LSDP Review Submission by Duchenne Foundation, on behalf of persons affected by Duchenne muscular dystrophy.

Introduction

Duchenne Foundation has acted as the peak information network for the Dystrophinopathies in Australia for over 10 yrs, conducting five national conferences with international programs. We were the lead organization in the establishment of the National Duchenne Muscular Dystrophy Registry which led to the Australian Neuromuscular Disorders Registry and the establishment of the Australasian Neuromuscular Network. Over the past decade, Duchenne Foundation has funded Australian research and advocated and assisted in the introduction of innovative treatment and education i.e. cardiac, respiratory and mobility interventions and equipment responsible for prolonging life and delaying the cascading milestones of Duchenne. e.g. Cough Assist machine, Sip Mouthpiece Ventilation (Duchenne Foundation, 2014)

Duchenne

Duchenne muscular dystrophy is an X-linked disease of muscle caused by an absence of the protein dystrophin, and affecting 1 in 3,500 live born males. Affected boys (and rare girls 1:50,000,000) begin manifesting signs of disease early in life, cease walking at the beginning of the second decade, and even with international consensus gold standard care, many struggle to survive past 25years. There is currently no cure or systemic therapy to regain dystrophin production or function but certain steps are taken to allow patients to remain mobile. Regular range-of-motion exercises can be used to keep joints flexible – delaying the progression of contractures and reducing/delaying the curvature of spine.

Prednisone, an anti-inflammatory corticosteroid, helps many improve muscle strength and delays the progression of DMD just as ace inhibitors and beta blockers are now used to delay cardiomyopathy. Respiratory equipment is also necessary to clear secretions and later, to enable adults to breathe. Mobility scooters and wheelchairs are used to assist in the mobility of patients.

Whilst our Foundation lacks the experience to address all the terms of reference, as a patient group, we would like to submit brief comments where applicable, in order to alert the LSDP to our upcoming interest in the scheme as it likely to affect a small percentage of our population.

Terms of Reference

- *Review the administration of the LSDP, including the Guidelines with which the programme is administered for each condition, and assess alternative administration systems.*

Upon examination of the patient conditions for subsidy for Gaucher Disease Type 1, it is a concern that a patient with a chronic condition may not be eligible if that patient develops another condition (No 3).

It has been our experience that in very rare instances a patient may develop another acute or chronic condition e.g. leukaemia, in addition to the underlying chronic diagnosis of Duchenne. It would be a concern that if an effective and readily available treatment can ameliorate the second

condition, that the patient should also qualify for a subsidy for an orphan drug to ameliorate his primary condition, either simultaneously or following on, depending upon medical advice.

- *Review emerging clinical treatments and diseases, including those that identify sub-groups by molecular target, which could potentially seek subsidisation through the LSDP in the future.*

Translarna, (formerly known as Ataluren), the first ultra-orphan drug to ameliorate the mechanism of a very small subset of patients with Duchenne muscular dystrophy (ie. approx 13% who have a nonsense mutation) has achieved conditional approval in Europe. Country specific arrangements and reimbursements have already commenced in some countries, e.g Ireland. (PTC, 2014)

Although in Australia, we only have a small number of patients participating in ongoing clinical trials and confirmatory studies for Translarna, we know that being a large country, the burden of regular travel to the two trial centres may impede participation. The eligibility criteria of a particular trial may also impede participation. However, PTC must conduct ongoing confirmatory studies in order to extend the label and we expect that both older and younger patients will be recommended eventually. Translarna will only be affective in a low incidence type of DMD, which would mean that there will only be a small number of patients who would require reimbursement per year. PTC estimate that there are approx. 40 patients in Australia with the ultra-orphan mutation that responds to Translarna; but other factors would make the requirement only a fraction of this number. Based on the new cases reported in Denmark and Norway annually, we estimate fewer than 4 new cases ongoing would be diagnosed in Australia each year. Therefore, we anticipate that TGA approval for Translarna will follow in Australia in the near future.

With respect to other potential ultra-orphan drugs in our pipeline, we understand that certain customized exon-skipping drugs (which are mutation dependent) and developed by companies like Prosensa (Prosensa, 2014) and Sarepta (Sarepta Therapeutics, 2014), may be approved for marketing within the next two years - once again for sub-groups of patients under the diagnosis of Duchenne, itself a rare disease.

