2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each pre-filled syringe contains 150 micrograms of corifollitropin alfa in 0.5 mL solution for injection.

3. PHARMACEUTICAL FORM

Solution for injection.

Clear and colourless aqueous solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Controlled Ovarian Stimulation (COS) in combination with a GnRH antagonist for the development of multiple follicles in women participating in an Assisted Reproductive Technology (ART) program.

4.2 Posology and method of administration.

Treatment with Elonva should be initiated under the supervision of a physician experienced in the treatment of fertility problems.

Posology

In the treatment of women of reproductive age, the dose of Elonva is based on weight and age.

- A single 150-microgram dose is recommended in women who weigh less than or equal to 55 kg and are younger than 35 years of age.
- A single 150-microgram dose is recommended in women: - who weigh more than 60 kilograms, regardless of age; - women older than 36 years of age who weigh less than 50 kilograms; or women who are older than 60 years of age.

Women older than 36 years of age who weigh less than 50 kilograms were not studied.

Table

<table>
<thead>
<tr>
<th>Age</th>
<th>Number of women</th>
<th>Weight</th>
<th>Median</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>18-30 years</td>
<td>100 micrograms</td>
<td>45 kg</td>
<td>40 kg-60 kg</td>
<td>25 kg-80 kg</td>
</tr>
<tr>
<td>31-36 years</td>
<td>150 micrograms</td>
<td>45 kg</td>
<td>40 kg-60 kg</td>
<td>25 kg-80 kg</td>
</tr>
<tr>
<td>&gt;36 years</td>
<td>150 micrograms</td>
<td>45 kg</td>
<td>40 kg-60 kg</td>
<td>25 kg-80 kg</td>
</tr>
</tbody>
</table>

The recommended doses of Elonva have only been established in a treatment cycle with a GnRH antagonist that was administered from stimulation day 5 or day 6 onwards (see also sections 4.1, 4.4, and 5.3).

Simulation day 1.

Elonva should be administered as a single subcutaneous injection, preferably in the abdominal wall, during the follicular phase of the menstrual cycle.

Simulation day 5.

Elonva should be administered as a single subcutaneous injection, preferably in the abdominal wall, during the follicular phase of the menstrual cycle.

Simulation day 7.

Elonva should be administered as a single subcutaneous injection, preferably in the abdominal wall, during the follicular phase of the menstrual cycle.

Simulation day 8.

Elonva should be administered as a single subcutaneous injection, preferably in the abdominal wall, during the follicular phase of the menstrual cycle.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients (See section 6.1 for list of excipients).
- Known or suspected pregnancy.
- Ovarian cyst or enlarged ovaries.
- A history of Ovarian Hyperstimulation Syndrome (OHSS).
- History of venous thromboembolism.
- Femoral veins of the anaesthetized with pregnancy.
- Polycystic ovarian syndrome (PCOS).

4.4 Special warnings and precautions for use (see section 4.1 ‘Infertility Evaluation Before Starting Treatment’)

- Before starting treatment, the couple’s infertility should be assessed as appropriate.
- In parturients, the woman should be evaluated for pregnancy, and appropriate specific treatment given. Medical conditions that contraindicate pregnancy should be evaluated before starting treatment with Elonva.

4.5 During the Stimulation Cycle

- Elonva is intended for single subcutaneous injection only. Additional injections of Elonva should not be given within the same treatment cycle. (See also section 4.2).
- Administration of Elonva, no additional FSH-containing product should be administered prior to stimulation day 8 (see also section 4.2).

4.6 Rare side effects

- In patients with renal insufficiency the rate of elimination of corifollitropin alfa may be reduced (see section 4.5 and 5.2). Therefore, the use of Elonva in these patients is not recommended.
- Not recommended with a GnRH Agonist Protocol

- There are limited data on the use of Elonva in combination with a GnRH agonist. Therefore, the use of Elonva is not recommended in combination with a GnRH agonist (see also section 4.2).
- Controlled Ovarian Hyperstimulation Syndrome (OHSS):

Elonva has not been studied in patients with polycystic ovarian syndrome (PCOS). In these women the use of Elonva is contraindicated (see also section 4.3).

- Ovarian Hyperstimulation Syndrome (OHSS):

Elonva has been studied in women with polycystic ovarian syndrome (PCOS). In these women the use of Elonva is contraindicated (see also section 4.3).

