PHARMACEUTICAL BENEFITS ADVISORY COMMITTEE GUIDELINES REVIEW

Submission by Baxalta

September 2015

EXECUTIVE SUMMARY

- **Baxalta is a global biopharmaceutical leader developing, manufacturing and commercialising transformative therapies to treat orphan and underserved disease conditions in haematology, immunology and oncology.**
- **The review of the PBAC guidelines include due consideration of the innovation cycle of pharmaceuticals.**
- **Review of the PBAC guidelines considers the differences inherent in cost-effectiveness evaluation in rare and underserved diseases and for treatments for oncology.**
- **Baxalta would be pleased to assist the review of the PBAC Guidelines in any way we can, particularly in the areas of rare and underserved diseases and oncology.**
- **We request that we be included in all consultation during this review of the PBAC guidelines.**

About Baxalta

Baxalta Incorporated (NYSE: BXLT) is a global biopharmaceutical leader developing, manufacturing and commercialising transformative therapies to treat orphan and underserved disease conditions in haematology, immunology and oncology. Launched on 1 July 2015, following separation from Baxter International Inc., Baxalta's heritage in biopharmaceuticals spans decades.

Its targeted innovation strategy and cutting-edge science, combined with strategic partnerships, come together to spark discovery and deliver innovation for patients with limited treatment options. Baxalta specialises in pioneering lifesaving and life-sustaining products, many of which were first of their kind, revolutionising care across a broad spectrum of rare and hard-to-treat diseases.

Baxalta employs 16,000 people worldwide and operates in over one hundred countries. Its global headquarters are in Bannockburn, Illinois and its global R&D innovation centre is located in Cambridge, Massachusetts.

Baxalta's haematology business is a global leader in delivering transformative and personalised treatments for people with haemophilia and other blood disorders.

Its immunology business is working to make a meaningful difference for patients by innovating to meet the unmet needs of patients with immune disorders. Already a leading global provider of differentiated immunoglobulin treatments for immune deficiency disorders, Baxalta's growing portfolio of immunology products and services aims to help transform patient lives.

Baxalta is committed to delivering innovative and life-changing cancer therapies. By addressing unmet patient needs with a combination of personalised, effective, and lasting therapies, Baxalta aims to help as many patients who are burdened with cancers.

Globally, Baxalta has announced that it intends to launch 20 new products in the next five years in the therapeutic areas of oncology, haematology, immunology as well as biosimilar products. Globally and locally we are very cognisant of the importance of preparing high quality submissions to demonstrate the value of our products.

Value of innovation

It is important to foster an environment that sustains and enhances innovation to ensure the continued discovery and development of new medicines that improve patients' health and their quality of life.

Over the past decade, growing numbers of patients and families have benefited enormously from innovative new medicines that address an ever wider range of acute and chronic diseases. Increasingly, people are living without the burden of disease as a result of improved treatment of diseases. This underscores the importance of continued medical innovation aimed at preventing, treating and curing costly, life threatening diseases.

The below case study of innovation in the treatment of haemophilia A is a real and typical example of how investment in research and development of treatments is extending life and improving quality of life.

To encourage these discoveries, it is important to understand the climate and incentives for innovation and how these incentives may be affected by a variety of public policies.

Recommendation

The review of the PBAC guidelines include due consideration of the innovation cycle of pharmaceuticals.

Case study: Innovation in Haemophilia A

Haemophilia A is a rare, congenital bleeding disorder caused by a deficiency of coagulation factor VIII, a protein in blood that controls bleeding. It affects 1 in every 5000 males. Haemophilia is a life-long and life-threatening disease which confers significant burden not only to the patient, but onto the patient's family, and the health care system.

Without therapy to manage bleeds, severe haemophilia patients suffer from spontaneous bleeds a few times per month. Repeated bleeding into joints, leads progressively to joint deformation and impaired joint function. Repeated bleeding into a "target" joint causes chronic inflammation and swelling, leading to chronic or permanent joint disease (permanent arthropathy). Joint deformation and joint disease causes the patient pain and impairs quality of life. (Bickert B, 2005) (US National Hemophilia Foundation, 2009) The key purpose of therapy is to prevent and manage bleeds, to avoid the crippling effect of haemophilic arthropathy, bringing the life expectancy to "near normal".

