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ORPHAN AUSTRALIA

Orphan Disease Know How
Orphan Drug Marketing
Orphan Drug R&D

ORPHAN AUSTRALIA AND THE ORPHAN DRUG PROGRAM

SUBMISSION TO THE HOUSE OF REPRESENTATIVES STANDING COMMITTEE ON HEALTH AND AGEING INQUIRY INTO HEALTH FUNDING

Background

- Orphan Australia, founded in 1985 and based in Melbourne, is committed to searching for and financing niche pharmaceutical products to treat serious, life threatening and rare diseases where current therapy is unavailable or inadequate

- In February 2000 Senator Tambling announced the findings of a review into the Pharmaceutical Benefits Scheme (PBS), which included the following recommendation: *"Further discussions on a mechanism encouraging applications for PBS listing of orphan drugs should occur between the PBAC, the APMA and the Pharmaceutical Benefits Branch"*

- In December 2001, consultant Tom Hayes AO completed his report into *The Orphan Drug Program and Improving Community Access to Effective Drugs for Rare Diseases* which focused on:
  - Examining the working of the Australian Orphan Drug program
  - Examining the experience of the Australian Orphan Drugs in obtaining access to public funding programs including PBS listing
  - Identifying options for further consideration that would improve the community's access to effective drugs for rare diseases

- The report identified five options for improving the orphan drug program to address the relatively low level of success of the orphan drug program at that time (i.e. 17 of the 42 drugs with designated orphan status had been registered in Australia; only two were funded under the PBS)

- Despite the fact that Government has yet to formally respond to the Hayes Report, there has been some progress in terms of increased drug registrations (i.e. two thirds of the 89 drugs with orphan designation are now registered in Australia) and PBS funding (i.e. approximately 17 products are now listed on the PBS). However, for Australians suffering from rare and life threatening diseases there remain a significant number of orphan drugs for which access is prohibitive.

Problem

- As a class, orphan drugs have a high 'failure rate' in PBAC applications.

- Orphan drugs are often developed to treat small and very specific patient populations. This creates significant challenges in collecting data to meet strict PBAC criteria for cost-effectiveness evaluation, for example:
  - Many of the treatments being discovered for rare diseases are generally biotech products which require complex and expensive manufacturing
  - Patient populations are very small and do not offer scales of economy
  - Orphan drugs generally lack a suitable comparator
  - Patient recruitment to clinical trials for orphan drugs is naturally limited. Patients with rare or end stage disease are often unwilling to take anything other than the active drug
  - A small study population (which is common in such trials) diminishes statistical significance

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Solutions

Preliminary investigations have identified a number of possible funding options to improve access to orphan drugs for the treatment of rare and life threatening disease. These include:

- Developing specific PBAC cost-effectiveness criteria (or dispensations) for orphan drugs
- Funding of orphan drugs through the Australian Health Care Agreements
- Funding of orphan drugs through the Public Health Outcomes Funding Agreements
- Supplier agreements with Government (as per blood products funding)

Orphan Australia Product Portfolio

Haemotology and Oncology

- **Agrylin**[1] (anagrelide hydrochloride) is used in the treatment of Essential Thrombocythemia (ET), which is characterised by an overproduction of platelets. Excessive levels of platelets can lead to thickened and slow flowing blood, which has a tendency to cause thrombosis (blood clots). Agrylin prevents overproduction of platelets.

- **Ferriprox**[1] (deferiprone) is PBS listed for the treatment of iron overload in children and adults with thalassaemia major (TM). Those with TM cannot manufacture normal haemoglobin (the oxygen carrying protein in blood). If left untreated children can develop potentially threatening heart failure. In the long term it can lead to stunted growth, delayed development, and multi-organ failure. The only cure is a bone marrow transplant.

- **Gliadel**[1] (carmustine) is used to treat newly diagnosed high-grade malignant glioma (brain tumours) following surgery. The wafer strips are applied directly to the tumour site following removal of the tumour, thus ensuring direct delivery of the drug to the target site. Gliadel kills residual cancer cells and /or stops cancer cells growing and multiplying.