- Infertility women undergoing ART: An increased incidence of ovulatory pregnancies is important to exclude the possibility of extraneous contraceptive

- Congenital Malformations

- General disorders and administration site conditions

- General disorders and administration site conditions

- Pregnancy, puerperium and postpartal conditions

- Reproductive system and breast disorders

- Hemorrhage, deep vein thrombosis and arterial or venous.

- In addition, ovulation pregnancy and multiple pregnancies have been reported. These are considered to be contraindications to ART or a subsequent pregnancy.

- Ovarian

More than one injection of Elonva within one treatment cycle or too high a dose of Elonva and/or (rec)FSH may increase the risk of OHSS. After administration of Elonva, no additional FSH-containing product should be administered prior to stimulation day 8, as this may also increase the risk of OHSS. For reasons to manage the risk of OHSS see section 4.4.

4.5 Interaction with other medicinal products and other forms of interaction

No serious studies with Elonva and other medicines have been performed. Since corifollitropin alfa is not a substrate of cytochrome P450 enzymes, no metabolic interactions with the medicinal products are anticipated.

4.6 Pregnancy and lactation

Pregnancy

The use of Elonva during pregnancy is not indicated. In case of inadvertent exposure to Elonva during pregnancy, clinical data are not sufficient to exclude an adverse outcome of pregnancy. In animal studies, reproductive toxicity has been observed (see preclinical safety data in section 5.3).

Lactation

The use of Elonva during breast-feeding is not indicated.

4.7 Effects on ability to drive and use machines

No studies on the ability to drive and use machines have been performed. Elonva may cause dizziness. Women should be advised if they feel dizzy, they should not drive or use machines.

5. PHARMACOLOGICAL PROPERTIES

5.1 Preclinical pharmacology

Animal models

5.2 Clinical trials

In the absence of human studies, no additional data are available to define the potential risk of OHSS or any other adverse effect, including that of ovulation induction. In one controlled study, an increased incidence of ovulatory pregnancies and one twin pregnancy arrestment were observed. In addition, there is an increased risk of spontaneous abortion and premature birth. In addition, there is an increased risk of spontaneous abortion and premature birth. In addition, there is an increased risk of spontaneous abortion and premature birth.

5.3 Safety data

5.4 Overdose

In cases of overdose, no additional FSH-containing product should be administered prior to stimulation day 8, as this may also increase the risk of OHSS. For reasons to manage the risk of OHSS see section 4.4.

RA 255001 CCDs 3 (REF 2)
**Pharmacokinetic properties**

Pharmacokinetic properties are described in the context of clinical trials and studies. The cumulative pharmacokinetic profile of corifollitropin alfa is characterized by a rapid rise in plasma concentration followed by a slower decline. The primary endpoints in the studies were to evaluate the pharmacokinetic profile and safety of corifollitropin alfa in comparison to recombinant follicle-stimulating hormone (rFSH).

**Pharmacodynamic properties**

Pharmacodynamic properties include efficacy endpoints such as the number of viable oocytes retrieved and pregnancy rates. These endpoints were compared against historical controls and other treatments.

**Exposure and Elimination**

The exposure to corifollitropin alfa is proportional to the dose within the range of 60 micrograms to 240 micrograms. The elimination of corifollitropin alfa occurs predominantly via the kidneys, and the rate of elimination may be reduced in patients with renal insufficiency. Hepatic metabolism contributes to a minor extent to the elimination of corifollitropin alfa.

**Pharmacokinetic parameters**

The pharmacokinetic parameters of corifollitropin alfa were evaluated after subcutaneous injection in women undergoing a COS treatment cycle. The parameters were compared against historical controls and other treatments.

**Clinical trial information**

Clinical trials were conducted to assess the safety and efficacy of corifollitropin alfa. The follow-up FTET trial for PURSUE included women who had at least one embryo thawed for use within two years of the date of the last cryopreservation for that woman. The use of these data in hepatically impaired patients is not available, hepatic impairment is unlikely to affect the pharmacokinetic profile of corifollitropin alfa.

**Precautional safety data**

Practical data showed no special hazard for humans based on conventional studies of single and repeated dose toxicity and safety. Pharmacologically, reproduction toxicology studies in rats and rabbits indicated that corifollitropin alfa does not adversely affect fertility. Administration of corifollitropin alfa to rats and rabbits, prior to and directly after mating, and during early pregnancy, resulted in embryotoxicity. No effects on pregnancy from the Frozen-Thawed Embryo Transfer (FTET) cycles from ENGAGE and PURSUE.

**Conclusion**

The use of corifollitropin alfa in clinical practice requires careful consideration of the potential risks and benefits. The availability of these findings for the clinical use of Elonva is limited.