Recent Initiatives in US Drug Policy to Promote Innovation, Value, Access, and Affordability

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KEY POINTS

21st Centuries Cures Act aims to fuel rapid innovation in drug development and patient access to innovative medical technologies while enhancing the ability to communicate value of innovation.

American Patients First Blueprint aims to modulate the rapid growth in healthcare costs of innovation by increasing competition, negotiation, and affordability.

Stakeholder implications of the 2 policies are significant across the US healthcare marketplace and in particular for HEOR professionals who can have major impact on the execution of both policies initiatives.

Pace of innovation in healthcare has reached a tipping point, and we are at the cusp of an era of curative therapies as well as those extending and enhancing quality of life. The promise of targeted immunotherapies in cancer, personalized gene therapy in rare disease, growth of biologic therapies, along with enhanced access to big data and digital innovation have fueled the US Market's tremendous appetite for healthcare innovation. However, innovation does not come without cost, which is a cause of daily discussion in national headlines. While overall pharmaceutical care costs have recently stabilized to a 1.4% annual increase, specialty products have continued to grow at an annual rate of 9%. [1] These cost and pricing trends have not been dented by the advent of competition, biosimilars, or any effective management strategy.

Value demonstration is now a cornerstone of any innovative healthcare intervention and is rapidly evolving with the availability of real-world evidence (RWE). Communication of this value to stakeholders, to enhance their decision making, is critical to the adoption and the contextualization of innovation, its cost, and its impact. Newer policy models that speed development and enhance regulatory pathways are required to further this innovation to ensure reach of its societal benefit. At the same time, managing costs and affordability takes critical priority. Two major policy initiatives in the last couple of years have been developed to address this fine balance, the 21st Century Cures Act and the American Patients First Blueprint. This article presents these key policy initiatives and their implications for stakeholders.

21ST CENTURIES CURES ACT

The 21st Century Cures Act (Cures Act) [2] passed the House of Representatives on November 30, 2016, and the Senate on December 7, 2016, and was signed into law on December 13, 2016, by President Obama. The Cures Act represents bipartisan legislation that provides $6.3 billion for medical research over the next several years to harness science, medicine, and technology to tackle challenges in healthcare. The Cures Act, formally known as HR 34, provides the FDA with the necessary resources to create a path for scientific advancements and patient access to innovative medical technologies. The key provisions in Title III of the Cures Act and other provisions that focus on medical product development build on the FDA's current efforts to streamline and transform regulatory activities. Subtitles A-D of Title III pertaining to medical product development and for patient access requires FDA compliance with statutory requirements and activities within the following subtitles and sections detailed below. Table 1 summarizes FDA's deliverables under Subtitles A-D of Title III of the Cures Act, as well as implementation and impact of the different subsections in the market. For example, the use of patient-reported outcome (PRO) data in drug development (eg, clinical endpoints) and commercial strategy can improve market differentiation and value. Likewise, competition-enhancing regulatory reforms as well as polices that promote innovation, market entry, and access can influence pharmaceutical prices.

SUBTITLE A: PATIENT FOCUSED DRUG DEVELOPMENT

More broadly, the provisions in Subtitle A, sections 3001-3004, under Title III of the Cures Act direct the FDA to incorporate patients' experiences, perspectives, needs,

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and priorities in drug development and evaluation. For example, section 3001 directs the Secretary "following approval of an application submitted under section 505(b) of the Act or section 351(a) of the Public Health Service, at least 180

days after the date of enactment", to make public a brief statement "regarding the patient experience data and related information, if any, submitted and reviewed as part of such application." The data and information refer to patient experiences, patient-focused drug development tools, and other relevant information. In addition, the Cures Act considers patient experience data to encompass information: (1) collected by patients, family members, caregivers, patient advocacy groups, disease research foundations, researchers, or drug manufacturers; and (2) provide information about patients' experiences with a disease or condition, "including—(a) the impact of such disease or condition, or a related therapy, on patients' lives; and (b) patient preferences with respect to treatment of such disease or condition." The patient-focused development provisions in Subtitle A create an opportunity for patient insights in drug development and benefit-risk assessment.

