Bemfola® follitropin alfa (recombinant human follicle stimulating hormone [r-hFSH])
Solution for injection in a pre-filled pen
Please refer to the SmPC before prescribing.
Bemfola Presentations: Pre-filled pens containing follitropin alfa 75 IU, 150 IU, 225 IU, 300 IU, 450 IU.
Indications: Anovulation (including polycystic ovarian syndrome, PCOS) in adult women who have been unresponsive to treatment with clomiphene citrate, stimulation of multifollicular development in women undergoing superovulation for assisted reproductive technologies (ART) such as in vitro fertilisation (IVF), gamete intra-fallopian transfer (GIFT) and zygote intra-fallopian transfer (ZIFT). Follitropin alfa in association with a luteinising hormone (LH) preparation is recommended for the stimulation of follicular development in women with severe LH (< 1.2 IU/l) and FSH deficiency. Follitropin alfa is indicated for the stimulation of spermatogenesis in adult men who have congenital or acquired hypogonadotropic hypogonadism with concomitant human chorionic gonadotropin (hCG) therapy.
Posology and Administration: Treatment with Bemfola should be initiated under the supervision of a physician experienced in the treatment of fertility disorders. Patients must be provided with the correct number of pens for their treatment course and educated to use the proper injection techniques. Dosage schemes depend on the ovarian response to be monitored through ultrasonography and measurement of serum oestradiol levels. Treatment should be tailored to the patient's response. Bemfola is given by subcutaneous injection.
Women with anovulation (including PCOS):
Daily injections, starting by Day 7 of the cycle.
Treatment typically commences at 75-150 IU FSH daily and is increased preferably by 37.5 or 75 IU at 7 or preferably 14-day intervals if necessary. Maximum daily dose is usually not higher than 225 IU FSH. If a patient fails to respond after 4 weeks of treatment, that cycle should be abandoned and patient re-evaluated after which treatment may recommence at a higher starting dose. When an optimal response is obtained, a single injection of 250 µg recombinant human chorionic gonadotropin (r-hCG) or 5,000 IU to 10,000 IU hCG should be administered 24-48 hours after the last Bemfola injection. The patient is recommended to have coitus on the day of, and day following, hCG administration. Alternatively intrauterine insemination (IUI) may be performed. If the response is excessive, treatment should be stopped and the hCG withheld (see Precautions). Treatment should recommence in the next cycle at a lower dose.
Women undergoing ovarian stimulation for multiple follicular development prior to in vitro fertilisation or other assisted reproductive technologies: A commonly used regimen for superovulation involves the administration of 150-225 IU of Bemfola daily, commencing on day 2 or 3 of the cycle. Treatment is continued until adequate follicular development has been achieved. Maximum daily dose is usually not higher than 450 IU daily. A single injection of 250 µg r-hCG or 5,000 IU to 10,000 IU hCG is administered 24-48 hours after the last Bemfola injection to induce final follicular maturation. Down-regulation with a gonadotropin-releasing hormone (GnRH) agonist or antagonist is commonly used in order to suppress the endogenous LH surge and to control tonic levels of LH. Bemfola is started approximately 2 weeks after the start of agonist treatment, both being continued until adequate follicular development is achieved.
Women with anovulation resulting from severe LH and FSH deficiency:
Follitropin alfa should be given as a course of daily injections simultaneously with lutropin alfa. Since these patients are amenorrhoeic and have low endogenous oestrogen secretion, treatment can commence at any time. Treatment may commence at 75 IU of lutropin alfa daily with 75 IU-150 IU FSH. If appropriate, the FSH dose should be adapted after 7-14 day intervals by 37.5 IU-75 IU increments for up to 5 weeks. When an optimal response is obtained, a single injection of 250 µg r-hCG or 5,000 IU to 10,000 IU hCG should be administered 24-48 hours after the last Bemfola and lutropin alfa injections. The patient is recommended to have coitus on the day of, and on the day following hCG administration. Alternatively, IUI may be performed. If the response is excessive, treatment should be stopped and the hCG withheld (see Precautions). Treatment should recommence in the next cycle at a lower dose.
Men with hypogonadotropic hypogonadism
150 IU Bemfola should be given three times a week, concomitantly with hCG, for a minimum of 4 months. If after this period, the patient has not responded, the combination treatment may be continued; current clinical experience indicates that treatment for at least 18 months may be necessary to achieve spermatogenesis.
Contraindications: Hypersensitivity to any of the active substance or to any of the excipients; tumours of the hypothalamus or pituitary gland; ovarian enlargement or ovarian cyst not due to PCOS; gynaecological haemorrhages of unknown aetiology; ovarian, uterine or

mammary carcinoma. Follitropin alfa must not be used when an effective response cannot be obtained eg. primary ovarian failure, malformations of sexual organs incompatible with pregnancy, fibroid tumours of the uterus incompatible with pregnancy, primary testicular insufficiency.

