. And as a result, an NCD is very unlikely to deny Aduhelm coverage without first pursuing every possible route to providing some form of limited coverage, he said. Additionally, although Biogen has requested for MACs to make coverage decisions while awaiting the NCD, it is unlikely any MAC would make a coverage decision given all the attention Aduhelm garners, the former CMS official said.

> "If the evidence gathered in the NCD process opposes Aduhelm, the CMS would likely cover the drug under CED over an outright coverage denial"

CED route last resort over denial

If the evidence gathered in the NCD process opposes Aduhelm, the CMS would likely cover the drug under CED over an outright coverage denial, the former CMS official said.



Although the CED process is exceedingly rare and normally unexpected for an FDA- approved drug, the unprecedented scrutiny of the Aduhelm decision and competing political pressures make it a much more likely outcome, said a Medicare healthcare consultant. Still, this decision would be largely unprecedented, as a CED designation is typically reserved for "close call situations" when the CMS decides more evidence is needed for a Medicare-specific population, the former CMS official explained.

Even with a CED, it is debatable whether additional data collected outside of a randomized control trial would be valuable, Chambers noted. Because Aduhelm is intended to slow disease progression rather than stop or reverse progression, it is unclear if patients who experience cognitive decline on Aduhelm are gaining no benefit, or if they would have been worse without it, said bioethicist Leonard Fleck, PhD, professor, Center for Bioethics and Social Justice, Michigan State University, East Lansing.

In a November 2020 FDA Advisory Committee, Aduhelm's efficacy was overwhelmingly rebuked by a panel of experts and biostatisticians. However, in June, the FDA granted Aduhelm accelerated approval after determining the demonstrated reduction in amyloid plaque is "reasonably likely" to translate to clinically meaningful improvement on cognitive decline.

As part of the accelerated approval process, Biogen has nine years to complete a confirmatory trial establishing whether a reduction in amyloid plaque does in fact translate to clinically meaningful disease outcomes. If the trial fails to do so, the FDA could remove marketing authorization for Aduhelm.

Precedent for narrower label

On 7 June, the FDA granted Aduhelm accelerated approval for all Alzheimer's disease patients, despite clinical testing only covering mild patients. Still, in an 8 July press release, Biogen said Aduhelm should be used in patients with "mild cognitive impairment or mild dementia stage of disease."

Beyond this initial narrowing, if the CMS does not pursue the CED route in favor of greater coverage, the coverage would likely come with even further restrictions, the former CMS official said. The CMS has several options available for limiting aducanumab's use, including restrictions on age groups, disease severity, disease biomarkers, and who can prescribe the treatment, the health care consultant explained.

Beyond the NCD label decision, the growing scrutiny of Aduhelm will likely further limit the label, said George Perry, PhD, Semmes Foundation Distinguished University chair in Neurobiology, University of Texas, San Antonio. Clinicians will be reluctant to prescribe the drug given its safety and efficacy concerns, and it is likely many would try and sway patients against its use, Perry explained.

Medicare hampered by bargaining, cost analysis restrictions

In an ideal scenario, Medicare would cover Aduhelm at the price of manufacturing, at approximately USD 2,500–5,000, plus a modest profit for Biogen, Fleck said. However, given the enormous restrictions on Medicare, this outcome is far from likely, he noted. Medicare cannot negotiate prescription drug prices, nor does it explicitly consider cost in its coverage decisions, Chambers explained. The FDA is tasked with determining if a drug is "safe and effective," while the CMS determines if a drug is "reasonable and necessary," with no specific mandate related to cost-effectiveness. Biogen announced Aduhelm will have a list price of USD 56,000 per patient per year. However, to be cost- effective, the Institute for Clinical and Economic Review (ICER) independently determined Aduhelm should be priced at USD 2,950–8,360 per person per year.

Overall, the NCD process can only determine if and to what extent a drug should be covered, and it does not deal with the amount Medicare will reimburse for a specific drug or device, the former CMS official explained. As a result, considering Medicare's many restrictions and the unprecedented scrutiny surrounding Aduhelm, the NCD process' flexibility to provide some level of coverage in the face of mounting criticism could be the best sign for Biogen, he said. W

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William Newton is a healthcare reporter for GlobalData focusing on central nervous system diseases and ophthalmology. Previously, he worked at the healthcare information firm Close Concerns, where he covered breaking news in diabetes therapeutics and technology for the company's industry-facing publication, and at the digital health startup Fitscript, where he assisted in researching digital health and lifestyle intervention approaches to treating diabetes. He graduated Williams College with a BA in Economics and Spanish and worked as a News Editor, Executive Editor, and Managing Editor of the Williams Record.

FOLLOW THE JOURNEY OF VIREAD

COMPLETE RESPONSE RESULTS AT YEAR 1...

#1 **Prescribed oral antiviral** according to US prescription data for treatment of CHB[1a]

AT YEAR 1
The primary endpoint—complete response*—was evaluated in Studies 102 and 103[2]

THROUGH YEAR 8
Resistance was evaluated as a secondary endpoint[2,3]

In Study 102 (HBeAg–, n=375) and Study 103 (HBeAg+, n=266), a combined total of 641 adult patients with chronic hepatitis B (CHB) and compensated liver disease who were primarily nucleoside treatment naïve entered a 48-week, randomized, double-blind, active-controlled treatment period comparing VIREAD 300 mg to adefovir dipivoxil 10 mg. Subjects who completed double-blind treatment at Week 48 were eligible to roll over with no interruption in treatment to open-label VIREAD. Of 641 patients enrolled in the initial trials, 412 (64%) completed 384 weeks of treatment.[2]

***The primary endpoint in Studies 102 and 103 was complete response to treatment at 48 weeks as defined by HBV DNA <400 copies/mL (69 IU/mL) + histological response (Knodell necroinflammatory score improvement of ≥2 points without worsening in Knodell fibrosis score). Annual evaluation of resistance was a prespecified secondary endpoint. Cumulative VIREAD genotypic resistance was evaluated annually for up to 384 weeks in Studies 102, 103, 106, 108, and 121.[2,3]**

71% of HBeAg– VIREAD patients vs **49%** of adefovir dipivoxil patients.[2-4]
67% of HBeAg+ VIREAD patients vs **12%** of adefovir dipivoxil patients.[2,3,5]

INDICATION AND USAGE

VIREAD® (tenofovir disoproxil fumarate) is indicated for the treatment of chronic hepatitis B in adults and pediatric patients 12 years of age and older.