As a result of innovative therapies and better access to care, life expectancy of haemophilia patients has increased significantly, from 16 years in the first half of the 20th century, to 60 years by the 1980s. Today, children born with haemophilia can have a normal life expectancy. (Haemophilia Australia Foundation, 2015)

Case study: Innovation in Haemophilia A (continued)

As frequent recipients of donated blood and blood-derived products, haemophilia patients were at much higher risk of exposure to blood-borne pathogens than almost any other group. During the last decades of the 20th century, fifty percent of hemophilia patients in Europe and the US contracted HIV; 60% were infected with hepatitis B; and 80% of patients were infected with hepatitis C. As a consequence, life expectancy amongst the hemophilia community in developed countries, which had been increasing from 16 years at the start of the 20th Century to 60 years in 1980, had fallen to 40 years in 1994. (Evatt, 2006)

Today, treatment for haemophilia A involves the replacement of FVIII by injection using either recombinant or plasma-derived products. Recombinant FVIII are genetically engineered, non-plasma-derived, products. The most innovative so-called 3rd generation recombinant FVIII treatments are plasma and albumin free and hence the chance of viral transmission is eliminated. Utilisation of 3rd generation recombinant FVIII eliminates the risk of patient exposure to blood borne pathogens. To date, there have been no confirmed spontaneous reports of Hepatitis, HIV, Parvovirus B19, or any other clinically significant infectious disease transmission that can be definitively linked to recombinant FVIII administration.

Patients receive either "episodic" (on-demand) treatment, after a bleed, or they receive replacement therapy through prophylaxis, when patients are infused regularly with factor concentrate to replace missing FactorVIII in their blood streams and thereby prevent bleeds. Prophylaxis can substantially reduce the number of bleeds per year and prevent joint damage. (Valentino LA, 2012) (Manco-Johnson MJ, 2007)

However, existing treatment has limitations. As factor administration and patient outcomes are not yet systematically captured in Australia, treatment optimization through adherence improvements as well as treatment personalization are still missing. Current prophylaxis treatments result in only 40-50% of patients with zero bleeds. Bleeds cause the joints to fill with blood and a single bleed can lead to joint damage. (Gringeri A, 2014) This results in progressive damage similar to arthritis creating significant health problems for patients. Intracranial haemorrhages can also develop, in some cases leading to brain damage and even premature death.

A new wave of innovation has led to products offering pharmacokinetic personalisation tools thereby allowing for personalised dosing and product innovation brought forward extended half-life products (EHL), which for some patients require less frequent infusions. EHL products are currently under development and are available now in some countries. These innovations are expected to lead to improved compliance for applicable patients and, importantly, lead to reduced bleeds. Further into the future, scientific research on the value of gene therapy for hemophilia A and B is likely to bring even better health solutions for people living with haemophilia.

Cost-effectiveness - Rare and underserved disease

Developing medicines in rare and underserved diseases provides special challenges for manufacturers and payors. Low patient numbers make it difficult for pharmaceutical companies to recoup research costs, and these medicines can be relatively expensive on a per patient basis. Consequently, the cost-effectiveness ratios for medicines serving rare diseases are typically higher when compared to other treatment interventions.

If it is accepted that individuals in a society are entitled to comparable levels of health, then we must accept that different cost-effectiveness thresholds for different diseases does not lead to inequitable outcomes. (Hughes DA, 2005) Patients suffering from rare conditions should be entitled to the same quality of treatment as other patients. In fact, the right to comparable health is implicit in most first world country health care systems and is even protected constitutionally in some. (Hughes DA, 2005)

Therefore, it is appropriate for the PBAC to recommend for PBS listing products with higher cost-effectiveness thresholds for rare and underserved diseases. It is not inequitable to accept different cost-effectiveness thresholds for different diseases as seeking to maximise overall public good (or public utility), that is, "bringing the greatest good to the greatest number", does not consider the individual's rights to healthcare. (Hughes DA, 2005)

It is also relevant to consider the budgetary impact. Given the relatively small number of patients with rare and underserved diseases, even in the context of a relatively higher cost per patient, the total cost impact on health budgets is typically limited. (Hughes DA, 2005)

It has been reported that in Europe (corresponding statistics are not available for Australia) five-year relative survival is worse for rare cancers (47%) than common cancers (65%) (Gatta G, 2011). This suggests that greater investment in treating rare cancers is required.

Recommendation

Review of the PBAC guidelines considers the differences inherent in cost-effectiveness evaluation in rare and underserved diseases.

Cost-effectiveness - Oncology

Clinical trial design in oncology regularly deviates from standard design for reasons including ethics, patients' risk / benefit assessments, patient prognosis and mode of delivery of treatments. Resultant clinical trial evidence is typically of a lower evidentiary standard. Many treatment regimens are evolving, often causing difficulties in identifying the appropriate place in therapy and target patient populations for new oncology products.

These factors create challenges when seeking to demonstrate of cost-effectiveness of oncology products, resulting in higher levels of uncertainty as compared to other therapies. This in turn makes reimbursement and pricing negotiations more difficult.

Recommendation

Review of the PBAC guidelines gives due consideration to the additional difficulties associated with the demonstration of cost-effectiveness in oncology.

Ongoing consultation

Baxalta would be pleased to assist the review of the PBAC Guidelines in any way we can, particularly in the areas of rare and underserved diseases and oncology. Baxalta looks forward to providing further comment on the consultation papers for reviewing the PBAC Guidelines.

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