MRx TREND ALERT

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YOUR QUARTERLY SOURCE FOR KEY TRENDS

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DID YOU KNOW? ICER REDUX

In our February 2016 issue, we reviewed the purpose, role, and structure of the independent, non-profit watchdog Institute for Clinical and Economic Review (ICER). ICER recently received a 3-year, $13.9 million grant, which will support their ability to review several new and existing drugs and classes, rather than focusing solely on high-profile agents.

Payers have begun to utilize these reports for price negotiations when ICER determines the drug does not meet cost-effectiveness at its current price point. The Pharmaceutical Research and Manufacturers of America (PhRMA) has expressed concern that ICER's reports could limit patient access to medications. However, select pharmaceutical manufacturers have worked with ICER to adjust drug pricing to better reflect their drug's worth based on ICER's analysis. Also, there are instances where ICER has found that very expensive treatments are currently priced such that their costs align with their clinical benefit for select uses. ICER also continues to fine-tune how they calculate price to adjust for other factors and, in March 2018, ICER released details on a pilot program to allow manufacturers to critique draft cost-effectiveness models. With continuous improvement in methods and findings that have resulted in either justified costs or, ultimately, an adjustment in price to reflect value, ICER clearly is making its mark.

ICER utilizes the quality-adjusted life year (QALY), a commonly used metric that provides a standardized approach to allow for comparability. The general construct of the QALY is that people can move through various health states over time, each of which is associated with a value under the assumption that health is valuable. A QALY is defined as a year of life adjusted for its quality or value. Thus, a year in perfect health is equivalent to 1 QALY, and death is equivalent to 0, while a year of ill health would be considered < 1 (e.g., 0.5 for a bedridden year). In brief, ICER's reports first examine clinical context, including treatment guidelines and coverage policies. Next, they assess the comparative outcomes from clinical studies, rating interventions of both health benefit and evidence certainty. Finally, they consider various factors, including utility and cost data, to model the cost-impact, resulting in estimates of total costs and QALYs gained. The ultimate cost per QALY reported can then be used to assess overall net gain from the product.

Most recently, ICER announced the formation of an advisory group consisting of key stakeholders, including pharma industry representatives, to guide a report on drug price increases that lack evidentiary support. ICER plans to release an initial report in the first quarter of 2019. With a focus on cost-containment for pharmaceuticals new and old, stakeholders are sure to be watching. ■

PROs: ESTABLISHING RELIABLE AND VALID TOOLS

As discussed in a previous issue, patient-reported outcomes (PROs) have demonstrated value in improving clinical outcomes for patient care. However, questions on how to accurately measure and implement PROs remain.

In clinical research, various instruments have been used to measure PROs. Several of these have been evaluated and catalogued within the National Institutes of Health (NIH) Patient Reported Outcomes Measurement Information System, or PROMIS®. Originally developed in 2004, PROMIS was funded as a 10-year project to construct an assessment system for self-reported health using large item banks and computer adaptive testing. The resulting PROMIS I and PROMIS II studies assessed PROs among a myriad of chronic conditions and populations in clinical research. PROMIS offers a publicly available resource, with reliable PROs across a wide variety of domains. More recently, an extension of the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) 2013 statement used an international, consensus-based approach to elaborate on these guidelines for clinical trials to address PROs, resulting in SPIRIT-PRO in February 2018.

Challenges with using intrinsically subjective PROs include lack of widespread use and limited established reliability to measure performance of healthcare. In addition, their heightened significance in the US Food and Drug Administration (FDA) approval process has raised questions on the rigor of drug approvals that emphasize PROs and "real-world" evidence, rather than focusing on traditional randomized, controlled trials. While much of the 21st Century Cures Act delegates the role determination of PROs in drug approval to FDA guidance, additional research and the PROMIS database improve the perceived reliability of PROs. In June 2018, the FDA announced the plans for 4 documents for industry and other stakeholders regarding patient-focused drug development. The first, currently in draft form, recommends how to operationalize and standardize the collection of information.

Operationalizing the role of PROs in healthcare coincides with an increased interest in incorporating other sources of patient-generated data into care, but it certainly has its own challenges. Guidance from provider and industry resources, like PROMIS, and the FDA's commitment to providing insight will continue to shape how these key measures for patient-perceived value will impact both drug approval and patient care. ■

KEEP ON YOUR RADAR: INDICATION-BASED PRICING AND BILLING CHALLENGES

The FDA approved 2 chimeric antigen receptor-T (CAR-T) cell therapies in 2017. As discussed in a prior issue, CAR-T cell therapy involves collecting a patient's own T cells, genetically modifying them, and infusing them back into the patient.