The following points should be considered when initiating therapy with VIREAD for the treatment of HBV infection:

- The indication in adults is based on data from treatment of subjects who were nucleoside–treatment-naïve and treatment-experienced with documented resistance to lamivudine. Subjects were adults with HBeAg-positive and HBeAg-negative chronic hepatitis B with compensated liver disease
- VIREAD was evaluated in a limited number of subjects with chronic hepatitis B and decompensated liver disease
- The numbers of subjects in clinical trials who had adefovir resistance-associated substitutions at baseline were too small to reach conclusions of efficacy

IMPORTANT SAFETY INFORMATION

BOXED WARNING: LACTIC ACIDOSIS/SEVERE HEPATOMEGALY WITH STEATOSIS and POST TREATMENT EXACERBATION OF HEPATITIS

- **Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported with the use of nucleoside analogs, including VIREAD, in combination with other antiretrovirals**
- **Severe acute exacerbations of hepatitis have been reported in HBV-infected patients who have discontinued anti-hepatitis B therapy, including VIREAD. Hepatic function should be monitored closely with both clinical and laboratory follow-up for at least several months in patients who discontinue anti-hepatitis B therapy, including VIREAD. If appropriate, resumption of anti-hepatitis B therapy may be warranted**

[a]Healthcare Analytics Monthly data, August 2014-June 2015.

Please see Brief Summary of full Prescribing Information including **BOXED WARNING** on the following pages.

GILEAD IS COMMITTED TO THE EDUCATION AND TREATMENT OF CHRONIC HEPATITIS B.

Viread® 300 mg tablets
tenofovir disoproxil fumarate

Not an actual patient, but is representative of a real patient type. Models are used for illustrative purposes only.

...AT 8 YEARS: NO RESISTANCE WAS

Annual evaluation of resistance was a prespecified secondary endpoint for Studies 102 and 103 in HBeAg- and HBeAg+ chronic hepatitis B patients[3]; no evidence of resistance was found. Cumulative VIREAD genotypic resistance was evaluated annually for up to 384 weeks in Studies 102, 103, 106, 108, and 121.[2,4,5]

- In the nucleotide-naïve population from Studies 102 and 103, HBeAg+ subjects had a higher baseline viral load than HBeAg– subjects and a significantly higher proportion of the subjects remained viremic at their last time point on VIREAD monotherapy (15% vs 5%, respectively)[2]
- HBV isolates from these subjects who remained viremic showed treatment-emergent substitutions; however, no specific substitutions occurred at a sufficient frequency to be associated with resistance to VIREAD (genotypic and phenotypic analyses)[2]

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS

- **New onset or worsening renal impairment:** Cases of acute renal failure and Fanconi syndrome have been reported with the use of VIREAD. In all patients, assess estimated creatinine clearance (CrCl) prior to initiating and during therapy. In patients at risk for renal dysfunction, including those who previously experienced renal events while receiving adefovir dipivoxil, additionally monitor serum phosphorus, urine glucose, and urine protein. In patients with CrCl <50 mL/min, adjust dosing interval and closely monitor renal function. Avoid concurrent or recent use with a nephrotoxic agent. Cases of acute renal failure, some requiring hospitalization and renal replacement therapy, have been reported after initiation of high dose or multiple NSAIDs in HIV-infected patients with risk factors for renal dysfunction; consider alternatives to NSAIDs in these patients. Persistent or worsening bone pain, pain in extremities, fractures and/or muscular pain or weakness may be manifestations of proximal renal tubulopathy and should prompt an evaluation of renal function
- **Coadministration with other products:**
  – Do not use in combination with other products containing tenofovir disoproxil fumarate
  – Do not administer in combination with adefovir dipivoxil
- **Patients coinfected with HIV-1 and HBV:** Due to the risk of development of HIV-1 resistance, VIREAD should only be used in HIV-1 and HBV coinfected patients as part of an appropriate antiretroviral combination regimen. HIV-1 antibody testing should be offered to all HBV-infected patients before initiating therapy with VIREAD
- **Bone effects:** Decreases in bone mineral density (BMD) and mineralization defects, including osteomalacia, have been seen in patients treated with VIREAD. Consider assessment of BMD in adult and pediatric patients who have a history of pathologic bone fracture or other risk factors for bone loss. In a clinical trial conducted in pediatric subjects 12 to <18 years of age with chronic hepatitis B, total body BMD gain was less in VIREAD-treated subjects as compared to the control group. In patients at risk of renal dysfunction who present with persistent or worsening bone or muscle symptoms, hypophosphatemia and osteomalacia secondary to proximal renal tubulopathy should be considered

ADVERSE REACTIONS

- **In HBV-infected subjects with compensated liver disease:** Most common adverse reaction (all grades) was nausea (9%). Other treatment-emergent adverse reactions reported in >5% of patients treated with VIREAD included: abdominal pain, diarrhea, headache, dizziness, fatigue, nasopharyngitis, back pain, and skin rash
- **In HBV-infected subjects with decompensated liver disease:** Most common adverse reactions (all grades) reported in ≥10% of patients treated with VIREAD were abdominal pain (22%), nausea (20%), insomnia (18%), pruritus (16%), vomiting (13%), dizziness (13%), and pyrexia (11%)

DRUG INTERACTIONS

- **Didanosine:** Coadministration increases didanosine concentrations. Use with caution and monitor for evidence of didanosine toxicity (e.g., pancreatitis, neuropathy). Didanosine should be discontinued in patients who develop didanosine-associated adverse reactions. In patients weighing >60 kg, the didanosine dose should be reduced to 250 mg once daily when it is coadministered with VIREAD and in patients weighing <60kg, the didanosine dose should be reduced to 200 mg once daily when coadministered with VIREAD

DETECTED AT YEAR 1 THROUGH YEAR 8

NO HBV RESISTANCE DEVELOPED
YEAR 1 through YEAR 8
in clinical trials (Studies 102 and 103)[2,3]*

*Data for Years 2 through 8 are from the open-label phase.[6]

- There was a 64% (412/641) retention rate at Year 8: 266/426 patients given VIREAD→VIREAD; 146/215 patients given adefovir dipivoxil→VIREAD[2,6]

IMPORTANT SAFETY INFORMATION (cont'd)

DRUG INTERACTIONS (cont'd)

