Exclusivity Program Has Mixed Economic Results

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As an incentive for pharmaceutical companies to conduct clinical trials in children, the Pediatric Exclusivity Program yields variable results, ranging from a generous economic net gain to a net loss, according to a study by Dr. Jennifer Li of Duke Clinical Research Institute, Durham, N.C., and colleagues (JAMA 2007;297:480-8).

Most drugs receive marketing approval in the United States based on clinical trials performed only in an adult population, although the drugs are often used to treat children. The Pediatric Exclusivity Program was designed to encourage pharmaceutical companies to obtain data concerning dosing, safety, and efficacy of marketed drugs in children. Written requests from the Food and Drug Administration specify the number of studies, the indication, sample sizes, and trial designs. In exchange for performing the requested pediatric studies, the pharmaceutical company receives an additional 6 months of marketing exclusivity.

The Best Pharmaceuticals for Children Act of 2002, which created the Pediatric Exclusivity Program, is due for renewal this year. However, despite its success in generating much-needed data on safety and efficacy of drugs given to children, the program has been criticized for providing "windfall" profits to the pharmaceutical industry. Dr. Li and her colleagues evaluated the economic return from marketing exclusivity in a subset of nine drugs that were granted pediatric exclusivity.

During 2002-2004, a total of 59 products received pediatric exclusivity. Of these, 13 (22%) were considered "blockbuster" drugs, with annual sales in the United States in excess of $1 billion. Median annual sales revenue from the 59 products was considerably lower, at $181.3 million, and 23 products had annual sales revenue under $150 million.

The investigators classified the 59 products into nine therapeutic areas and selected one drug from each category for evaluation.

The indications for the nine selected drugs were asthma, tumors, attention-deficit/hyperactivity disorder, diabetes mellitus, gastroesophageal reflux, bacterial infection, and bone mineralization. The selection was heavily weighted toward products that were expected to yield a high economic return, with five "blockbusters" among the nine drugs.

Costs to the pharmaceutical companies in coordinating the clinical trials were estimated from information culled from the final clinical study reports. The estimated costs did not include costs of regulatory filings, costs of juvenile preclinical studies, or costs associated with development of special formulations for pediatric use.

Estimates of after-tax cash inflow over a 6-month period of extended patent protection were extrapolated from market sales data from the previous 3 years. For each of the nine drugs, the investigators calculated the net economic return by subtracting the estimated after-tax cash outflow resulting from the requested pediatric trials from the after-tax cash inflow projected over a 6-month period of extended patent protection.

In the group of nine drugs, 16 efficacy studies, 10 pharmacokinetic studies, and 1 safety study were performed in response to written requests. Median cost per written request was estimated to be $12.3 million (range, $5.1 million-$43.8 million).

Eight of the nine drugs underwent a labeling change as a result of the clinical trials conducted under pediatric exclusivity. "Importantly, several were associated with substantial safety concerns and lack of effectiveness in the pediatric population," wrote Dr. Li and colleagues.

For 6 months' market exclusivity, the median net economic benefit for the nine drugs was estimated to be $134,265,456, ranging from a loss of $8,946,033 to a gain of $507,899,374, with a net return:cost ratio ranging from –0.68 to 73.63. With a 3-month market exclusivity, the median net economic return decreased to $64,041,833, ranging from a loss of $11,088,214 to a gain of $250,500,635. The net return:cost ratio decreased to a range of –0.84 to 36.31.

The investigators predicted that the reduction of marketing protection from 6 to 3 months would likely dissuade pharmaceutical companies from requesting pediatric exclusivity for products that were unlikely to generate a high economic return. ■