Tisagenlecleucel (Kymriah®) was approved on August 30, 2017 for the treatment of relapsed/refractory B cell acute lymphoblastic leukemia (ALL) in patients up to 25 years old. At that time, Novartis launched Kymriah with a wholesale acquisition cost (WAC) of $475,000 for the one-time treatment. On May 1st of this year, the FDA approved Kymriah for a second indication of relapsed/refractory diffuse large B cell lymphoma (DLBCL) in adult patients. Meanwhile, Gilead's axicabtagene ciloleucel (Yescarta®) was approved for DLBCL on October 18, 2017. The WAC price for Yescarta was set at $373,000. In response, Novartis set the price for Kymriah when used to treat DLBCL at a parity price of $373,000.

The Centers for Medicare and Medicaid Services (CMS) assigned a temporary Q-code of Q2040 for Kymriah effective January 1, 2018, which will be used for both Kymriah indications. Novartis has assigned 2 different National Drug Codes (NDCs) for Kymriah to address the different indications. Both agents also have a handful of other potential indications in the pipeline (Table 1). Health plans will need to pay close attention to how medical claims for Kymriah will be reimbursed based on patient diagnosis. Some health plans do not accept/receive NDC numbers on the medical claims for medications when billed through the medical benefit. If

Table 1: CAR-T Pipeline Indications in the Pipeline

DRUG	INDICATION	ESTIMATED APPROVAL DATE
Kymriah	Relapsed/refractory follicular lymphoma	2020 (Phase 3)
	Chronic lymphocytic leukemia	2021 (Phase 3)
	Relapsed/refractory DLBCL (+ pembrolizumab)	2022 (Phase 3)
	Relapsed/refractory DLBCL in first relapse	> 2022 (Phase 2)
Yescarta	Indolent non-Hodgkin's lymphoma	> 2022 (Phase 2)
	Relapsed/refractory mantle cell lymphoma	> 2022 (Phase 2)
	Refractory DLBCL (+ atezolizumab)	To Be Determined (Phase 1 & 2)

a health plan is only accepting the assigned temporary Q-code, the claim could be reimbursed at the wrong rate, causing a potential over or under payment of around $102,000. Most health plans are currently adjudicating CAR-T medical claims on a case-by-case basis due to the high cost, so chances of the wrong payment being reimbursed are lessened. As these treatments become more common and additional indications are approved, health plans will need to ensure they have automated NDC-level claim information to reimburse for Kymriah.

It will be interesting to see how many more pharmaceutical manufacturers will follow Novartis in the adoption of indication-based pricing for new medications. ■

MEDICAL PHARMACY CORNER

DRUG SUPPLY CHAIN OPTIONS: WILL THAT ORDER BE CARRY OUT?

The drug supply chain is one of the many differences between drugs that are dispensed under the pharmacy benefit versus the medical benefit. With pharmacy benefit drugs, patients usually fill prescriptions at a local pharmacy or through mail order. In contrast, medical benefit drugs are usually dispensed (and administered) at the provider's office; however, recent models may be changing this paradigm.

The method by which physicians obtain drugs for office administration differs based on several variables. The most common supply chain for these drugs is referred to as "buy and bill" (Figure 1). Under the buy and bill system, doctors' offices usually purchase the drugs through a specialty distributor. Doctors practicing in hospital-based outpatient clinics often receive their drugs from an internal pharmacy. Under buy and bill, the physician's office or clinic is responsible for all inventory management of the medication.

Drugs managed under the medical benefit are often very expensive and typically account for a large percentage of health plan drug costs. "Brown bagging" or "white bagging" has been identified as a possible drug supply chain strategy to potentially defray some of these costs (Figure 2). Brown bagging refers to a system whereby the patient obtains the drug from a local or specialty pharmacy and brings it to the provider's office to be administered. White bagging is similar except the drug is shipped directly to the provider's office.

The pros and cons of each system differ according to the stakeholder. With brown bagging or white bagging, the payer has greater control over the cost due to contracted network pharmacy rates. It also removes incentives for prescribing a more costly medication; provider reimbursement is independent of the drug cost. Increased cost due to wasted medications would be among the disadvantages, if problems occur with shipping or if the patient's dose changes.

Many providers are against the practice of brown bagging or white bagging. One reason is due to lost revenue because they are only reimbursed for drug administration and lose the markup on drug charges. Lack of certainty regarding proper storage and the added cost of maintaining separate, patient-specific inventory records are other concerns. For these reasons, some providers have declined to treat patients in brown bagging- or white bagging-mandated plans.

Patients may experience advantages or disadvantages with either system. The patient's copayment or coinsurance amount may differ depending on which drug supply channel is utilized. Specialty pharmacies dispensing drugs for brown bagging or white bagging programs may identify patient copay assistance programs, but this service may or may not be offered in the provider office under buy and bill. Depending on the benefit design, patient out-of-pocket costs may be drastically different.