- **HIV-1 protease inhibitors:** Coadministration decreases atazanavir concentrations and increases tenofovir concentrations; use atazanavir given with ritonavir. Coadministration of VIREAD with atazanavir and ritonavir, darunavir and ritonavir, or lopinavir/ritonavir increases tenofovir concentrations. Monitor for evidence of tenofovir toxicity
- **Drugs affecting renal function:** Coadministration of VIREAD with drugs that reduce renal function or compete for active tubular secretion may increase concentrations of tenofovir

DOSAGE AND ADMINISTRATION

- Recommended dose, in adults and pediatric patients ≥12 years of age (≥35 kg), for the treatment of chronic hepatitis B: one 300 mg tablet, once daily, taken orally, without regard to food
- In the treatment of chronic hepatitis B, the optimal duration of treatment is unknown
- Safety and efficacy in pediatric patients <12 years of age or weighing <35kg with chronic hepatitis B have not been established
- The dosing interval of VIREAD should be adjusted (using recommendations in the table below) and renal function closely monitored in patients with baseline creatinine clearance <50 mL/min

DOSAGE ADJUSTMENT FOR PATIENTS WITH ALTERED CREATININE CLEARANCE

	Creatinine clearance (mL/min)[a]			Hemodialysis patients
	≥50	30-49	10-29	
Recommended 300 mg dosing interval	Every 24 hours	Every 48 hours	Every 72 to 96 hours	Every 7 days or after a total of approximately 12 hours of dialysis[b]

[a]Calculated using ideal (lean) body weight.

[b]Generally once weekly assuming three hemodialysis sessions a week of approximately 4 hours duration. VIREAD should be administered following completion of dialysis.

- The pharmacokinetics of tenofovir have not been evaluated in non-hemodialysis patients with creatinine clearance <10 mL/min; therefore, no dosing recommendation is available for these patients
- No dose adjustment is necessary for patients with mild renal impairment (creatinine clearance 50-80 mL/min). Routine monitoring of estimated creatinine clearance, serum phosphorus, urine glucose, and urine protein should be performed in these patients
- No data are available to make dose recommendations in pediatric patients with renal impairment

Please see Brief Summary of full Prescribing Information including **BOXED WARNING** on the following pages.

References: 1. Data on file, Gilead Sciences, Inc. Healthcare Analytics. **2.** VIREAD [package insert]. Foster City, CA: Gilead Sciences, Inc.; May 2015. **3.** Marcellin P, Heathcote EJ, Buti M, et al. Tenofovir disoproxil fumarate versus adefovir dipivoxil for chronic hepatitis B. *N Engl J Med.* 2008;359(23):2442-2455. **4.** Data on file, Gilead Sciences, Inc. Study 102 CSR. **5.** Data on file, Gilead Sciences, Inc. Study 103 CSR. **6.** Marcellin P, Gane EJ, Flisiak R, et al. Long term treatment with tenofovir disoproxil fumarate for chronic hepatitis B infection is safe and well tolerated and associated with durable virologic response with no detectable resistance: 8 year results from two phase 3 trials [AASLD abstract 229]. *Hepatology.* 2014;60(4)(suppl):313A-314A.

For more information, visit www.viread.com/hcp

300mg tablets
Viread®
tenofovir disoproxil fumarate

VIREAD® (tenofovir disoproxil fumarate) tablets

Brief summary of full Prescribing Information. Please see full Prescribing Information including Boxed WARNING. Rx only

WARNING: LACTIC ACIDOSIS/SEVERE HEPATOMEGALY WITH STEATOSIS and POST TREATMENT EXACERBATION OF HEPATITIS

- **Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported with the use of nucleoside analogs, including VIREAD, in combination with other antiretrovirals *(See Warnings and Precautions)***
- **Severe acute exacerbations of hepatitis have been reported in HBV-infected patients who have discontinued anti-hepatitis therapy, including VIREAD. Hepatic function should be monitored closely with both clinical and laboratory follow-up for at least several months in patients who discontinue anti-hepatitis B therapy, including VIREAD. If appropriate, resumption of anti-hepatitis B therapy may be warranted *(See Warnings and Precautions)***

INDICATIONS AND USAGE: VIREAD is indicated for the treatment of chronic hepatitis B in adults and pediatric patients 12 years of age and older.

The following points should be considered when initiating therapy with VIREAD for the treatment of HBV infection:

- The indication in adults is based on safety and efficacy data from treatment of subjects who were nucleoside-treatment-naïve and subjects who were treatment-experienced with documented resistance to lamivudine. Subjects were adults with HBeAg-positive and HBeAg-negative chronic hepatitis B with compensated liver disease *(See Adverse Reactions)*
- VIREAD was evaluated in a limited number of subjects with chronic hepatitis B and decompensated liver disease *(See Adverse Reactions)*
- The numbers of subjects in clinical trials who had adefovir resistance-associated substitutions at baseline were too small to reach conclusions of efficacy

DOSAGE AND ADMINISTRATION: For the treatment of chronic hepatitis B the recommended dose, in adults and pediatric patients ≥12 years of age (≥35 kg), is one 300 mg tablet, once daily, taken orally, without regard to food. In the treatment of chronic hepatitis B, the optimal duration of treatment is unknown. Safety and efficacy in pediatric patients <12 years of age with chronic hepatitis B weighing <35 kg have not been established. **Dose Adjustment for Renal Impairment in Adults:** Significantly increased drug exposures occurred when VIREAD was administered to subjects with moderate to severe renal impairment. Therefore, the dosing interval of VIREAD tablets 300 mg should be adjusted in patients with baseline creatinine clearance <50 mL/min using the recommendations in Table 1. These dosing interval recommendations are based on modeling of single-dose pharmacokinetic data in non-HIV and non-HBV infected subjects with varying degrees of renal impairment, including end-stage renal disease (ESRD) requiring hemodialysis. The safety and effectiveness of these dosing interval adjustment recommendations have not been clinically evaluated in patients with moderate or severe renal impairment, therefore clinical response to treatment and renal function should be closely monitored in these patients *(See Warnings and Precautions)*. No dose adjustment of VIREAD tablets 300 mg is necessary for patients with mild renal impairment (creatinine clearance 50–80 mL/min). Routine monitoring of calculated creatinine clearance, serum phosphorus, urine glucose and urine protein should be performed in patients with mild renal impairment *(See Warnings and Precautions)*.

Dosage Adjustment for Adult Patients with Altered Creatinine Clearance

	Creatinine clearance (mL/min)[a]			Hemodialysis patients
	≥50	30-49	10-29	
Recommended 300 mg dosing interval	Every 24 hours	Every 48 hours	Every 72 to 96 hours	Every 7 days or after a total of approximately 12 hours of dialysis[b]

a. Calculated using ideal (lean) body weight.

b. Generally once weekly assuming three hemodialysis sessions a week of approximately 4 hours duration. VIREAD should be administered following completion of dialysis.