Warnings and Precautions: To improve the traceability of biological medicinal products; the name and batch number of the administered product should be recorded. Follitropin alfa is a potent gonadotrophic substance capable of causing mild to severe adverse reactions, and should only be used by physicians who are thoroughly familiar with infertility problems and their management. Patients with porphyria or a family history of porphyria should be closely monitored. Deterioration or a first appearance of this condition may require cessation of treatment.

Treatment in women:

Before starting treatment, patients should be evaluated for hypothyroidism, adrenocortical deficiency, hyperprolactinemia and should be treated accordingly. Ovarian hyperstimulation should be avoided by ultrasonic control of follicular development and regular assessment of serum oestradiol levels, which may rapidly rise to excessive values. In case of threatening unwanted hyperstimulation, the dose of Bemfola should be reduced, or in case of an excessive response, administration must be stopped and hCG withheld. Symptoms of mild and moderate hyperstimulation syndrome are abdominal pain, nausea, diarrhoea, and moderate enlargement of ovaries and ovarian cysts. Symptoms of severe hyperstimulation syndrome are large ovarian cysts (prone to rupture), abdominal distension, dyspnoea, weight gain, and (in rare cases) arteriothromboembolic processes.

In patients undergoing ovulation induction, the incidence of multiple pregnancy is increased compared with natural conception. The incidence of pregnancy loss by miscarriage or abortion is higher in patients undergoing stimulation of follicular growth for ovulation induction or ART than following natural conception. Women with a history of tubal disease are at risk of ectopic pregnancy. There have been reports of ovarian and other reproductive system neoplasms in women who have undergone multiple treatment regimens for infertility treatment. The prevalence of congenital malformations after ART may be slightly higher than after spontaneous conceptions. In women with recent or ongoing thromboembolic disease or with risk factors for thromboembolic events, treatment with gonadotropins may further increase the risk for aggravation or occurrence of such events.

Treatment in men:

Semen analysis is recommended 4 to 6 months after the beginning of treatment in men as part of the assessment of the response.

Interactions: Concomitant use of follitropin alfa with other medicinal products used to stimulate ovulation (e.g. hCG, clomiphene citrate) may potentiate the follicular response, whereas concurrent use of a GnRH agonist or antagonist to induce pituitary desensitisation may need an increased dose of follitropin alfa to elicit an adequate response. **Pregnancy and Lactation**: There are no indications for use of Bemfola during pregnancy or during breastfeeding.

Undesirable Effects: *Very common (≥ 1/10)*: Women - Headache; ovarian cysts. Women & men - Injection site reactions (e.g. pain, erythema, haematoma, swelling and/or irritation at the site of injection). *Common (≥ 1/100 to < 1/10)*: Women - Abdominal pain; abdominal distension; abdominal discomfort; nausea; vomiting; diarrhoea; mild or moderate OHSS. Men - Acne; gynaecomastia; varicocele; weight gain. *Uncommon (≥ 1/1,000 to < 1/100)*: Women - Severe OHSS. *Rare (≥ 1/10,000 to < 1/1,000)*: Women - Complication of severe OHSS. *Very rare (< 1/10,000)*: Women - Thromboembolism (may be associated with severe OHSS). Women & men - Mild to severe hypersensitivity reactions including anaphylactic reactions and shock; exacerbation or aggravation of asthma.

Special Precautions for Storage: Store in a refrigerator (2°C-8°C). Do not freeze. Store in the original package to protect from light.

Legal Category: POM

UK Cost:

75 IU/0.125 ml	£23.50
150 IU/0.25 ml	£47.00
225 IU/0.375 ml	£70.50
300 IU/0.5 ml	£94.00
450 IU/0.75 ml	£141.00

Marketing Authorisation (MA) Numbers and Packs. EU/1/13/909/001-15. Packs of 1, 5 and 10 pre-filled pens containing either 75 IU / 0.125 ml, 150 IU / 0.25 ml, 225 IU / 0.375 ml, 300 IU / 0.50 ml or 450 IU / 0.75 ml, with needles.

Marketing Authorisation Holder: Gedeon Richter Plc, Gyömrői út 19-21., 1103 Budapest, Hungary

Date of Authorisation: 27th March 2014

Date of Preparation: 12th November 2018

Further information available from:

Prescribing Information UK & ROI

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Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard. Adverse events should also be reported to Gedeon Richter (UK) Ltd on 0207 604 8806 or drugsafety.uk@gedeonrichter.eu

Adverse events should be reported to the HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2, Tel: +353 1 6764971, Fax: +353 1 6762517, Website: www.hpra.ie, e-mail: medsafety@hpra.ie. Adverse events should also be reported to Gedeon Richter (UK) Ltd on 0207 604 8806 or drugsafety.uk@gedeonrichter.eu