Tuberous Sclerosis Alliance

WE'LL GIVE EVERYTHING. BUT UP.

Medicaid and CHIP Payment and Access Commission (MACPAC)1800 M
Street NW, Suite 650 South
Washington, DC 20036

Via email to: comments@macpac.gov

RE: MACPAC's Work on Medicaid Rebate and Accelerated Approval Drugs

Dear MACPAC Commissioners:

The Tuberous Sclerosis Alliance (TS Alliance) appreciates the opportunity to comment on the Medicaid and CHIP Paymentand Access Commission's (MACPAC) proposed recommendations regarding differential Medicaid rebates for accelerated approval drugs.

The TS Alliance is a 501(c)(3) non-profit organization dedicated to finding a cure for tuberous sclerosis complex (TSC), while improving the lives of those affected. TSC is a rare is a genetic disorder that can cause tumor growth in all of the body's vital organs. Symptoms can include seizures, kidney failure, brain and lung tumors, autism spectrum disorder, and severe learning disabilities. We deliver on our core mission to accelerate research, improve access and quality of care, support and empower constituents, educate, and mobilize to increase investment, and build and strengthen organization. Essential to this mission is our commitment to educate policymakers and other stakeholders about the unique circumstances of rare diseases with respect to product development, commercialization, and equitable access to care.

The TS Alliance shares MACPAC's interest in ensuring manufacturers gaining approval for their drug products through the FDA accelerated approval pathway should demonstrate diligence in completing the confirmatory post-market studies identified in their FDA approval letter. MACPAC's Recommendation 1 is unlikely to achieve this goal as it applies an increased minimum rebate percentage on accelerated approval drugs *from day one of accelerated approval until the manufacturer has completed the confirmatory trial and been granted traditional FDA approval.* This is not an incentive toward manufacturer completion of FDA-mandated confirmatory studies; it is a disincentive on expediting patient access to treatments that address an unmet need in serious conditions, and that qualify for accelerated approval. We are similarly concerned that MACPAC's proposed recommendation will inject economic calculations into manufacturer accelerated approval decisions that could outweigh the disease severity and unmet need considerations at the heart of this FDA pathway.

Manufacturers are not "bad actors" for gaining market access through an accelerated approval pathway. Recommendation 1 treats them as such, shifting the balance between R&D and price controls too far in one direction. MACPAC appears to ignore the fact that the clear and definite

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point at which companies fail to meet their commitments is the point at which penalties shouldbe implemented.

Where MACPAC's Recommendation 2 conditions its penalty/disincentive on action or inaction within the manufacturer's control that are contrary to public policy (i.e., excessive price increases and failure to complete confirmatory clinical studies), Recommendation 1 penalty/disincentive is conditioned on action that is aligned with public policy – developing treatments addressing unmet need in serious medical conditions and receiving accelerated approval.

This failure to align with policy priorities will be catastrophic for our constituents as this would further delay access for much needed treatment options for life -limiting and life-threatening conditions to those who already have astronomical unmet medical needs. As MACPAC has noted, under Recommendation 1, "[b]eneficiaries would maintain similar access once a drug enters the market, but may lose early access to some products if manufacturers decide to forego accelerated approval pathway." Proposals such as Recommendation 1 that, while tied to a public policy interest unrelated to cost, are designed primarily to cut Medicaid expenditures pose a heightened risk of unintended, disproportionate, and potentially profound impacts. This would be devastating for the rare disease community, including our constituents with TSC who have minimal treatment options to reduce disease burden or slow disease progression, and for whom early access to a therapy is critical.

As MACPAC is aware, economic calculations of research and development (R&D) costs, projected risk, and population-based revenue estimates can tip the scales for or against pursuing a specific drug candidate for an orphan indication. For patient populations approaching the 200,000 - patient orphan disease limit, current incentives may be sufficiently robust to mitigate clinical trial and reimbursement risks, and there may be adequate pricing elasticity to accommodate an enhanced Medicaid rebate. However, TSC has an even lower population of 50,000 people affected in the US, and the balance can be far more fragile, and risks or uncertainties can discourage the investor interest required to take product candidates from bench to market. For these very rare conditions, the ability to pursue an accelerated approval pathway affords innovators an opportunity to recoup investment that could be significantly impaired if accompanied by a penalty on sales associated with Medicaid patients.

We expect that manufacturer considerations might include:

- Payer mix, i.e., what percentage of likely patient population is served by Medicaid;

- Overall size of patient population;

- Whether product is "one-and-done" or used long term;

- Anticipated use among 340B covered entities; and

- Likely length of time required to complete confirmatory studies.

Depending on the answers manufacturers receive, they could decide to (1) pursue accelerated approval and absorb the additional rebate, (2) pursue accelerated approval and decline to execute a Medicaid Rebate Agreement; (3) continue to develop the product but decline to pursue an accelerated approval, or (4) stop/decline to initiate product development efforts.