The pharmacokinetics of tenofovir have not been evaluated in non-hemodialysis patients with creatinine clearance <10 mL/min; therefore, no dosing recommendation is available for these patients. No data are available to make dose recommendations in pediatric patients with renal impairment.

CONTRAINDICATIONS: None.

WARNINGS AND PRECAUTIONS: Lactic Acidosis/Severe Hepatomegaly with Steatosis: Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported with the use of nucleoside analogs, including VIREAD, in combination with other antiretrovirals. A majority of these cases have been in women. Obesity and prolonged nucleoside exposure may be risk factors. Particular caution should be exercised when administering nucleoside analogs to any patient with known risk factors for liver disease; however, cases have also been reported in patients with no known risk factors. Treatment with VIREAD should be suspended in any patient who develops clinical or laboratory findings suggestive of lactic acidosis or pronounced hepatotoxicity (which may include hepatomegaly and steatosis even in the absence of marked transaminase elevations). **Exacerbation of Hepatitis after Discontinuation of Treatment:** Discontinuation of anti-HBV therapy, including VIREAD, may be associated with severe acute exacerbations of hepatitis. Patients infected with HBV who discontinue VIREAD should be closely monitored with both clinical and laboratory follow-up for at least several months after stopping treatment. If appropriate, resumption of anti-hepatitis B therapy may be warranted. **New Onset or Worsening Renal Impairment:** Tenofovir is principally eliminated by the kidney. Renal impairment, including cases of acute renal failure and Fanconi syndrome (renal tubular injury with severe hypophosphatemia), has been reported with the use of VIREAD *(See Adverse Reactions)*. It is recommended that estimated creatinine clearance be assessed in all patients prior to initiating therapy and as clinically appropriate during therapy with VIREAD. In patients at risk of renal dysfunction, including patients who have previously experienced renal events while receiving adefovir dipivoxil, it is recommended that estimated creatinine clearance, serum phosphorus, urine glucose, and urine protein be assessed prior to initiation of VIREAD, and periodically during VIREAD therapy. Dosing interval adjustment of VIREAD and close monitoring of renal function are recommended in all patients with creatinine clearance <50 mL/min *(See Dosage and Administration)*. No safety or efficacy data are available in patients with renal impairment who received VIREAD using these dosing guidelines, so the potential benefit of VIREAD therapy should be assessed against the potential risk of renal toxicity. VIREAD should be avoided with concurrent or recent use of a nephrotoxic agent (e.g., high-dose or multiple non-steroidal anti-inflammatory drugs (NSAIDs)) *(See Drug Interactions)*. Cases of acute renal failure after initiation of high dose or multiple NSAIDs have been reported in HIV-infected patients with risk factors for renal dysfunction who appeared stable on tenofovir DF. Some patients required hospitalization and renal replacement therapy. Alternatives to NSAIDs should be considered, if needed, in patients at risk for renal dysfunction. Persistent or worsening bone pain, pain in extremities, fractures and/or muscular pain or weakness may be manifestations of proximal renal tubulopathy and should prompt an evaluation of renal function in at-risk patients. **Coadministration with Other Products:** VIREAD should not be used in combination with the fixed-dose combination products ATRIPLA®, COMPLERA®, STRIBILD® or TRUVADA® since tenofovir disoproxil fumarate is a component of these products. VIREAD should not be administered in combination with adefovir dipivoxil *(See Drug Interactions)*. **Patients Coinfected with HIV-1 and HBV:** Due to the risk of development of HIV-1 resistance, VIREAD should only be used in HIV-1 and HBV coinfected patients as part of an appropriate antiretroviral combination regimen. HIV-1 antibody testing should be offered to all HBV-infected patients before initiating therapy with VIREAD. It is also recommended that all patients with HIV-1 be tested for the presence of chronic hepatitis B before initiating treatment with VIREAD.

Bone Effects

Bone Mineral Density: In clinical trials in HIV-1 infected adults, VIREAD was associated with slightly greater decreases in bone mineral density (BMD) and increases in biochemical markers of bone metabolism, suggesting increased bone turnover relative to comparators. Serum parathyroid hormone levels and 1,25 Vitamin D levels were also higher in subjects receiving VIREAD *(See Adverse Reactions)*.

Clinical trials evaluating VIREAD in pediatric and adolescent subjects were conducted. Under normal circumstances, BMD increases rapidly in pediatric patients. In HIV-1 infected subjects aged 2 years to less than 18 years, bone effects were similar to those observed in adult subjects and suggest increased bone turnover. Total body BMD gain was less in the VIREAD-treated HIV-1 infected pediatric subjects as compared to the control groups. Similar trends were observed in chronic hepatitis B infected adolescent subjects aged 12 years to less than 18 years. In all pediatric trials, skeletal growth (height) appeared to be unaffected *(See Adverse Reactions)*.

The effects of VIREAD-associated changes in BMD and biochemical markers on long-term bone health and future fracture risk are unknown. Assessment of BMD should be considered for adults and pediatric patients who have a history of pathologic bone fracture or other risk factors for osteoporosis or bone loss. Although the effect of supplementation with calcium and vitamin D was not studied, such supplementation may be beneficial for all patients. If bone abnormalities are suspected then appropriate consultation should be obtained.

Mineralization Defects: Cases of osteomalacia associated with proximal renal tubulopathy, manifested as bone pain or pain in extremities and which may contribute to fractures, have been reported in association with the use of VIREAD *(See Adverse Reactions)*. Arthralgias and muscle pain or weakness have also been reported in cases of proximal renal tubulopathy. Hypophosphatemia and

Brief Summary (Cont'd)

osteomalacia secondary to proximal renal tubulopathy should be considered in patients at risk of renal dysfunction who present with persistent or worsening bone or muscle symptoms while receiving products containing tenofovir DF *(See Warnings and Precautions).*

ADVERSE REACTIONS: Clinical Trials in Adult Subjects with Chronic Hepatitis B and Compensated Liver Disease: *Treatment-Emergent Adverse Reactions:* In controlled clinical trials in subjects with chronic hepatitis B (0102 and 0103), more subjects treated with VIREAD during the 48-week double-blind period experienced nausea: 9% with VIREAD versus 2% with adefovir dipivoxil. Other treatment-emergent adverse reactions reported in >5% of subjects treated with VIREAD included: abdominal pain, diarrhea, headache, dizziness, fatigue, nasopharyngitis, back pain, and skin rash. No significant change in the tolerability profile was observed with continued treatment with VIREAD for up to 384 weeks.

