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**Optimization Models for Faster and Affordable Access to Rare Disease Treatments.**

Although 350 million patients are suffering from more than 7,000 known rare diseases, only 500 rare diseases have drug treatments available. Even when a treatment (known as orphan drugs) exists, the average cost is seven times higher than non-orphan drugs. The limited availability and accessibility of orphan drugs have created a rallying cry for change. As a corrective measure, several orphan drug initiatives are being proposed. In this research, we present multi-stage game theoretic models to analyze different initiatives to improve the availability and accessibility of treatments for rare diseases. First, we evaluate the impact of subsidy, pricing and payment mechanisms on improving patient access. In addition to the traditional setting in which the manufacturer sets the price, we consider an "exogenous pricing scheme" under which a consortium sets the price. We also examine an outcome-based payment scheme, which offers the drug for free if it is not efficacious. Second, we analyze the impact of converting a drug from "off-label" to on-label use for rare diseases. As most rare diseases have no approved treatments available, doctors often prescribe existing drugs for "off-label" use in the sense that a drug is prescribed for a medical condition that is different from the original condition approved by regulatory authorities. In this research we provide an initial attempt to investigate the effectiveness of different types of government subsidies (e.g., offer subsidies to manufacturers, patients or both) for improving patient welfare through the drug conversion strategy. Third, we analyze the adaptive approval program. Adaptive approval is a novel regulatory program that enables earlier patient access to new drugs for rare diseases. The program has been in place for almost a decade; however, industry participation has been surprisingly low. In this research, we analyze various redesigns of the adaptive approval programs, such as the inclusion of subsidies, a change in the market exit requirement, and an extension of the market exclusivity period. Finally, we analyze magistral drug preparation by a pharmacist as a complement to industrial drugs. With magistral drug preparation, a drug is prepared for an individual patient by a pharmacist, instead of a commercial firm. However, it is unclear what the implications of magistral drug preparation are on the patient welfare, the firm's profit and payer welfare. In this research, we provide one of the first attempts in modeling and analyzing the impact of magistral drugs on patient welfare.