Gonal-F® gains first centralized approval from EMEA

In October 1995, the first marketing approval issued via the centralized system of the new European Agency for the Evaluation of Medicinal Products (EMEA) was granted to Ares-Serono for the new recombinant human follicle stimulating hormone (r-hFSH), Gonal-F®. Approvals granted through the centralized procedure by the new agency are valid in all EU countries.

Gonal-F® is indicated in the treatment of infertility; it stimulates the development of ovarian follicles in patients undergoing assisted reproduction treatments, such as *in vitro* fertilization. The production of r-hFSH has proved particularly challenging; Gonal-F® was the first heterodimeric glycoprotein to be produced by recombinant DNA technology. Problems associated with existing gonadotrophin treatments relate to the availability and variability of the natural source (human urine) and to difficulties in isolating pure gonadotrophin from the raw material. The manufacturers claim that the use of Gonal-F® eliminates concerns regarding possible side-effects associated with proteins coextracted from urine. The company is also pursuing the development of recombinant human luteinizing hormone and recombinant human chorionic gonadotrophin.

Gonal-F® received marketing approvals in Sweden, Finland and Switzerland in 1994. A New Drug Application (NDA) has been filed with the FDA in the USA.

New approvals system

In contrast to the FDA, the EMEA is a small organization with headcount projections of 100 and 250 for 1996 and the year 2000, respectively. From 1998, all pharmaceutical products must be submitted for a single European marketing approval. This may be achieved either through a central mechanism under the auspices of the agency itself, or through a decentralized system whereby approvals will be granted following successful application directly to the national agency of a European Member State and following ratification by other Member States (the EMEA acting as arbiter in areas of dispute).

Application under the centralized procedure is obligatory now for those drugs that can be categorized as being derived from biotechnology by means of one of the following processes:

- recombinant DNA technology
- controlled expression of genes coding for biologically active proteins in prokaryotes and eukaryotes including transformed mammalian cells
- hybridoma and monoclonal antibody methods

In the centralized procedure, the evaluation is performed by a team selected from an international panel of some 1600 independent experts (400 of these are experts in veterinary products). The team is selected by a member of the Committee for Proprietary Medicinal Products (CPMP; a committee convening under the auspices of the EMEA), who is referred to as the 'rapporteur'. The rapporteur assigned to any given application is chosen by the Committee itself, bearing in mind the wishes of the company concerned. The Director of the EMEA, Mr Fernand Sauer, is pleased to point out that in all applications to date, the rapporteur of choice has been assigned. In the case of Gonal-F®, the UK acted as rapporteur and Belgium as co-rapporteur.

In the first year of operation, companies have appeared hesitant to use the EMEA; many had already 'emptied their draws' in advance of the implementation of the reforms, and debates regarding the levels of fees levied on companies submitting approvals meant that submissions were slow. However, Mr Sauer has expressed clear aims in what the EMEA should achieve for the single European market and is optimistic for the future.

The first Annual Report of the EMEA is available directly from the agency: EMEA, 7 Westferry Circus, Canary Wharf, London, UK E14 4HB. tel: +44 171 418 8400, fax: +44 171 418 8416.

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