Laboratory Abnormalities: in Studies 0102 and 0103 (0–48 Weeks) laboratory abnormalities (Grades 3–4) reported in ≥1% of subjects treated with Viread (n=426) and adefovir dipivoxil (n=215), respectively, were: any ≥Grade 3 laboratory abnormality (19%, 13%); creatine kinase (M: >990 U/L; F: >845 U/L) (2%, 3%); serum amylase (>175 U/L) (4%, 1%); glycosuria (≥3+) (3%, <1%); AST (M: >180 U/L; F: >170 U/L) (4%, 4%); and ALT (M: >215 U/L; F: >170 U/L) (10%, 6%). Laboratory abnormalities (Grades 3–4) were similar in subjects continuing VIREAD treatment for up to 384 weeks in these trials.

The overall incidence of on-treatment ALT flares (defined as serum ALT >2 × baseline and >10 × ULN, with or without associated symptoms) was similar between VIREAD (2.6%) and adefovir dipivoxil (2%). ALT flares generally occurred within the first 4-8 weeks of treatment and were accompanied by decreases in HBV DNA levels. No subject had evidence of decompensation. ALT flares typically resolved within 4-8 weeks without changes in study medication. The adverse reactions observed in subjects with chronic hepatitis B and lamivudine resistance who received treatment with VIREAD were consistent with those observed in other hepatitis B clinical trials in adults. *Clinical Trial in Adult Subjects with Chronic Hepatitis B and Decompensated Liver Disease:* In a small randomized, double-blind, active-controlled trial (0108), subjects with CHB and decompensated liver disease received treatment with VIREAD or other antiviral drugs for up to 48 weeks. Among the 45 subjects receiving VIREAD, the most frequently reported treatment-emergent adverse reactions of any severity were abdominal pain (22%), nausea (20%), insomnia (18%), pruritus (16%), vomiting (13%), dizziness (13%), and pyrexia (11%). Two of 45 (4%) subjects died through Week 48 of the trial due to progression of liver disease. Three of 45 (7%) subjects discontinued treatment due to an adverse event. Four of 45 (9%) subjects experienced a confirmed increase in serum creatinine of 0.5 mg/dL (1 subject also had a confirmed serum phosphorus <2 mg/dL through Week 48). Three of these subjects (each of whom had a Child-Pugh score ≥10 and MELD score ≥14 at entry) developed renal failure. Because both VIREAD and decompensated liver disease may have an impact on renal function, the contribution of VIREAD to renal impairment in this population is difficult to ascertain. One of 45 subjects experienced an on-treatment hepatic flare during the 48 week trial.

Clinical Trials in Pediatric Subjects 12 Years of Age and Older with Chronic Hepatitis B: Assessment of adverse reactions is based on one randomized study (0115) in 106 pediatric subjects (12 to less than 18 years of age) infected with chronic hepatitis B receiving treatment with VIREAD (N = 52) or placebo (N = 54) for 72 weeks. The adverse reactions observed in pediatric subjects who received treatment with VIREAD were consistent with those observed in clinical trials of VIREAD in adults. In this study, both the VIREAD and placebo treatment arms experienced an overall increase in mean lumbar spine BMD over 72 weeks, as expected for an adolescent population. The BMD gains from baseline to Week 72 in lumbar spine and total body BMD in VIREAD-treated subjects (+5% and +3%, respectively) were less than the BMD gains observed in placebo-treated subjects (+8% and +5%, respectively). Three subjects in the VIREAD group and two subjects in the placebo group had significant (greater than 4%) lumbar spine BMD loss at Week 72. At baseline, mean BMD Z-scores in subjects randomized to VIREAD were –0.43 for lumbar spine and –0.20 for total body, and mean BMD Z-scores in subjects randomized to placebo were –0.28 for lumbar spine and –0.26 for total body. In subjects receiving VIREAD for 72 weeks, the mean change in BMD Z-score was –0.05 for lumbar spine and –0.15 for total body compared to +0.07 and +0.06, respectively, in subjects receiving placebo. As observed in pediatric studies of HIV-infected patients, skeletal growth (height) appeared to be unaffected *(See Warnings and Precautions).*

Postmarketing Experience: The following adverse reactions have been identified during postapproval use of VIREAD. Because postmarketing reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure: allergic reaction, including angioedema, lactic acidosis, hypokalemia, hypophosphatemia, dyspnea, pancreatitis, increased amylase, abdominal pain, hepatic steatosis, hepatitis, increased liver enzymes (most commonly AST, ALT gamma GT), rash, rhabdomyolysis, osteomalacia (manifested as bone pain and which may contribute to fractures), muscular weakness, myopathy, acute renal failure, renal failure, acute tubular necrosis, Fanconi syndrome, proximal renal tubulopathy, interstitial nephritis (including acute cases), nephrogenic diabetes insipidus, renal insufficiency, increased creatinine, proteinuria, polyuria, asthenia. The following adverse reactions listed above, may occur as a consequence of proximal renal tubulopathy: rhabdomyolysis, osteomalacia, hypokalemia, muscular weakness, myopathy, hypophosphatemia.

