

New drugs

Some of the views expressed in the following notes on newly approved products should be regarded as tentative, as there may be limited published data and little experience in Australia of their safety or efficacy. However, the Editorial Executive Committee believes that comments made in good faith at an early stage may still be of value. As a result of fuller experience, initial comments may need to be modified. The Committee is prepared to do this. Before new drugs are prescribed, the Committee believes it is important that full information is obtained either from the manufacturer's approved product information, a drug information centre or some other appropriate source.

Corifollitropin alfa

Elonva (Schering-Plough)

prefilled syringes containing 100 microgram and 150 microgram/0.5 mL

Approved indication: ovarian stimulation

Australian Medicines Handbook section 10.5

Follicle stimulating hormone is used in the management of infertility. Two recombinant forms are available, follitropin alfa and follitropin beta. Women preparing for *in vitro* fertilisation need daily injections to stimulate follicular development.

To reduce the number of injections, the hormone has been genetically engineered to form corifollitropin which has a more prolonged effect on the ovaries.

Corifollitropin combines follicle stimulating hormone with part of the human chorionic gonadotropin molecule. This extends the time to peak serum concentration and approximately doubles the half-life. A single injection can therefore sustain the growth of multiple follicles for a week. Corifollitropin is distributed and metabolised like follicle stimulating hormone with most of the dose being excreted in the urine. The appropriate dose is determined by the patient's weight.

In a placebo-controlled dose-ranging study of 55 women with anovulatory infertility, the follicular response increased with the dose of corifollitropin. Although a single subcutaneous dose induced a follicular response in 28 of the women, only eight ovulated.¹

An open-label study compared different doses of corifollitropin alfa with daily injections of recombinant follicle stimulating hormone. The 99 women who were randomised were preparing for *in vitro* fertilisation or intracytoplasmic sperm injection. More oocytes were retrieved from the women given corifollitropin than from the ovaries of women given recombinant follicle stimulating hormone. However, there was no significant difference in the number of good quality embryos produced.²

Corifollitropin and recombinant follicle stimulating hormone were then compared in a double-blind trial involving 1506 women weighing 60–90 kg. The women either had daily injections of follicle stimulating hormone or one injection of corifollitropin followed, after a week, by daily follicle stimulating hormone. Significantly more oocytes were retrieved from the women who had corifollitropin in the first week of treatment.³

Similar results were found in a trial of 396 women weighing 60 kg or less.⁴

In the trial of women of normal weight, 2.1% of those given corifollitropin discontinued treatment because of serious adverse effects compared with 0.4% of the group given recombinant follicle stimulating hormone. Ovarian hyperstimulation syndrome affected 7% of the corifollitropin group and 6.3% of the control group. Other adverse events also occurred with similar frequencies in each group.³ Common adverse effects include pelvic pain, headache, breast symptoms and nausea.

Although, statistically, significantly more oocytes were retrieved from women given corifollitropin rather than recombinant follicle stimulating hormone, the difference between treatments was only 1.2 oocytes. Embryo quality was similar and there was no significant difference in the pregnancy rate. Pregnancies lasting at least 10 weeks occurred in 38.9% of the corifollitropin group and 38.1% of the control group, with multiple pregnancies in 28.2% and 23.1%.³

T T manufacturer provided additional useful information

References †

1. Balen AH, Mulders AG, Fauser BC, Schoot BC, Renier MA, Devroey P, et al. Pharmacodynamics of a single low dose of long-acting recombinant follicle-stimulating hormone (FSH-carboxy terminal peptide, corifollitropin alfa) in women with World Health Organization group II anovulatory infertility. *J Clin Endocrinol Metab* 2004;89:6297-304.
2. Devroey P, Fauser BC, Platteau P, Beckers NG, Dhont M, Mannaerts BM. Induction of multiple follicular development by a single dose of long-acting recombinant follicle-stimulating hormone (FSH-CTP, corifollitropin alfa) for controlled ovarian stimulation before *in vitro* fertilization. *J Clin Endocrinol Metab* 2004;89:2062-70.
3. Devroey P, Boostanfar R, Koper NP, Mannaerts BM, Ijzerman-Boon PC, Fauser BC; ENGAGE Investigators. A double-blind, non-inferiority RCT comparing corifollitropin alfa and recombinant FSH during the first seven days of ovarian stimulation using a GnRH antagonist protocol. *Hum Reprod* 2009;24:3063-72.
4. The corifollitropin alfa Ensure study group. Corifollitropin alfa for ovarian stimulation in IVF: a randomized trial in lower-body-weight women. *Reprod Biomed Online* 2010;21:66-76.

