



## Access to Rare Indications

### **ENSURE RARE DISEASE PARITY IN ACCESSING MEDICALLY NECESSARY CARE IN MEDICARE AND MEDICAID**

**Problem.** There are often so few patients with a very rare condition that drug companies will not, or often cannot, do a clinical trial for every subtype of a rare condition. Patients are then left fighting for off-label access to a treatment. For patients relying on Medicare Part D, access to off-label treatments within the standard of care can be particularly problematic since Part D plans are *prohibited* from including off-label uses not listed in compendia in the Part D benefit. For these patients, there is not even an appeal or reconsideration mechanism available to overcome the “fact” that the prescribed use is outside of the Part D benefit.

Additionally, these treatments are often used in combination with other FDA approved treatments, making the FDA approved treatment more effective or supporting the effectiveness of the FDA approved treatment. Managing all of this can be quite challenging for a patient attempting to live as best they can with a rare disease and navigate the complexity of the healthcare system.

**Solution.** Ensure parity in coverage for Medicare and Medicaid beneficiaries with low-prevalence conditions by aligning the statutory definition of “medically accepted use” for low-prevalence conditions with sources likely to include the standard of care, i.e., FDA label, compendia, peer-reviewed literature, and opinion of disease experts identified by relevant societies.

**Precedent.** Over a decade ago, oncologists and cancer patients faced a similar situation and Congress passed a law deeming certain uses of anti-cancer treatments as “medically accepted,” effectively requiring Medicare to cover anti-cancer treatments for off-label indications *if* those indications were listed in a compendia or there were two or more peer-reviewed articles supporting an off-label use. The circumstances that drove that legislation for oncology all those years ago, is very much the circumstance that rare patients find themselves in today. 7,000+ rare conditions, most without treatments, means an off-label use is often patients’ only hope.

**Example 1.** Pemphigus is a rare group of blistering autoimmune diseases that affect the skin and mucous membranes. The mainstay of treatment is corticosteroids that also suppress the normal function of the immune system. While not usually fatal, patients with uncontrolled/untreated pemphigus can die from opportunistic infections. Several studies completed before 2007 noted clear benefits of Rituximab in a subset of patients with refractory disease and severe adverse effects from long-term steroid therapy. Patients who may have found relief from **Rituximab** were unable to access it through Medicare or other insurers for over a decade until FDA approved Rituxan for pemphigus in 2018, and it is now considered a first-line therapy.

**Example 2.** Tuberous sclerosis complex. The most severe cases of denials based on prior



authorizations were for children between the ages of 2 and 9 (outside of label). The treatment was labeled for **1 month to 2 years of age** for infantile spasms and **ages 10+** for complex partial seizures. The patient group finally approach Lundbeck in Spring 2018 about applying for label change to FDA using global guidance for extrapolation of complex partial seizures. The group supported the collection of supplemental information from 200 patient chart reviews and in 2019 submitted with Lundbeck to the FDA. FDA approved the label change in January 2020, but the impact on these children and their families is hard to accept

**Example 3.** Cutaneous lymphoma -- Off-Label use of interferon, topical steroids and other drugs used to treat skin conditions is frequent and quite helpful in managing the disease. The increase in prices for these drugs or lack of access to them because an insurer will not cover it due to being off-label, creates limitations for effective treatment for some patients as there may be no alternatives suitable to managing their form of the disease.

## **CREATE PRIVATE PAYER EXPEDITED REVIEW FOR RARE CONDITIONS**

**Today.** Clinical trial sponsors have long had to walk a fine line between including patients in clinical trials that sick enough to benefit from a potential treatment and yet, not so sick that it is too late for the potential treatment to be impactful. Criteria for who to include and exclude from a clinical trial is carefully considered.

**Ultra-Rare Circumstance.** It is difficult to find enough patients to enroll in a trial for ultra-rare conditions because, by definition, there are far fewer patients to choose from. Sometimes there are multiple sub-types of a very rare condition to consider, sometimes age, progression of disease, and other factors are critical for really rare conditions. Most ultra-rare disorders lack a patient advocacy organization, or they rarely have resources to develop patient registries and natural disease history data.

In the end, the FDA weighs the results of the clinical trial and decides how broad (or narrow) the labeled indication should be -- and it does so with all the same scientific rigor it brings to bear on more common conditions. There is nothing “lesser” about the science applied to treatments for very rare conditions.

**Problem.** However, payers have begun a steady drumbeat of “concern” that there is no evidence to support giving a FDA-approved treatment to their patients. FDA and patients are rightfully concerned that this narrative undermines FDA’s decisions on safety and efficacy, and goes against public policy priorities on getting those treatments to patients who need them to halt or stop disease progression, or enable relief from high disease burden.

**Solution.** Require private payers to implement a mechanism for expedited formulary exception, reconsideration, and/or appeal of any denial of coverage for a drug or biological prescribed for treatment of a low-prevalence condition.

**Example 1.** The clinical trial for Choroideremia (CHM), an inherited retinal degenerative



disease with the prevalence of 1/50,000 is a good example. CHM patients maintain good central vision until their later years, losing their peripheral vision from the outside in until there is complete blindness. Most patients still have 20/20 central vision, likely into their 40s– the blindness is more due to reduced field of vision than gradual loss of acuity. The trial for a novel gene therapy limited inclusion in the clinical trial to patients with vision worse than 20/40 to assess improvement. So even though younger patients could benefit from not having their vision deteriorate in the first place, they're sometimes prevented from getting the therapy until their vision is as bad as the patients who were in the clinical trial.

Since the goal of this therapy is to make the retina cells healthy so they would not degrade and die, patients with the most to gain (patients with little or no loss in field of vision) are sometimes denied access if coverage follows trial population rather than the FDA's broader label.

The ultimate hope would be that a genetically confirmed CHM patient could be treated at the age of four or five with the hopes of never having any vision loss or diminished vision.

**Example 2:** Payers are also combing through other clinical trial requirements for ways to burden clinicians and patients to reduce access to new treatments. In one case, the clinical trial required a biopsy of tissue for amyloid for confirmation of HATTR Amyloidosis. Upon approval of the drug, the manufacturer made a genetic confirmation test available for free to patients, so that a biopsy would not be required. Nonetheless, some payers put a PA for a biopsy in place, not only incurring a cost to the health care system, but unnecessary copay costs to the patient. Such biopsies are not readily available, for example in rural areas, nor are pathologists always able to translate biopsy results easily outside of academic centers. This wasn't required by the FDA or the label, but the payer used the clinical trial criteria to deny or delay access.