DRUG INTERACTIONS: Didanosine: Coadministration of VIREAD and didanosine should be undertaken with caution and patients receiving this combination should be monitored closely for didanosine-associated adverse reactions. Didanosine should be discontinued in patients who develop didanosine-associated adverse reactions. When administered with VIREAD, C_{max} and AUC of didanosine increased significantly. The mechanism of this interaction is unknown. Higher didanosine concentrations could potentiate didanosine-associated adverse reactions, including pancreatitis and neuropathy. Suppression of $CD4^+$ cell counts has been observed in patients receiving VIREAD with didanosine 400 mg daily. In patients weighing >60 kg, the didanosine dose should be reduced to 250 mg once daily when it is coadministered with VIREAD. In patients weighing <60 kg, the didanosine dose should be reduced to 200 mg once daily when it is coadministered with VIREAD. When coadministered, VIREAD and didanosine EC may be taken under fasted conditions or with a light meal (<400 kcal, 20% fat). For additional information on coadministration of VIREAD and didanosine, please refer to the full Prescribing Information for didanosine. **HIV-1 Protease Inhibitors:** VIREAD decreases the AUC and C_{min} of atazanavir. Viread should not be coadministered with atazanavir without ritonavir. Lopinavir/ritonavir, atazanavir coadministered with ritonavir, and darunavir coadministered with ritonavir have been shown to increase tenofovir concentrations. Tenofovir disoproxil fumarate is a substrate of P-glycoprotein (Pgp) and breast cancer resistance protein (BCRP) transporters. When tenofovir disoproxil fumarate is coadministered with an inhibitor of these transporters, an increase in absorption may be observed. Patients receiving VIREAD concomitantly with lopinavir/ritonavir, ritonavir-boosted atazanavir, or ritonavir-boosted darunavir should be monitored for VIREAD-associated adverse reactions. VIREAD should be discontinued in patients who develop VIREAD-associated adverse reactions. **Drugs Affecting Renal Function:** Since tenofovir is primarily eliminated by the kidneys, coadministration of VIREAD with drugs that reduce renal function or compete for active tubular secretion may increase serum concentrations of tenofovir and/or increase the concentrations of other renally eliminated drugs. Some examples include, but are not limited to cidofovir, acyclovir, valacyclovir, ganciclovir, valganciclovir, aminoglycosides (e.g., gentamicin), and high-dose or multiple NSAIDs *(See Warnings and Precautions).* In the treatment of chronic hepatitis B, VIREAD should not be administered in combination with adefovir dipivoxil.

USE IN SPECIFIC POPULATIONS: Pregnancy: *Pregnancy Category B:* There are no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, VIREAD should be used during pregnancy only if clearly needed. *Antiretroviral Pregnancy Registry:* To monitor fetal outcomes of pregnant women exposed to VIREAD, an Antiretroviral Pregnancy Registry has been established. Healthcare providers are encouraged to register patients by calling 1-800-258-4263. *Animal Data:* Reproduction studies have been performed in rats and rabbits at doses up to 14 and 19 times the human dose based on body surface area comparisons and revealed no evidence of impaired fertility or harm to the fetus due to tenofovir. **Nursing Mothers: The Centers for Disease Control and Prevention recommend that HIV-1-infected mothers not breastfeed their infants to avoid risking postnatal transmission of HIV-1.** Samples of breast milk obtained from five HIV-1 infected mothers in the first post-partum week show that tenofovir is secreted in human milk. The impact of this exposure in breastfed infants is unknown. Because of both the potential for HIV-1 transmission and the potential for serious adverse reactions in nursing infants, **mothers should be instructed not to breastfeed if they are receiving VIREAD. Geriatric Use:** Clinical studies of VIREAD did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. In general, dose selection for the elderly patient should be cautious, keeping in mind the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy. **Patients with Impaired Renal Function:** It is recommended that the dosing interval for VIREAD be modified in patients with estimated creatinine clearance <50 mL/min or in patients with ESRD who require dialysis *(See Dosage and Administration).*

For detailed information, please see full Prescribing Information. To learn more call 1-800-GILEAD-5 (1-800-445-3235) or visit www.VIREAD.com.

CVH

Center for Viral Hepatitis

바이러스간염진료센터

- To promote the awareness of hepatitis B
- To screen in high risk population
- To facilitate the linkage to care

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Earn what's new on viral hepatitis

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LINKAGE TO CARE
Engage yourself to access health care

www.cureHep.org

Happy smile and hope after pain

D.K. Lee has related to It's A Wig that she will promote to cancer patients about the beauty classes and healing programs she attended. The beauty classes are held at Kyung Hee Medical Center and it is for cancer patients to help them feel more womanly during their hard times. She would like to thank all the people who gave her hope. "Thank you for giving me a second chance to live as a woman. With the hopes and gifts that I have received, it encourages me to work harder to volunteer my time for the people who are fighting against cancer."

Kyung Hee Medical Center patient
D. K. Lee

Cancer-free D.K. Lee

D.K. Lee attending
beauty classes while chemotherapy treatment

Conference Alerts

North America

2021 JAX Healthcare Forum
October 27-28, 2021 | Virtual Conference

Website: https://www.jax.org/education-and-learning/education-calendar/2021/10-october/forum
Contact: https://www.jax.org/global-contact-form

2021 JAX Healthcare Forum is a gathering of decision makers from across the healthcare industry. It is the centerpiece of The Jackson Laboratory's efforts to create a new paradigm for biomedical innovation. This year's conference theme, "Post-COVID World.", focus areas include biology and epidemiology, population dynamics, regulatory landscape, future of vaccine development, post pandemic economic and business impacts.

LM 2021 (Lifestyle Medicine)
November 7-10, 2021 | Virtual Conference

Website: https://lmconference.org/index.asp
Contact: events@lifestylemedicine.org

Lifestyle Medicine 2021 and ACLM's Corporate Roundtable bring together all stakeholder groups that comprise healthcare: physicians, health professionals, medical education, health systems, health insurers, benefits consultants, self-insured employers, purveyors of products and services that support the clinical practice of lifestyle medicine, as well as the tip of the spear, our providers--the physicians and allied health professionals who are on the front lines.

STAT Summit 2021
November 16-18, 2021 | Virtual Conference

Website: https://www.statnews.com/2021/summit/stat-summit/
Contact: summit@statnews.com

STAT Summit 2021 will gather the top minds in the life sciences and bring to life the coverage that has earned STAT its reputation: deep analysis and fearless discussion around the most important topics in biotech, medicine, and policy, brought to you by the industry's top talent.

2021 Global Wellness Summit
November 30-December 3, 2021 | Boston, Massachusetts, USA

Website: https://www.globalwellnesssummit.com/2021-global-wellness-summit/
Contact: kendra.kobler@globalwellnesssummit.com

The unifying force of the Global Wellness Summit (GWS) is an annual gathering, the most important global conference on the business of wellness. The 15th of the annual Global Wellness Summit is with the theme of "A New New Era of Health & Wellness." The conference will bring together leaders and visionaries to positively impact and shape the future of the global wellness industry.

63rd ASH Annual Meeting and Exposition
December 11-14, 2021 | Atlanta, Georgia, USA

Website: https://www.hematology.org/meetings/annual-meeting
Contact: 202-776-0544

The 63rd ASH Annual Meeting and Exposition is the world's most comprehensive hematology event of the year for an invaluable educational experience and the opportunity to review thousands of scientific abstracts highlighting updates in the hottest topics in hematology.

Europe

World Health Summit
October 24-26, 2021 | Berlin, Germany

Website: https://www.worldhealthsummit.org/
Contact: contact@worldhealthsummit.org

The World Health Summit is one of the world's leading strategic forums for global health and brings together leaders from politics, science and medicine, the private sector, and civil society to set the agenda for a healthier future.

