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Early Scientific Advice Obtained Simultaneously from Regulators and Payers: Findings from a Pilot Study in Australia

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ABSTRACT

Objective: There is scope for better interaction between regulators, payers/HTA agencies, and medicines developers in their common objective of getting new medicines to patients. This paper reports on a tripartite early scientific advice pilot conducted by a pharmaceutical company (developer), the Therapeutic Goods Administration (TGA: regulator) and the Pharmaceutical Benefit Advisory Committee (PBAC) Secretariat (HTA agency) in Australia. The objective was to explore the practicality, feasibility, and sustainability of means of obtaining simultaneous scientific advice from both a regulatory and reimbursement perspective. **Methods:** Advice was sought for two development compounds in different disease areas. The focus was on matters of common interest to the TGA and the PBAC (i.e. the clinical evidence). Briefing books were prepared by the developer and supplied eight weeks prior to the meeting and only verbal advice was provided. **Results:** The pilot meeting took place in 2009. Each session lasted for approximately two hours and was structured around the questions in the briefing books. The representatives from the TGA and PBAC Secretariat provided well-informed, considered and careful advice for both compounds, which was predominantly actionable and practical. **Discussion:** The sessions proved highly informative and permitted better alignment of the possible positioning of new medicines with the clinical evidence that regulators and HTA agencies might subsequently require for favorable assessment. The process provided early and clear signals to inform major development investments and the probability of successful market access. A number of challenges need to be addressed before tripartite scientific advice can be provided on continual basis.

Keywords: Australia, health technology assessment, payer, regulatory, scientific advice.

Introduction

It is increasingly being recognized that there is considerable scope for better, coordinated, and early interactions between those who make decisions on the marketing authorization of new medicines (regulators), those who make recommendations/decisions on their pricing and reimbursement coverage (payers/health technology assessment [HTA] agencies), and those who develop medicines (developers). For many years, developers of new medicines have used the procedures offered by regulators to obtain early scientific advice about the clinical evidence plans necessary to support the marketing authorization of new medicines.

Despite the fact that payers/HTA agencies base their coverage recommendations/decisions on criteria that include a detailed review of the same clinical evidence package submitted to regulators, it is only recently that developers have been able to engage early and directly with them on evidence requirement issues such as the design of phase 3 clinical development programs. For example, Backhouse et al. [1] recently reported the results of a medicine developer's early scientific advice engagement with payers/HTA agencies in seven countries on the design and conduct of the clinical trial program for a new oral treatment for patients with chronic plaque psoriasis.

A logical extension of bipartite early scientific advice engagements (meetings involving only regulators and developers or only payers and developers) is to conduct tripartite interactions involving each of the three stakeholders. There are clear potential benefits to all parties from tripartite dialogue. For example, an early and more comprehensive mutual understanding of the expected phase 3 evidence needs of both regulators and payers/HTA agencies might lead to developers producing a single concise clinical evidence file (one dossier) that simultaneously meets the needs of both decision makers and that is sufficient to ensure quicker patient access [2]. The case for tripartite scientific meetings has taken on greater relevance in Australia with the introduction of new parallel regulatory and reimbursement processes in 2011 [3]. Moreover, there is an ongoing debate in certain jurisdictions about whether regulators or payers/HTA agencies should be responsible for making decisions on comparative (relative) efficacy and comparative (relative) effectiveness [4].

Frønsdal et al. [5] recently reported that meetings for scientific advice in Australia before phase 3 have to date most often been tripartite. While they were able to state that the national regulator

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(Therapeutic Goods Administration [TGA]) and the national HTA agency (Pharmaceutical Benefits Advisory Committee [PBAC] Secretariat) have found such meetings useful in terms of enhanced understanding and trust, they did not provide any details of any actual meetings. This article reports on a tripartite early scientific advice pilot project that we conducted with representatives of the TGA and the PBAC Secretariat. The meeting was conducted on behalf of the product development sponsor, a large multinational pharmaceutical company. As far as we are aware, it was the first process pilot of this type. This article provides an important contribution to the international discussion and debate on models of increased engagement and co-operation between technology developers, regulators, and payers/HTA agencies.

Objectives

The primary objective of the pilot was to explore the practicality, feasibility, and value of obtaining simultaneous scientific advice for a development compound from both a regulatory and reimbursement perspective with a view to identifying issues that might promote or impede the establishment of a sustainable tripartite (payer, regulator, developer) scientific advice process. Additional objectives were to obtain scientific advice, to ascertain whether or not the perspectives of the two agencies could be aligned with respect to evidence plans for the compound, to gain a deeper understanding on each party's function and objectives, and to foster mutual respect and trust.

