GONAL-f® RFF Pen (follitropin alfa injection)

DESCRIPTION

Gonal-f® RFF Pen is a potent gonadotropic substance capable of causing Ovarian Hyperstimulation Syndrome (OHSS) in women with or without pulmonary or vascular problems. OHSS causes fluid to suddenly build up in the stomach area, chest area, and heart area. It may result in death if not treated. OHSS may occur more severely and last longer in women with primary ovarian failure, a condition that stops ovulation (egg release) before menopause. Gonal-f® RFF Pen is also indicated for the development of multiple follicles in the ovulatory patient participating in in vitro fertilization (IVF) vs. intrauterine insemination (IUI) treatment cycles. Gonal-f® RFF Pen is a recombinant human follicle-stimulating hormone (FSH) product for the stimulation of ovarian follicle development and maturation.

WARNINGs

• Do not use Gonal-f® RFF Pen for a condition for which it was not prescribed. Do not give Gonal-f® RFF Pen to other people, even if they have the same symptoms.
• Do not use Gonal-f® RFF Pen for the treatment of men. It is not known whether Gonal-f® RFF Pen is effective in men.

INDICATIONS

Gonal-f® RFF Pen is used:
• for Assisted Reproductive Technologies (ART) after pituitary down-regulation with a GnRH agonist. Patients were randomized to either Gonal-f® RFF (n=237), administered subcutaneously, or a comparator recombinant human FSH. The use of insulin-sensitizing agents was allowed. Median treatment duration in days (range) 9.7 [3‑21] (230) d. Cycle 2 92% d. Cycle 3 45% d.
• for in vitro fertilization, to help their ovaries make more eggs.

CONTRAINDICATIONS

• Do not use Gonal-f® RFF Pen in women with a history of severe OHSS.
• Do not use Gonal-f® RFF Pen if you have had a stroke or a blood clot.

PRECAUTIONS

• Use Gonal-f® RFF Pen only as prescribed by your doctor.
• Special populations: Safety and effectiveness in pediatric patients have not been established.

ADVERSE REACTIONS

The most frequent adverse reactions included:

1. Gastrointestinal reactions: Nausea, vomiting, diarrhea, severe ovarian enlargement, abdominal pain, weight gain, dyspnea, and oliguria.
2. Skin and Appendages: Acne, rash, urticaria, and pruritus.
3. Reproductive, Female: Vaginal bleeding, menorrhagia, and premenstrual syndrome.

Table 4: Common Adverse Reactions on Gonal-f® RFF Pen

<table>
<thead>
<tr>
<th>Reaction</th>
<th>Patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acne</td>
<td>3 (3.6%)</td>
</tr>
<tr>
<td>Rash</td>
<td>3 (3.6%)</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>10 (12.0%)</td>
</tr>
<tr>
<td>Vaginal haemorrhage</td>
<td>5 (6.0%)</td>
</tr>
<tr>
<td>Nausea</td>
<td>3 (3.6%)</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>10 (12.0%)</td>
</tr>
<tr>
<td>Vaginal haemorrhage</td>
<td>5 (6.0%)</td>
</tr>
<tr>
<td>Nausea</td>
<td>3 (3.6%)</td>
</tr>
</tbody>
</table>

Gonal-f® RFF Pen is given by an injection just under the skin (subcutaneous injection). Your doctor's office will teach you how to inject yourself. See the end of this leaflet for directions on how to use the pen. Gonal-f® RFF Pen is at room temperature before using. Gonal-f® RFF Pen is given by an injection just under the skin (subcutaneous injection). Your doctor's office will teach you how to inject yourself. See the end of this leaflet for directions on how to use the pen. Gonal-f® RFF Pen is at room temperature before using. Gonal-f® RFF Pen. Your doctor may do regular ultrasound tests and blood tests to check your progress and to make sure you are responding to treatment. Your doctor will continue to monitor your response to treatment. Your doctor may adjust your dose if necessary. This may result in the development of multiple follicles in the ovulatory patient participating in in vitro fertilization (IVF) vs. intrauterine insemination (IUI) treatment cycles. Gonal-f® RFF Pen is a recombinant human follicle-stimulating hormone (FSH) product for the stimulation of ovarian follicle development and maturation.

For the complete list of adverse reactions, please see the Summary of Product Characteristics (SmPC).