CPhl Worldwide 2021
October 24-26, 2021 | Milan, Italy

Website: https://www.cphi.com/europe/en.html
Contact: https://www.cphi.com/europe/en/about/contact-us.html

CPhI Worldwide, together with co-located events ICSE, P-MEC, FDF, InnoPack, and BioProduction, hosts more than 36,000 visiting pharma professionals. 2,500+ exhibitors from 170+ countries gather at the event to network and take advantage of more than 100+ onsite conferences and seminars. It will be a great opportunity to establish new business relationships, meet with global partners and stay updated on the latest industry trends. The exhibition showcases cover the whole spectrum of pharmaceutical manufacturing and ingredients sourcing, offering products and services that cover the entire supply chain.

Total Health Europe: Adapt to the New Age of European Healthcare
November 29-30, 2021 | Virtual Conference

Website: https://reutersevents.com/events/healthcare-europe/
Contact: jack.tiplady@thomsonreuters.com

Post-pandemic European healthcare providers face overburdened workforces and patients that struggle to access the care that they require. At Total Health Europe 2021, attendees will seize the opportunity to connect with 2,000+ stakeholders and find the solutions from the key decision makers. The healthcare meeting provides solutions to the most pressing European issues: Release data-driven healthcare with digitalized patient records, Leverage virtual and remote care, Address the European health workforce crisis, and Improve patient access to care.

Conference Alerts

Asia

HIMSS21 APAC Conference & Exhibition

October 18-19, 2021 | Singapore, Singapore

Website: https://www.himss.org/event-himss-singapore
Contact: Evelyn.Wee@himss.org

HIMSS21 APAC Conference and Exhibition will be convened under the theme of Future-Proof Healthcare: The Emergence of Asia Pacific. Hear from speakers and thought leaders as they explore future-proof capabilities to help organizations enhance quality of care and reduce costs by focusing on consumers, harnessing the power of technology, and bringing together solutions to be developed and implemented for a sustainable and resilient health ecosystem.

APCCMI Singapore 2021: 18th Asia Pacific Congress of Clinical Microbiology and Infection

November 11-13, 2021 | Virtual Conference

Website: https://apccmi2021.com
Contact: https://apccmi2021.com/contact-us

The Asia Pacific Congress of Clinical Microbiology and Infection (APCCMI) is the bi-annual conference for the Asia Pacific Society of Clinical Microbiology and Infection (APSCMI). The forum is with a very strong scientific program and is expected to bring together over 1,200 delegates. It will focus on COVID-19, advances in infection control, microbiome vaccines, microbiology, challenges, and progress in the three pandemic infections of HIV, Malaria, and Tuberculosis, and etc.

The 10th International Conference on Biomedical Engineering and Biotechnology

November 15-18, 2021 | Suzhou, China

Website: http://www.icbeb.org/
Contact: icbeb@icbeb.org

The 10th International Conference on Biomedical Engineering and Biotechnology (ICBEB 2021), hosted by Institute of Biomaterials and Medical Devices, Jiangsu Industrial Technology Research Institute & Institute of Biomedical Devices (Suzhou), Southeast University. As an annual gathering, it provides an opportunity and unique platform for scientists, researchers, and scholars to present various research activities and latest findings in Biomedical Engineering and Biotechnology, discuss the practical challenges encountered, recommend better solutions for human health, and explore avenues to collaborate with top experts from various countries.

8th China Healthcare Summit: The Bridge to Innovation

November 16-19, 2021 | Virtual Conference

Website: https://conferences.biocentury.com/china-healthcare-summit
Contact: https://www.biocentury.com/contact-us

The BioCentury-BayHelix China Healthcare Summit: The Bridge to Innovation is a VIP event organized in collaboration with McKinsey & Co. The conference will gather top thinkers from industry, academia, and finance to identify who will lead China's biopharma innovation ecosystem, how innovation will be funded, and the business strategies required to transform both domestic and multinational biopharma companies as China advances its innovation agenda.

LATEST HEALTHCARE INDUSTRY NEWS

JUL - SEP 2021

1. FDA Revises Labeling of Biogen's Alzheimer's Drug to Emphasize Early Treatment

The Food and Drug Administration, under heavy criticism over its decision last month to approve Biogen's Alzheimer's drug Aduhelm, has revised the medicine's prescribing information in an effort to focus treatment to the type of patients who were included in clinical testing. The FDA's June 7 approval of Aduhelm was made more controversial by the agency's decision to clear the drug for broad use, even though Biogen's studies only enrolled patients with mild Alzheimer's. Under the FDA's initial approval of Aduhelm, patients in the United States would be eligible for treatment, despite Biogen never having studied the drug in patients in later stages of disease.

https://www.biopharmadive.com/news/fda-biogen-alzheimers-revise-prescribing-information/603008/

2. Related Cos., CareMax Partner Up to Develop Senior Health Centers in Underserved Communities

Related Cos., one of the largest owners of affordable housing in the U.S., is acquiring as much as a 9% stake in healthcare provider CareMax Inc. as part of its plan to develop scores of senior health centers in underserved urban communities throughout the U.S. Related, a developer of office buildings, malls and upscale apartments as well as affordable housing, will act as an investor, adviser, developer and, in some cases, landlord of CareMax health centers. As part of the deal, Related will buy $5 million in CareMax stock and receive warrants to purchase up to 8 million shares at $11.50 a share.

https://www.wsj.com/articles/related-cos-caremax-partner-up-to-develop-senior-health-centers-in-underserved-communities-11626168602

3. FDA Approves First Biosimilar to Top-Selling Eye Drug Lucentis

The U.S. Food and Drug Administration on Monday approved the first biosimilar version of Lucentis, a blockbuster biologic drug for age-related macular degeneration and two other eye conditions. The biosimilar, called Byooviz, was developed by Samsung Bioepis and will be sold by partner Biogen when patents protecting Lucentis expire next year. Byooviz is the second biosimilar to be approved in the U.S. in 2021 after the agency cleared Mylan and Biocon's Semglee as interchangeable with Sanofi's Lantus. The FDA approved three biosimilars last year and to date has approved 31 of the copycat drugs.

https://www.biopharmadive.com/news/fda-approves-first-biosimilar-to-top-selling-eye-drug-lucentis/606855/