SUBTITLE B: ADVANCING NEW DRUG THERAPIES

The provisions in Subtitle B, sections 3011-3016, under Title III of the Cures Act aims to accelerate medical product development and approval processes and bring medical advances to the market faster and more efficiently. The Cures Act directs the Secretary, acting through the FDA, to establish a process for the qualification of Drug Development Tools for a proposed context of use, which includes determining the acceptability of a qualification submission based on scientific merit. Drug Development Tools (DDTs) (ie, biomarkers, clinical outcome assessments (COAs), and animal models) are methods, materials, or measures that have the potential to facilitate drug development and market entry. The rare disease space is another example where the Cures Act aims to bring new drug therapies to the market to address an unmet need. Section 3012 is intended to "(1) facilitate the development, review, and approval of genetically targeted drugs and variant protein-targeted drugs to address an unmet medical need in one or more patient subgroups, including subgroups of patients with different mutations of a gene, with respect to rare diseases or conditions that are serious or life-threatening; and (2) maximize the use of scientific tools or methods, including surrogate endpoints and other biomarkers" in clinical research (eg, clinical endpoints to assess efficacy, enrichment designs). Similarly, the provision in section 3013 on the reauthorization program for rare pediatric diseases will allow individuals from birth to 18 years to gain access to potentially life-saving and life-changing treatments by accelerating and promoting development of therapies in this space.

Table 1: Key sections of 21st Century Cures Act, Statutory Deliverables, and Potential Impact in the Market Place[3]

Title III Section Number	Title III Subsection	Statutory Deliverable	Impacts
3001	Patient experience data		Value
3002	Patient-focused drug development guidance	Plan, Draft & Final Guidance	Value
3004	Report on patient experience drug development	Public Report	
3011	Qualification of drug development tools	Plan, Public Report, Draft & Final Guidance, FR Notice, Public Meeting, Public Report	Innovation, Access
3014	GAO study of priority review voucher programs	GAO Report	Access
3016	Grants for studying continuous manufacturing	Grants	Access, Pricing
3021	Novel clinical trial designs	Public Meeting, Draft Guidance, Final Guidance	Innovation
3022	Real world evidence	Plan, Framework, Draft Guidance, Final Guidance	Access, Pricing, Innovation
3023	Protection of human research subjects	Regulation or Guidance, Report to Congress	Access
3024	Informed consent waiver or alteration for clinical investigations	Other	Innovation
3031	Summary level review	Other	
3034	Guidance regarding devices used in the recovery, isolation, or delivery of regenerative advance therapies	Final Guidance	Pricing
3035	Report on regenerative advanced therapies	Report to Congress	Pricing, Value
3036	Standards for regenerative medicine and regenerative advanced therapies	Plan	Innovation
3038	Combination product innovation	Final Guidance	Value

Source Adapted from: 21st Century Cures Act Deliverables. https://www.fda.gov/regulatoryinformation/lawsenforcedbyfda/significantamendmentstothefdcact/21stcenturycuresact/ucm562475.htm

SUBTITLE C: MODERN TRIAL DESIGN AND EVIDENCE DEVELOPMENT

Included in the Cures Act are provisions in Subtitle C on modern approaches to designing and conducting clinical trials. Section 3021, novel clinical trial designs under Subtitle C directs the FDA to incorporate complex adaptive and other novel trial designs into proposed clinical protocols and applications for new drugs and biological products. The Secretary, acting through the FDA, shall update or issue guidance addressing the use of novel approaches such as complex adaptive and other novel trial designs in clinical development. This provision helps us to address the needs of innovation and efficiency in clinical trial conduct while maximizing patient access. Section 3022 on RWE directs the FDA to evaluate how such data can be used to support approval of new indications for approved drugs or to support or satisfy post-approval study requirements. The law also requires a draft framework for implementation for the RWE program that includes information describing the sources of RWE, "including ongoing safety surveillance, observational studies, registries, claims, and patient-centered outcomes research activities; the gaps in data collection activities; the standards and methodologies for collection and analysis; and the priority areas, remaining challenges, and potential pilot opportunities." In discussing the acceptance of RWE to support regulatory decisions, the FDA has used historical controls in rare disease drug development and approval (eg, Myozyme, Carbaglu). >

SUBTITLE D: PATIENT ACCESS TO THERAPIES AND INFORMATION

The provisions in Subtitle D, sections 3032-3033, increase patient access to new drug therapies through the expanded access policy and accelerated approval for regenerative advanced therapies (eg, Regenerative Medicine Advanced Therapy (RMAT) designation program) and provide more timely access to potentially life-saving therapeutic alternatives. The provisions in section 3031 to 3033 could present an opportunity to address pricing and access for therapies showing evidence of clinical effect in early stages of development, for example.

