Senate Community Affairs Committee

ANSWERS TO ESTIMATES QUESTIONS ON NOTICE

HEALTH AND AGEING PORTFOLIO

Supplementary Budget Estimates 2010-11, 20 October 2010

Question: E10-045

OUTCOME 1: Population Health

Topic: AVANDIA

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Senator Xenophon asked:

a) What steps has the TGA taken to review the approval of Avandia since September?
b) What independent assessments and tests of the drug were used in this process?
c) Were independent assessments and tests used in the original approval of the drug and any subsequent reassessments?
d) What steps will the TGA be taking in the future to continue monitoring the effects of this drug?
e) Does the TGA acknowledge that the actions of some GSK executives in withholding information about the drug make a strong argument for more independent testing of drugs and medical devices?

Answer:

a) The Therapeutic Goods Administration (TGA) is currently in the process of reviewing the benefit-risk profile of rosiglitazone (Avandia). This matter has been referred by the TGA to the Advisory Committee on the Safety of Medicines (ACSOM) for advice on the significance of recent data on the safety of rosiglitazone. The TGA has also worked with its international regulatory counterparts at the FDA and EMA to seek clarity on the different regulatory positions currently taken on this matter in the US and Europe.

b) The ACSOM has reviewed rosiglitazone. ACSOM is an independent statutory committee that provides advice to TGA about the safety, risk assessment and risk management of medicines and other matters related to pharmacovigilance. Members of ACSOM have expertise in pharmacoepidemiology, clinical pharmacology, clinical pharmacy, general medicine, paediatrics, clinical immunology, hepatology, vaccines and consumer issues.

   The safety matters currently under consideration with rosiglitazone relate to epidemiological data suggesting a higher than anticipated rate of cardiovascular side effects in some patients taking the medicine. This effect cannot be analysed through laboratory “tests”, rather it is detected, analysed and proven or disproven via clinical trials and epidemiological studies involving many thousands of patients.

c) Rosiglitazone was initially approved around the world and in Australia following analysis of phase I, II and III trials that demonstrated the safety and efficacy of the medicine in clinical trial settings in the patient groups for which it was indicated in the trials. The guidelines pertaining to the scientific data necessary to register a new prescription medicine are summarised in the Australian Regulatory Guidelines for Prescription Medicines. These guidelines are based on an internationally harmonised framework of scientific evaluation that defines the standards that a medicine needs to meet before being acceptable for marketing approval. In Australia, that evaluation process includes independent review of clinical trials, toxicological, pharmaceutical chemistry, chemistry and microbiological data by the Australian Government regulator, the TGA.

Standards of clinical trial design and oversight are defined in NHMRC and international guidelines, and studies to support registration of a new medicine must comply with these guidelines. In addition, the TGA utilises independent statutory advisory committees made up of clinical, scientific and epidemiological experts to review data relating to new medications and advise on issues that should be considered by the TGA in making its regulatory decisions.

d) When the issue of cardiovascular safety of rosiglitazone first arose the TGA took a number of regulatory activities. This included:
   - boxed warnings
   - changing the Product Information
   - reducing patient population indicated for use
   - writing to prescribers/colleges
   - working with NPS

   The effect of this action was to reduce the number of patients using rosiglitazone in Australia from 42,000 to approximately 16,000. These actions were taken 2 years prior to the recent action in Europe and the US. It is important to note that there has been no new safety data provided since the TGA's actions of 2008 and the recent actions in the US and Europe appear to relate to the issues the TGA acted on in 2008.

   The TGA is continuing to work with the US FDA and the EMA to further analyse emerging data related to rosiglitazone and will take further regulatory action if indicated.

e) The current approach to regulating medicines and medical devices in Australia is fundamentally the same as that used in all comparable developed countries. That is to say that an independent government regulator assesses compliance with prescribed standards of safety, quality and efficacy before allowing therapeutic products onto the market, and then monitors the ongoing safety of these products once they are on the market. It is important to note that for all new medicines, only a proportion of potential side effects are known at the time of market authorisation approval, as many more side effects only become known when a medicine is used in large numbers of people, or for a long period of time. For that reason the TGA, like the FDA and the EMA, has active post-market procedures to monitor and analyse the significance of side effects arising once a medicine is released to the market.