4. Startup EQRx to Take Drug Price Mission Public through $1.8B SPAC Deal

EQRx, a startup with lofty ambitions to develop competitors to top-selling drugs at much reduced prices, will go public through a merger with a blank-check company backed by the biotech venture firm Casdin Capital and the hedge fund Corvex Management. The deal, announced Friday by EQRx and the special-purpose acquisition company CM Life Sciences II, will give EQRx access to $1.8 billion in new funds, dramatically increasing the resources it has on hand to support a business plan. EQRx's business plan remains unproven, however. It is unclear how well EQRx can deliver on its promise of cheaply developing dozens of other drugs as good as, or better than, established medicines.

https://www.biopharmadive.com/news/startup-eqrx-to-take-drug-price-mission-public-through-18b-spac-deal/604590/

5. Merck Wins Approval for Cancer Drug Acquired in 2019 Biotech Buyout

Merck & Co. on Friday said it has won Food and Drug Administration approval for a targeted cancer drug it acquired two years ago in a $1 billion buyout of biotech Peloton Therapeutics. The drug, which will be sold as Welireg, is cleared to treat several types of tumors that are associated with a rare genetic condition called von Hippel-Lindau disease, or VHL. In a small clinical trial of 61 people with VHL-associated cancer, treatment with Welireg shrank tumors in the kidney, nervous system and pancreas. Welireg is the first drug of its type to win FDA approval, Merck said in a August 16 statement.

https://www.biopharmadive.com/news/merck-welireg-fda-approval-peloton/605047/

6. Pandemic Special Enrollment Period Led to Record Number of ACA Enrollees

More than 2.8 million people signed up for healthcare coverage during the special enrollment period for Affordable Care Act plans that ran from February 15 through August 15, putting the number of people enrolled in an ACA plan at its highest level ever, according to a release from HHS. The American Rescue Plan passed earlier this year also expanded premium tax credits and helped drive down premiums — over 90% of those who enrolled during the SEP saw their premiums reduced, and 48% of new HealthCare.gov enrollees pay $10 or less a month in premiums after tax credits, according to the release. Existing enrollees have also benefited, saving an average of $67 a month on premiums, according to HHS.

https://www.healthcaredive.com/news/pandemic-special-enrollment-period-led-to-record-number-of-aca-enrollees/606699/

7. Pfizer Stocks Cancer Drug Pipeline with $2.3B Deal for Trillium

Pfizer is building up its pipeline of experimental cancer medicines, announcing a deal to buy the Cambridge, Massachusetts-based biotech Trillium Therapeutics for nearly $2.3 billion. The acquisition marks a dramatic turnaround for Trillium, which was worth less than $50 million at the start of last year. Under deal terms, Pfizer agreed to pay $18.50 per share of the biotech, valuing the company at a premium of more than 200% to the stock's closing price on Friday. By buying Trillium, Pfizer gains access to two drugs in early stages of clinical testing for a range of blood cancers, like lymphoma, as well as certain solid tumors.

https://www.biopharmadive.com/news/pfizer-trillium-acquisition-deal-cancer-cd47/605389/

8. Google Disbands Health Unit as Chief Departs for Cerner

Google is dissolving its health division, Google Health, after three years as the head of the unit, David Feinberg, departs to become CEO of health IT vendor Cerner. Google is splitting its health projects and teams across several other divisions of the company. Alphabet's Google created the Google Health division in 2018 to bring its health initiatives under a single umbrella. The Mountain View, California-based company remains committed to healthcare and will continue to invest in the space, but the goal of the reshuffling is to put its teams in the areas that make the most sense for its projects.
https://www.healthcaredive.com/news/google-disbands-health-unit-as-chief-departs-for-cerner/605387/

9. Business Groups Withdraw Suit Challenging Health-Price Transparency Rule

The U.S. Chamber of Commerce and a Texas affiliate withdrew a suit filed to block parts of a federal rule requiring insurers and employers to disclose prices they pay for healthcare services and drugs. The withdrawal came after the Biden administration delayed enforcement of provisions of the rule that were the focus of the suit. The suit, which was filed against the U.S. Department of Health and Human Services and other federal agencies on August 10, claimed provisions of the rule, which required disclosure of prices for healthcare services and drugs in machine-readable files, went beyond federal authority and could raise healthcare costs. Enforcement of some provisions of the rule was delayed to July 1, 2022, from January 1, 2022. Enforcement of a requirement to disclose drug prices was delayed indefinitely pending new rule making.
https://www.wsj.com/articles/business-groups-withdraw-suit-challenging-health-price-transparency-rule-11629998986

10. Headspace, Ginger to Merge, Creating $3B Mental Health Company

Meditation and mindfulness startup Headspace and on-demand mental healthcare app Ginger have announced plans to merge into a single company, called Headspace Health, valued at $3 billion. The two startups focused on mental health and wellness have each raised more than $200 million in venture funding from investors. As Headspace Health, the two companies will offer support for mental health symptoms from anxiety to depression to more complex diagnoses, selling direct to consumers and to employers and health plans. Financial terms of the deal, which is expected to close in the fourth quarter this year, were not disclosed.
https://www.healthcaredive.com/news/headspace-ginger-to-merge-create-3b-mental-health-company/605632/

11. BioMarin Wins European Approval to Sell Drug for Dwarfism

BioMarin Pharmaceutical can sell its drug for dwarfism in Europe after regulators there granted a market authorization, two months following the European Medicines Agency's endorsement of the California biotech company's treatment. BioMarin's drug, which it will sell under the brand name Voxzogo, is the first medicine to be made available in Europe for achondroplasia, the most common cause of dwarfism. Under an access plan with authorities in France, BioMarin plans to charge roughly $300,000 per patient per year.
https://www.biopharmadive.com/news/biomarin-voxzogo-european-approval-dwarfism/605703/

12. FDA Approves First-of-Its-Kind Stroke Rehabilitation System

The U.S. Food and Drug Administration today approved the MicroTransponder Vivistim Paired VNS System (Vivistim System), a first-of-its-kind, drug-free rehabilitation system intended to treat moderate to severe upper extremity motor deficits associated with chronic ischemic stroke—a stroke caused by a blockage of blood flow to the brain with long-lasting symptoms—using vagus nerve stimulation (VNS). The Vivistim System is not approved for use outside of its intended use to stimulate the vagus nerve during chronic ischemic stroke rehabilitation therapy for moderate to severe loss of upper extremity function. It should not be used in patients with vagotomy, which is surgical removal of part of the vagus nerve.
https://www.fda.gov/news-events/press-announcements/fda-approves-first-its-kind-stroke-rehabilitation-system

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