As the number of drugs billed under the medical benefit continues to expand, payers and providers need to collaborate to ensure patients can receive safe, effective, and affordable drug therapy. ■

Figure 1: Buy & Bill

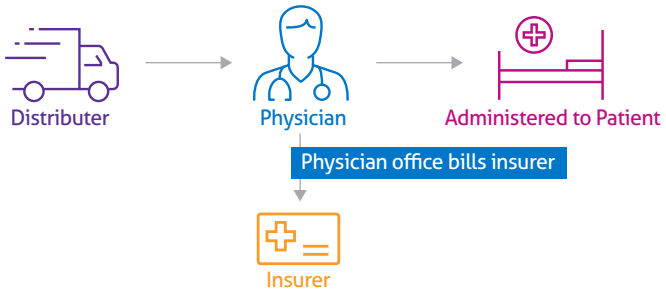
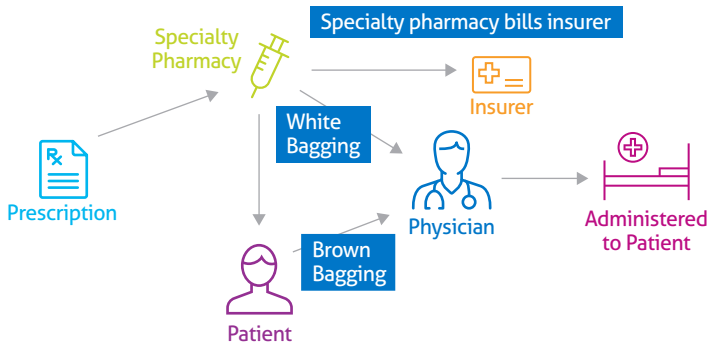


Figure 2: White Bagging versus Brown Bagging



PIPELINE REPORT: 3RD AND 4TH QUARTER 2018

DRUG MANUFACTURER	CLINICAL USE	ANTICIPATED DATE	PROJECTED MARKET IMPACT
Select Branded Pipeline Agents: Potential New Emerging Expenses for Health Plans			
fremanezumab Teva	Migraine prevention	September 14, 2018	Subcutaneous (SC) calcitonin gene-related peptide (CGRP) inhibitor; will compete with erenumab (Aimovig™) and galcanezumab as new class of anti-migraine agents; Fast track; Priority review
galcanezumab Eli Lilly	Migraine prevention	September 28, 2018	SC CGRP inhibitor; will compete with erenumab (Aimovig) and fremanezumab as new class of anti-migraine agents; Fast track
omadacycline Paratek	Bacterial skin and skin-structure infections and community-acquired pneumonia	October 2, 2018	Intravenous (IV) and oral broad-spectrum, tetracycline-derived, first-in-class aminomethylcycline antibiotic; appears unaffected by select common resistance mechanisms; Fast track; Priority review; Qualified infectious diseases product
levodopa Acorda	"Off" periods in Parkinson's disease	October 5, 2018	Inhaled dopamine precursor; offers fast-acting alternative to SC apomorphine (Apokyn®)
doravirine and doravirine/ lamivudine/ tenofovir disoproxil fumarate Merck	Human immunodeficiency virus-1 (HIV-1) infection	October 23, 2018	Oral non-nucleoside reverse transcriptase inhibitor (NNRTI) as a once-daily tablet for use in combination with other antiretroviral agents and oral NNRTI combined with 2 nucleos(t)ide reverse transcriptase inhibitors (NRTIs) in a once-daily, fixed-dose tablet as a complete regimen
cemiplimab Regeneron	Cutaneous squamous cell carcinoma	October 26, 2018	IV programmed cell death protein-1 (PD-1) checkpoint inhibitor; Breakthrough therapy; Priority review
Select New Generics/ Patent Expirations			
testosterone generic for Abbvie's Androgel® 1.62%	Hypogonadism	2H 2018	Settlement agreement with Perrigo; US sales of > $952 million in 2017
silodosin generic for Allergan's Rapaflo®	Benign prostatic hyperplasia	4Q 2018	Settlement agreement with multiple manufacturers; US sales of $206 million in 2017
azelaic acid generic for Bayer's Finacea® Gel	Rosacea	November 18, 2018	Patent expiration; multiple generic manufacturers anticipated; US sales of $66 million in 2017
Select Biosimilars			
SB3 – biosimilar to Genentech's Herceptin® Merck/ Samsung Bioepis	Breast cancer (HER2+)	October 19, 2018	Trastuzumab; IV HER2/neu receptor antagonist; product launch likely to be delayed due to regulatory hurdles; Herceptin had US sales of $2.8 billion in 2017
CHS-1701 – biosimilar to Amgen's Neulasta® Coherus	Neutropenia associated with chemotherapy; neutropenia associated with radiation	November 3, 2018	Pegfilgrastim; SC colony stimulating factor; product launch likely to be delayed due to regulatory hurdles; Neulasta had $4.2 billion in US sales in 2017