- **Litak**[1] (cladribine) is used in the treatment of hairy cell leukaemia and is the only product registered for use as second-line treatment of Waldenström's Macroglobulinaemia (WM), a type of non-Hodgkin's lymphoma. It is PBS listed for hairy cell leukaemia, which is a slow-growing malignant disorder affecting white blood cells. These cells accumulate in bone marrow and spleen preventing the production of normal blood cells. In WM, abnormal lymphocytes in the bone marrow produce an antibody (IgM) that can potentially thicken the blood plasma, causing nosebleeds, dizziness, gum bleeding and blurred vision.

- **Busulfex**[2] (IV busulfan) is indicated for use in combination with other chemotherapeutic agents and/or radiotherapy as a pre-conditioning regimen for haematopoietic progenitor cell transplantation. Haematopoiesis is the process of blood cell production and differentiation. Busulfex is used to restore normal haematopoiesis in patients affected by a number of blood and bone marrow related diseases.

Metabolic Disorders

- **Cystagon**[3] (cysteamine bitartrate) is used in the management of nephropathic cystinosis in children and adults. Nephropathic cystinosis is a rare inherited disorder characterised by the build up of cystine in organs, such as kidneys. This can cause kidney damage and excretion of excess amounts of glucose, proteins and electrolytes, resulting in slow growth, weak bones and progressive kidney failure.

- **Cystadane**[3] (betaine anhydrous powder) is used for the treatment of homocysteine in children and adults. Homocysteine causes cardiovascular thrombosis leading to premature death, osteoporosis, skeletal abnormalities, and optic lens dislocation.

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[1] TGA designated orphan drug.

[2] Product is currently only available under a Special Access Scheme. Orphan designation and registration is pending (PBS application to be considered in due course).

[3] This product meets the TGA criteria for orphan drug designation but was registered prior to the introduction of the relevant legislation and is therefore not included on the TGA's orphan drug list.

- **Adagen**[4] (pegademase bovine injection) is used in the treatment of adenosine deaminase (ADA) deficiency in children and adults with severe combined immunodeficiency disease (SCID). Adagen replenishes ADA, which allows an increase in white blood cells and decreases the risk of infection in conditions such as SCID.

- **Buphenyl**[4] (sodium phenylbutyrate) is used as adjunctive therapy in the chronic management of children and adults with urea cycle disorders (UCD). UCD's cause a build up of waste products, such as nitrogen, which can lead to brain damage and death.

- **Carnitor**[4] (levocarnitine) is used to treat carnitine deficiency in children and adults. A deficiency of carnitine can happen due to long-term haemodialysis and can result in extreme muscle weakness, cardiomyopathy and other related symptoms.

- **Orfadin**[4] (NTBC, nitisinone) is used in the treatment of hereditary tyrosinemia type 1. This condition, usually seen in children, leads to an abnormal accumulation of tyrosine in the liver and can potentially cause severe liver disease and failure to thrive.

- **Sucraid**[4] (sacrosidase) is used to treat genetically determined congenital sucrase-isomaltase deficiency or CSID in children. Children with CSID cannot break down certain sugars and starches. Symptoms include diarrhoea, dehydration, malnutrition and failure to thrive. The condition usually improves with age.

Cardiovascular

- **Remodulin**[1] (treprostinil sodium) is used to treat Pulmonary Arterial Hypertension or PAH (i.e. blood pressure in the lungs is higher than normal). Remodulin widens the blood vessels supplying the lungs and the body and also stops clotting. Increased blood pressure in the lungs places a strain on the heart causing less blood to be pumped into the lungs, resulting in shortness of breath, tiredness and as heart failure develops, swelling in the feet and abdomen.

Gastro Intestinal

- **Ursofalk**[3] (ursodeoxycholic acid) is TGA-approved for the treatment of liver diseases such as primary biliary cirrhosis (PBC), primary sclerosing cholangitis (PSC) and cystic fibrosis-related cholestasis. It is PBS listed for PBC. All these conditions impact on flow of bile and bile precursors leading to a build up in the liver causing conditions such as cirrhosis and liver failure.

Central Nervous System (CNS)

- **LAX101**[1] (ethyl eicosapentaenoic acid) is an innovative agent undergoing development for the treatment of Hungtingdon's Disease (HD). HD is a progressive and debilitating neurological condition that gradually renders the patient incapable of normal day-to-day function including employment and self-care. Mean age of onset is about 40 years with a duration of15-20 years.

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[4] Product is only available through a Special Access Scheme. Despite meeting TGA criteria for orphan drug designation there is no incentive to register the product (i.e. very small patient populations and relatively high cost of preparing registration dossier).