Meningococcal A, C, W₁₃₅ and Y conjugate vaccine

Menveo (CSL)

vials containing powder for reconstitution

Approved indication: prevention of meningococcal disease

Australian Medicines Handbook section 20.1

Meningococcal disease is caused by the Gram-negative bacterium *Neisseria meningitidis*. The most prevalent disease-causing serogroups are A, B, C, W₁₃₅ and Y. Asymptomatic carriage of meningococci in the upper respiratory tract is relatively common, but occasionally the bacteria invade and cause septicaemia and meningitis. Infection can be rapid and fatal and mainly affects children under two years. However, there is also a peak of incidence in adolescents associated with increased carriage rates.

Currently in Australia there are two types of meningococcal vaccine – meningococcal C conjugate vaccines and polysaccharide vaccines. The conjugate vaccines consist of serogroup C polysaccharide conjugated to a carrier protein. These vaccines are immunogenic in babies and are given from two months of age. However, they only protect against serogroup C disease. The polysaccharide vaccines contain serogroups A, C, W₁₃₅ and Y, but because they are not conjugated to protein they may only protect for a short duration, do not induce immunological memory and are relatively ineffective in young children.

This new vaccine is a quadrivalent conjugate vaccine containing oligosaccharides from serogroups A, C, W₁₃₅ and Y individually attached to *Corynebacterium diphtheriae* CRM₁₉₇ protein. In a clinical trial of people aged 11 and over, one intramuscular dose of the vaccine was immunogenic and seemed to be non-inferior to a similar conjugate vaccine (Menactra).¹ In another trial of 11–17 year olds, the vaccine seemed to be comparable to a quadrivalent polysaccharide vaccine (Menomune).² Adverse events were generally mild and included injection-site reactions, headache, nausea and malaise.

Based on immunological data, this vaccine should protect against meningococcal infections caused by serogroups A, C, W₁₃₅ and Y. However, it is important to remember that it will not prevent serogroup B disease. The vaccine is currently only indicated for people aged 11 years or older. The US Food and Drug Administration has requested additional safety data in infants before considering approval in this age group.

T **T** manufacturer provided additional useful information

References *†A

1. Reisinger KS, Baxter R, Block SL, Shah J, Bedell L, Dull PM. Quadrivalent meningococcal vaccination of adults: phase III comparison of an investigational conjugate vaccine, MenACWY-CRM, with the licensed vaccine, Menactra. *Clin Vaccine Immunol* 2009;16:1810-15.

2. Jackson LA, Jacobson RM, Reisinger KS, Anemona A, Danzig LE, Dull PM. A randomized trial to determine the tolerability and immunogenicity of a quadrivalent meningococcal glycoconjugate vaccine in healthy adolescents. *Pediatr Infect Dis* 2009;28:86-91.

The T-score (**T**) is explained in 'New drugs: T-score for transparency' in this issue, *Aust Prescr* 2011;34:26–7.

- * At the time the comment was prepared, information about this drug was available on the website of the Food and Drug Administration in the USA (www.fda.gov).
- † At the time the comment was prepared, a scientific discussion about this drug was available on the website of the European Medicines Agency (www.ema.europa.eu).
- A At the time the comment was prepared, information about this drug was available on the website of the Therapeutic Goods Administration (www.tga.gov.au/pmeds/auspar.htm)

Correction

Vaccinia smallpox vaccine (*Aust Prescr* 2009;32:169-70)

T the manufacturer provided only the product information, not the clinical evaluation

New education program

NPS's latest education program for health professionals will be launched this month, focussing on managing lipids. It encourages greater use of risk assessment calculators to identify patients at risk of cardiovascular events, and early commencement of appropriate therapies. Resources have been developed to support conversations with patients about their cardiovascular health and provide information they can take home. For more information go to www.nps.org.au/health_professionals