Section 3037 on healthcare economic information (HCEI), which amended FDAMA 114, expands the scope of drug manufacturers' communication to payers, formulary committees, or other similar entities about the value of their products. The Cures Act defines HCEI as any analysis (including the clinical data, inputs, clinical or other assumptions, methods, results, and other components underlying or comprising the analysis) that identifies, measures, or describes the economic consequences, which may be based on the separate or aggregated clinical consequences of the represented health outcomes of the use of a drug [2]. The preapproval information exchange (eg, product pricing information) under this provision provides an opportunity for better communication on product value.

AMERICAN PATIENTS FIRST BLUEPRINT

In May 2018, the White House released the American Patients First (APF) Blueprint [4] aimed to lower drug prices and reduce out-of-pocket costs. The APF blueprint outlines President Trump's agenda to spur new entrants, improve competition, and create incentives for pharmaceutical companies to lower list prices, amongst other things. The administration's vision to lower drug prices and reduce out-of-pocket costs is centered around key issues identified as challenges in the pharmaceutical market, namely rebates and discounts that favor high list prices, patent exclusivity, the expansion of the 340B drug discount program, international price controls, and government programs lacking modern negotiation tools. The Health and Human Services Secretary (HHS) introductory message in the APF blueprint echoed the administration's commitment to bring immediate relief while also delivering long-term reforms. The secretary states that "the time to act is now: not only are costs spiraling out of control, but the scientific landscape is changing as well." HHS has identified 4 challenges in the American pharmaceutical market:

1. High list prices for drugs
2. Seniors and government programs overpaying for drugs due to lack of the latest negotiation tools
3. High and rising out-of-pocket costs for consumers
4. Foreign governments free-riding from American investment in innovation

In the APF Blueprint, HHS proposes to address these challenges using 4 key strategies for reform: (1) improved competition; (2) better negotiation; (3) incentives for lower list prices; and (4) lowering out-of-pocket costs. This is to be accomplished through 2 phases: 1) actions the President may direct HHS to take immediately and 2) actions HHS is actively considering, on which feedback is being solicited. The blueprint introduced immediate actions and proposals to lower list prices and out-of-pocket costs[4]:

Incentives for Lower List Prices

Immediate Actions

- FDA evaluation of requiring manufacturers to include list prices in advertising
- Updating Medicare's drug-pricing dashboard to make price increases and generic competition more transparent

Lowering Out-of-Pocket Costs

Immediate Actions

- Prohibiting Part D contracts from preventing pharmacists telling patients when they could pay less out-of-pocket by not using insurance
- Improving the usefulness of the Part D Explanation of Benefits statement by including information about drug price increases and lower cost alternatives

These recent policy initiatives will likely have short and long-term implications to key stakeholders.

Implications of these policy initiatives: are significant across the 5 key stakeholders:

1. **Regulatory Authorities:** Should have a clear mandate in speeding the process of drug development for rare diseases (eg, validation of biomarkers); driving use of RWE of patient origin in drug development; enhancing sharing of information; and clarifying FDA authority on development of orphan drugs. Furthermore, the APF Blueprint provides new rules for the FDA to govern the implementation of pricing transparency and disclosure in direct-to-consumer advertising.
2. **Payer Organizations:** Regulations on sharing HCEI will allow rapid determination of value assessment, formulary decision making, and medical policy implementation. The potential to accelerate the value-based purchasing per the APF Blueprint will allow plans to negotiate innovative agreements with manufacturers.
3. **Value Assessment Organizations:** Will need to recognize the potential of patient-derived RWE in their assessments beyond cost-effectiveness and budget impact analysis.
4. **Patients:** Enhanced access to compassionate-use medications, expedited regulatory pathways for rare diseases, and enhanced visibility to drug pricing will provide significant choice in making decisions impacting their care.
5. **Pharmaceutical Manufacturers:** Speeding trial performance, mitigating paperwork and regulations on review, enhanced trial designs, and guidance on combination products will drive innovation to market. Balancing the ability to get innovation to market will be the responsibility to demonstrate value through pricing strategy reform and lowering overall healthcare system costs. HEOR professionals will significantly benefit from the provisions of the new policy initiatives, as they are the key experts at the heart of developing RWE, communicating HCEI to payers, and developing value-based contracts.

Successful implementation of the Cures Act and policies outlined in the APF Blueprint has the potential to remove obstacles and unnecessary cost to the healthcare system. The key to their actual impact will depend on the implementation plan, timing, and absorption of the policy initiatives into the healthcare marketplace.

Note: This article reflects the views of the author and should not be construed to represent the FDA's views or policies.

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