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CARDIOVASCULAR MEDICINE & SOCIETY

Role of Payers in the Development of Cardiovascular Therapeutics

Misalignment Between Approval and Reimbursement

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ABSTRACT

Regulators and payers have contrasting priorities that can lead to divergent decisions and delays in patient access to new treatments. Those involved in coverage decisions have not routinely been integrated in the drug development process. Theoretically, inclusion of payer representatives early in development could help discern discordance among stakeholder priorities; facilitate cooperation to align objectives; foster agreement on the evidence required for approval and reimbursement; improve transparency, accountability, and consistency of payer decision making; and ideally, minimize delays in patient access to new therapies. However, early participation by payers may not provide these expected benefits if payers' decision-making processes are not evidence based or cannot be reliably predicted. This paper describes current interactions among regulatory agencies, payers, sponsors, and investigators and proposes collaboration among all stakeholders earlier in the development process. The premise that a priori discussions might facilitate the delivery of advances in cardiovascular care is a hypothesis worth testing. (J Am Coll Cardiol 2017;70:2822–30)
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In both the United States and Europe, the average time from initial filing to regulatory approval for new cardiovascular drugs is 6 to 7 years (1,2). Yet, timelines for payer reimbursement decisions, termed the "fourth hurdle" (3,4), may further delay patient access to new treatments by months (5) to years (2), or indefinitely if coverage is denied, high levels of coinsurance are transferred to patients, or repetitive administrative documentation is required. Although these concerns affect many parts of the world, this

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paper focuses on considerations relevant to the United States and the European Union (EU).

Regulators are responsible for ensuring the safety, efficacy, and quality of drug, biologic, or device therapeutics for an intended use in a specified population. Generally, a single body of scientific evidence derived from active or placebo-controlled large randomized trials forms the basis of regulatory decision making for new cardiovascular treatments. However, payer or health technology assessment (HTA) organizations have a different purview; they determine whether "an intervention offers useful, appropriate and affordable benefits for patients in a particular healthcare system" (6), and they focus heavily on whether the treatment provides value for money in relation to current therapies (**Table 1**) (7–10). This is particularly true as new high-cost specialty pharmaceuticals enter the market (11). Contrasting priorities can lead to delays between regulatory approval and payer reimbursement. When available evidence is deemed convincing for regulatory approval but not for reimbursement (12), patient access to new treatments is hindered. Payers have not, in general, been systematically engaged in the development process pre-approval, but their engagement may enable value-based information to be generated pre-approval, potentially minimizing delays in patient access post-approval. In this document, we consider involvement of payers in pre-approval drug development, focusing on therapies that offer a demonstrable advance over existing care but do not reach the public in a timely manner because of reimbursement barriers. We will not discuss "me-too" drugs with marginal or uncertain incremental benefits. Differentiation between these scenarios is essential in identifying true advances with potential to reduce morbidity and mortality.

The Global CardioVascular Clinical Trialists (CVCT) Forum is an opportunity for cardiovascular clinical trialists, clinicians, biostatisticians, European and United States regulators, government and industry sponsors, and patient representatives to convene and discuss relevant challenges facing cardiovascular clinical research. Concerns about the misalignment between regulatory approval and reimbursement decisions were raised during the annual meeting, December 1 to 3, 2016, in Washington, DC, and it was a specific topic of discussion during the CVCT Workshop, December 4 to 5, 2016, in Washington, DC. This paper summarizes the issues that were brought forth and proposes actions to address obstacles and hasten the delivery of effective, safe, and affordable treatments to patients with cardiovascular disease.

OVERVIEW OF CURRENT SYSTEMS AND COMPLEXITIES

UNITED STATES. Medical coverage in the United States is complex (13), in large part because multiple public and private payers operate within the health care system. The U.S. Centers for Medicare and Medicaid Services (CMS) provide medical and hospital coverage for approximately 57 million individuals over 65 years of age (Medicare); 41.5 million of these receive prescription drug coverage through the Medicare Part D benefit administered by Medicare-approved private insurers (14). Medicaid provides coverage for approximately 74 million eligible low-income individuals (15). Private insurers provide coverage for an additional 174.5 million people (16).

There is substantial variation in reimbursement practices among the various payers in the United States (17,18). In addition, reimbursement decision making is not transparent among the broad group of payers. Although it is appealing to think that payers' needs could be addressed if they were involved in the design and execution of pre-approval clinical trials, it is not clear that payers (especially private payers) are able to describe their requirements or specify formal criteria early in development. As neither the benefits nor the price of a new treatment have been determined at this point in time, payers who rely on value or outcome-based pricing approaches may not be able to define their response in advance of a new approval (17,19). Nonetheless, efforts to actively involve payers in the process of evidence generation could improve post-approval communications, as outlined in a recent Food and Drug Administration (FDA) guidance document (20).

EUROPE. The process for reimbursement decisions in the European Union is more streamlined than in the United States, owing to the predominance of single-payer systems and the ability of national organizations to negotiate pricing (21). Nevertheless,

ABBREVIATIONS AND ACRONYMS

CMS = Centers for Medicare and Medicaid Services

CED = Coverage with Evidence Development

CVCT = CardioVascular Clinical Trialists

EMA = European Medicines Agency

EU = European Union

FDA = Food and Drug Administration

HTA = health technology assessment

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