The remainder of the article is divided into three sections. The Methods section focuses on a description of the engagement process adopted for the pilot. This is followed by the Results section in which key observations from the perspective of a technology developer are presented. The general findings and implications are addressed in the Discussion section.

Methods

Selection of Country

Australia was identified as a good country in which to conduct a pilot for a number of reasons. First, the Australian medicine regulatory and reimbursement (Pharmaceutical Benefits Scheme) systems are well established and widely respected. Australia has what is seen to be one of the most, if not the most, rigorous medicine reimbursement systems, and its decisions are widely "referenced" by other countries [6]. Second, Australia has one national public medicine regulator (TGA) and one national public HTA agency (PBAC). They work for the same level of government, under the same portfolio (Minister of Health) and department (Department of Health and Ageing) [7]. This meant that conducting the pilot was administratively straightforward. Third, there were local political initiatives to improve collaboration between the TGA and the PBAC (i.e., the piloting of the parallel lodgment of registration and reimbursement dossiers) [3]. Fourth, the Australian reimbursement system is referenced internationally such that procedural developments in Australia are likely to have ramifications in other countries. Finally, the PBAC Secretariat participated in an earlier bipartite payer/HTA agency engagement pilot project and was willing to experiment with this logical extension [1].

Tripartite Engagement Process

The engagement process was agreed during a number of preparatory meetings between the developer and representatives from the PBAC Secretariat in Canberra beginning in 2008. The agreed process was similar to that developed for the earlier payer/HTA agency bipartite engagement pilot involving the PBAC Secretariat with any such advice being nonbinding on the PBAC [1]. Key elements of the process are shown in Figure 1 and are summarized briefly in the following text.

The focus of the engagement was on matters of common interest to the TGA and the PBAC (i.e., the clinical evidence). Matters of interest to the TGA but not to the PBAC (e.g., pharmaceutical chemistry, animal toxicity, and manufacturing) and those of interest to the PBAC but not to the TGA (e.g., economic evidence, measurement of patient utility, cost-effectiveness, budget impact, risk-sharing arrangement, and quality use of medicine) were not considered. While acceptable cost-effectiveness is an important decision-making criterion of the PBAC, such determinations are underpinned by the strength and relevance of the supporting clinical evidence.

The technology developer selected two compounds for the pilot engagement: one was a compound to treat patients with cardiovascular disease and the other was a compound for patients with a musculoskeletal condition. In both cases, the proposed phase 3 clinical trials were presented for discussion with well advanced (but not yet finalized) trial designs. In other words, the timing was planned to allow for any changes that might be deemed necessary following the scientific advice received. Arrangements had been made with other agencies to discuss the clinical development plans for these two compounds, but the joint discussion with the TGA and the PBAC Secretariat was one of the first of such scientific advice meetings.

At the time the TGA did not have an established process for giving early scientific advice unlike regulators in other countries. While the PBAC Secretariat has a well established pre-submission consultation process, such meetings have tended to occur close to the lodgment of a reimbursement submission when substantive phase 3 data have been realized.

Participants

Participants would include the developer's decision makers for the pilot compounds (i.e., key members of the compound's global project team— clinical, regulatory, reimbursement, and marketing) and expert scientific advisors from both the TGA and the PBAC Secretariat. It was agreed that participating advisors would be excluded from any downstream assessment of a submission to support a request for subsidy. Legally, it was not possible for the actual decision makers (i.e., TGA delegate and/or PBAC members) to participate as advisors in the pilot because any advice given might be considered as an interim decision.

Briefing Documentation

It was agreed that the developer would produce a briefing book for each compound outlining a proposed clinical development program and submit it to the agencies 8 weeks in advance of a face-to-face meeting. In each case, the briefing book focused on proposed target patient population(s), indication(s), comparator (s), trial outcomes, and duration of follow-up of the proposed phase 3 clinical trials and how they had been determined. Each briefing book included questions for the agencies aimed at testing the suitability of the proposed evidence plans for the purposes of supporting payer as well as regulatory decisions. The questions needed to be of an active rather than a passive nature, for example, "Comparator X is proposed because…" rather than "Which comparator should the developer choose?" Figure 2 outlines some indicative questions.

Format of Advice

The TGA and the PBAC Secretariat agreed that they would liaise with each other before the meeting to ensure that their approach