

Facts about once-a-month injectable contraceptives: Memorandum from a WHO meeting*

This Memorandum reviews the results of research undertaken in animals and human subjects on once-a-month injectable contraceptives containing a progestogen and an estrogen, in particular the products Cyclofem and Mesigyna. Results from clinical trials, including effectiveness and side-effects, are evaluated and issues arising from health service research are discussed. The Memorandum concludes with a statement regarding the use of Cyclofem and Mesigyna as options for potential contraceptive users.

Introduction

In 1981 WHO convened a meeting of experts to review progestogen-only injectable contraception. The report of the meeting stressed the need for long-acting reversible contraceptive methods but gave menstrual irregularity as the major reason for discontinuation of these progestogen-only methods (1). In order to try to overcome this problem, combined progestogen/estrogen formulations have been developed and extensively reviewed (2-7). In 1993, approximately 2 million women were using once-a-month combined injectable contraceptives mainly in Latin

America and China, with several other countries participating in the development and introduction of two new preparations.

Development of once-a-month combined injectables

Since the first report of a long-acting combined preparation by Siegel in 1963 (8), several different preparations have been tested. Of these preparations, two are now widely used. (1) one, known as *Chinese Injectable No. 1*, is used in China and a few neighbouring countries and is said to be used by at least 1% of all contraceptive users in China; and (2) the other, used in Latin America, is marketed under different brand names. Two new preparations will soon be available to national family planning programmes: (1) *Cyclofem*, previously known as HRP112 or Cycloprovera (this formulation originated with Upjohn and was further developed by WHO); and (2) *Mesigyna*, previously called HRP102 (this was developed by WHO and made available by Schering AG) (see Table 1). Both preparations have been tested in phase-III studies and some introductory studies undertaken on Cyclofem. Registration has been approved in some countries and further registrations are imminent.

17 α -Hydroxyprogesterone caproate plus estradiol valerate. This formulation is only manufactured in China. Two injections are given during the first month, the second 10 to 12 days after the first to achieve high efficacy. Some 5500 women have been studied in Shanghai for some 54 200 months of use and it was found to be acceptable, despite short cycles and to be relatively free from side-effects (9). It was subsequently assessed in comparison with Cyclofem and Mesigyna (see below).

* This Memorandum is based on the report of a WHO meeting that was held in Geneva on 1-3 June 1993. The participants were A. Andrade, Juiz de Fora, Brazil; S. Bassol, Torreon, Mexico; Wisut Boonkasemsanti, Bangkok, Thailand; L. Dorflinger, Research Triangle Park, NC, USA; J. Findlay, Clayton, Victoria, Australia (Co-Chairman); I. S. Fraser, Sydney, New South Wales, Australia; H.L. Gabeinick, Arlington, VA, USA; O.F. Giwa-Osagie, Lagos, Nigeria; Lely N.E. Hadjar, Jakarta, Indonesia; K. Hagenfeldt, Stockholm, Sweden (Co-Chairman); S. Hajri, Tunis, Tunisia; R. Heywood, Huntingdon, Cambridgeshire, England; R. Holt, Seattle, WA, USA; C. Huerdo, London, England; M. El Hussein, Cairo, Egypt; Suporn Koetsawang, Bangkok, Thailand; F. Lubis, Jakarta Pusat, Indonesia; R.F. McConnell, Flemington, NJ, USA; J.R. Newton, Birmingham, England (Rapporteur); E.S.P. Pandi, Jakarta, Indonesia; Sang G.-W., Hangzhou, Zhejiang China; B.N. Saxena, New Delhi, India; R. Simmons, Ann Arbor, MI, USA; D.C.G. Skegg, Dunedin, New Zealand; and M. Topozada, Alexandria, Egypt. Representative from Drug Regulatory Authority: P.A. Corlman. Representatives from the Pharmaceutical Industry: K.M. Cookson, P. Gunzel, B. Seibert and K. Schmidt-Gollwitzer. Observer: R. Lande. WHO Secretariat: C. d'Arcangues (Secretary) and P.E. Hall. Special Programme of Research, Development and Research Training in Human Reproduction, World Health Organization, 1211 Geneva 27, Switzerland. Requests for reprints should be sent to this address. A French translation of this article will appear in a later issue of the *Bulletin*.