Table 3: Cumulative Ovulation and Clinical Pregnancy Rates on Gonal-f® RFF Pen

<table>
<thead>
<tr>
<th>Cycle</th>
<th>Ovulation (%)</th>
<th>Clinical Pregnancy (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cycle 1</td>
<td>14</td>
<td>1</td>
</tr>
<tr>
<td>Cycle 2</td>
<td>28</td>
<td>28</td>
</tr>
<tr>
<td>Cycle 3</td>
<td>42</td>
<td>42</td>
</tr>
</tbody>
</table>

Grace approved by the European Medicines Agency (EMA) for the management of the Ovarian Hyperstimulation Syndrome (OHSS) in women with or without pulmonary or vascular problems. OHSS causes fluid to suddenly build up in the stomach area, chest area, and heart area. It may result in death if not treated. OHSS may occur more severely and last longer in women with primary ovarian failure, a condition that stops ovulation (egg release) before menopause. Gonal-f® RFF Pen is also indicated for the development of multiple follicles in the ovulatory patient participating in in vitro fertilization (IVF) vs. intrauterine insemination (IUI) treatment cycles.
Before you start, wash your hands with soap and water. Be a closer look by not touching anything you need.

Preparing the Pen

Step 1: Open the package and remove the 415 IU, 568 IU, or 1026 IU follitropin alfa to deliver a minimum total of 300 IU in 0.5 mL, 450 IU in 0.75 mL, or 900 IU in 1.5 mL, respectively, in a single injection. Before you start, wash your hands with soap and water. On a clean surface, lay out everything you need.

• Remove the protective pen cap. Clean threaded tip of pen with an alcohol swab.
• Tap the drug reservoir gently with your finger so that any air bubbles rise towards the needle. (If a few small air bubbles remain, do not worry; this is normal.)
• Remove the inner needle cap and hold the Pen with the needle pointing upwards.
• Check to make sure the dose arrow is set at 37.5. If not, turn the dosage dial (black numbers) to align the dose arrow with 37.5.

Step 2: Check the drug reservoir to ensure that the correct dose has been loaded. Dial your dose and pull out the injection button. It will go out only as far as the marked end of the red dosage confirmation scale. The amount of drug left in the Pen will be indicated by the last mark (flat arrow) on the red dosage confirmation scale.

Step 3: Injecting the dose

• Replace the inner needle cap. Do NOT remove the protective pen cap.
• If you are traveling, keep the Gonal-f® RFF Pen refrigerated (2°‑8°C/36°‑46°F) or at room temperature (20°‑25°C/68°‑77°F) for up to 28 days. Protect from light. Do not freeze. Discard unused material after 28 days.

Step 4: Dispose of used needles

• Do not use the Gonal-f® RFF Pen to store the drug. Use only the single‑use disposable needles provided within the Gonal‑f® RFF Pen carton or compatible needles distributed separately by EMD Serono, Inc.

Step 5: Expiration date

• If more than 3 years have passed since the last use, the needle should not be used. The manufacturer does not guarantee the effectiveness or safety of used needles.

Step 6: No more than 10% of patients receiving Gonal-f® RFF Pen in this study

• Use only the single‑use disposable needles provided within the Gonal‑f® RFF Pen carton or compatible needles distributed separately by EMD Serono, Inc.

Step 7: How it works

• Use only the single‑use disposable needles provided within the Gonal‑f® RFF Pen carton or compatible needles distributed separately by EMD Serono, Inc.

Step 8: After the injection is complete, make sure the needle is removed from the skin. Apply pressure using a gauze pad. If you have questions or problems, speak to your doctor or other healthcare professional.

Step 9: Further information and advice

• You can turn the dosage dial to the correct dose and pull out the injection button again. If the set dose is higher than the dose to be administered, discard the Pen. If the set dose is lower than the dose to be administered, dial the remaining amount of drug that is left in the Pen. The amount of drug left in the Pen will be indicated by the last mark (flat arrow) on the red dosage confirmation scale. In this case, turn the dosage dial to the correct dose and pull out the injection button again. If the set dose is lower than the dose to be administered, discard the Pen. If the set dose is higher than the dose to be administered, dial the remaining amount of drug that is left in the Pen.

Step 10: How the Gonal‑f® RFF Pen works

• If more than 3 years have passed since the last use, the needle should not be used. The manufacturer does not guarantee the effectiveness or safety of used needles.

Step 11: What is this medication for

• Use only the single‑use disposable needles provided within the Gonal‑f® RFF Pen carton or compatible needles distributed separately by EMD Serono, Inc.

Step 12: Side effects

• Use only the single‑use disposable needles provided within the Gonal‑f® RFF Pen carton or compatible needles distributed separately by EMD Serono, Inc.

Step 13: YOUR RESPONSIBILITY

• Use only the single‑use disposable needles provided within the Gonal‑f® RFF Pen carton or compatible needles distributed separately by EMD Serono, Inc.