In June, 2014, Prof Aartsma-Rus (Head of TREAT-NMD) summarized a complete list of developing therapies and their current status for Duchenne including gene, cell and drug therapies. (Aartsma-Rus, 2014). This summary provides both an indication of the range of therapies and her esteemed view of their individual stage of development. Also, May, 2014 saw the first Guidance for Industry for Duchenne, submitted by a patient group to the FDA in order to expedite the development and review of compounds and encapsulate the unique patient perspective of risk/benefit. (PPMD, 2014)

With accompanying improvements in early diagnosis and intervention, a positive effect of the availability of these orphan drugs will be to significantly delay disease progression; reducing co-morbidities, significantly lengthening lifespan, improving quality of life and the patient's ability to self-manage. (Population Health, WA. 2013)

Clinical Research Fact sheets for Duchenne are also available on the website of the US Registry, Duchenne Connect. (PPMD, 2014)

- *Establish a framework for data collection on rare diseases in Australia and assess how this could function internationally.*

Our representatives, along with representatives from various rare disease patient organizations, have most recently participated in nationwide workshops throughout 2014, to discuss the necessity for a Rare Diseases Policy in Australia. Data collection is crucial to the scoping of all rare diseases in Australia. We know the economic burden for the top 10 most expensive genetic diseases equates to $100m for paediatric cases and over $350m for adult cases. By altering the natural history for even one ultra-orphan disease such as the specific mutation of Duchenne requiring the drug, Translarna, there would be a significant decrease in social cost. However, at this stage, we have no further information about solutions, proffered during the RD workshops, to the all important issue of data collection, than what has been written in the scoping paper. (Population Health, WA., 2013)

Additionally, as a patient representative on the advisory board of the Australian National Neuromuscular Registry, it is apparent how this type of database might be developed for all rare diseases and utilized with similar ethical and privacy guidelines to benefit patients, health service provision, the pharmaceutical industry and scientists recruiting for clinical trials or surveillance studies. (Population Health, WA, 2014)

It is important to note that national neuromuscular databases are melded internationally into the global TREAT-NMD database. Dr Hugh Dawkins, our national curator is in fact the incoming chair of the The TREAT-NMD Global Database Oversight Committee (TGDOC).

Problems encountered by our clinical jurisdictional stakeholders in the national registry include; the lack of time to update data regularly and oversee the adult or remote patients who do not attend the paediatric clinics where the state curators have regular contact with patients. A pending self-registry function should partially address this barrier to a currency problem. Our experiences demonstrate that it is essential to provide the infrastructure and labour for a curator to validate, follow-up and update entries in the database or perhaps sub-groups within the database. Interestingly, from discussions with at least one other peak body who self-administer their own registry, the challenges are surprisingly similar. If this is so for separate health groups, each monitoring only hundreds of patients, imagine the difficulty for 1.2million persons affected by rare disease (RD).

A ready solution may exist in existing government health records. Since all Australians should activate their online eHealth profile and certainly this will be a priority for both persons with a rare disease and their health providers, the ability to export or integrate all eHealth portfolios in order to delimit a rare disease(s) database for national and international purposes, would seem both a cost effective and an accessible solution to RD data management. Presently we are encouraging our parents to enter consensus emergency considerations into the allergy section of the Personal Health Summary area of their child's eHealth record, in order to have life-saving information available to all medical staff. By doing so we are aiming to ensure that lives may be saved since parents of patients who have died in emergency rooms, report forgetting about their iphone App or Emergency Wallet Card, which we distribute. It follows that the eHealth record has even greater individual and collective potential (after some ethical adjustments) when utilized to benefit over a million Australians with a rare disease.

Conclusion

Thank you for this opportunity to make the LSDP aware that in the near future, our population are expecting PTC Therapeutics to be seeking reciprocal marketing approval for Translarna, which will be clinically effective in a very small number of Duchenne patients; followed by our hopes for no less than two other ultra-orphan drug therapies currently in the clinical trials pipeline. These efficacious therapies give us confidence, and the stimulus to focus our research efforts on the challenges for the remaining untreated mutations of Duchenne. More importantly, new treatments for even a small portion of persons with Duchenne, will decrease the cost and psycho-social impact upon patients, family members and their communities.

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