The TS Alliance has serious concerns that MACPAC's differential rebate mechanism could not only delay access as manufacturers opt to pursue traditional approvals,

but could substantially deter R&D in very rare diseases. The premise that price controls and forced discounting can chill innovation, is supported by economic models[1] [2] [3] and observational data on manufacturer response to implemented or threatened price controls.

Nearly all European Union nations have regulated pharmaceutical prices for decades, and successfully achieved drug pricing that is 20-40% lower than US prices.[4] [5] Direct price controlsamong nineteen Organization for Economic Co-operation and Development (OECD) countries have, however, reduced pharmaceutical company revenues by an average of 16.8%, and contributed to an average difference of 4.9% in aggregate profitability between USand EU pharmaceutical firms.[6] [7] Although EU pharmaceutical R&D spending was 24% higher than US spending in 1986, by 2004 US R&D spending outpaced that of EU nations by 14%.[8] The US has continued to invest more funds into R&D and has brought more products tomarket than its EU counterparts in recent years.[9]

Although it can be debated whether or not the right manufacturer incentives are currently in place, their effect on R&D for orphan diseases has been positive from the rare patient perspective.[10] Disease groups work hard to raise research dollars, create patient registries, fund natural history studies and ultimately partner with companies interested in developing therapies for their very rare conditions. The risk of failure is high for all. Hurdles to R&D such as MACPACis proposing in Recommendation 1 are not appropriate or fair for populations suffering from extremely low prevalence conditions.

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[1] Giaccotto, Carmelo, Rexford E. Santerre, and John A. Vernon. 2005. "Drug Prices and Research and Development Investment Behavior in the Pharmaceutical Industry." The Journal of Law & Economics 48 (1): 195–214. The authors simulations were based on multiple-regression model indicating that the capitalized value of pharmaceutical R&D spending would have been about 30 percent lower if the federal government had limited the rate of growth in drug price increases to the rate of growth in the general consumer price index during the period 1980–2001. This would have resulted in 330–65 fewer new drugs, representing over one-third of all actual new drug launches brought to the global market during that time period.

[2] Lichtenberg, Frank R. 2001. "Probing The Link Between Gross Profitability And R&D Spending." Health Affairs 20(5): 221–22.

[3] Vernon, John A. 2005. "Examining the Link between Price Regulation and Pharmaceutical R&D Investment." Health Economics 14 (1): 1–16. The author identifies two mechanisms through which price regulation may exert an influenceon R&D: an expected-profit effect and a cash-flow effect and simulated how a new policy regulating pharmaceutical prices in the U.S. will affect R&D investment. Modeling suggested that such a policy would lead to a decline in industry R&D by between 23.4 and 32.7%.

[4] Golec, Joseph, and John A. Vernon. 2010. "Financial Effects of Pharmaceutical Price Regulation on R&D Spendingby EU versus US Firms." PharmacoEconomics 28 (8): 615–28.

[5] Vernon, supra.

[6] Eger, Stephan, and Jörg C Mahlich. 2014. "Pharmaceutical Regulation in Europe and Its Impact on Corporate R&D." Health Economics Review 4 (October).

[7] Sood, N., H. de Vries, I. Gutierrez, D. N. Lakdawalla, and D. P. Goldman. 2009. "The Effect Of Regulation On Pharmaceutical Revenues: Experience In Nineteen Countries." Health Affairs 28 (1): w125–37.

[8] Golec, supra.

[9] Eger, Stephan, and Jörg C Mahlich. 2014. "Pharmaceutical Regulation in Europe and Its Impact on Corporate R&D." Health Economics Review 4 (October).

[10] Haffner, M.E., J. Whitley, and M. Moses, Two decades of orphan product development. Nat Rev Drug Discov, 2002. 1(10): p. 821-5.

The TS Alliance urges MACPAC to:

- Withdraw Recommendation 1 and focus disincentives/penalties on manufacturer actions and failures to act that are contrary to public policy and within the manufacturer's control;

- Delay action directed toward manufacturer delays in completing confirmatory studies following accelerated approval until Medicaid programs have fully implemented coverage for costs associated with clinical trials and the impact of this coverage expansion can be evaluated;

- Clarify that the costs of accelerated approval drugs provided in connection with an FDA-mandated confirmatory study will be covered by Medicaid programs without application of an additional rebate percentage. Applying the differential rebate in these circumstances is inherently inconsistent with the stated goal of the Recommendation.

- To the extent that MACPAC retains Recommendation 1, it should devise an exception for rare disease treatments addressing populations 50, 000 and under US patients and for 5 years following the earlier of pivotal study completion or accelerated approval date; and

- Adopt Recommendation 2 providing an additional rebate percentage for manufacturers that engage in excessive price increases and fail to complete confirmatory studies.

Conclusion

The TS Alliance appreciates MACPAC's efforts to hold manufacturers accountable for the post-market trials that are critical for the patients depending on their products. We look forward to working with MACPAC as it finalizes its recommendations. If you have any questions or need further information, please do not hesitate to contact Chief Executive Officer, Kari Rosbeck, at krosbeck@tsalliance.org or Director of Medical Affairs, Ashley Pounders MSN, FNP – C, at apounders@tsalliance.org.