

A redesigned follitropin alfa pen injector for infertility: results of a market research study

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Background: The purpose of this study was to evaluate patient-learning and nurse-teaching experiences when using a redesigned prefilled, ready-to-use follitropin alfa pen injector.

Methods: Seventy-three UK women of reproductive age either administering daily treatment with self-injectable gonadotropins or about to start gonadotropin treatment for infertility (aged 24–47 years; 53 self-injection-experienced and 20 self-injection-naïve) and 28 nurses from UK infertility clinics were recruited for the study. Following instruction, patients and nurses used the redesigned follitropin alfa pen to inject water into an orange and completed questionnaires to evaluate their experiences with the pen immediately after the simulated injections.

Results: Most (88%, n = 64) patients found it easy to learn how to use the pen. Among injection-experienced patients, 66% (n = 35) agreed that the redesigned pen was easier to learn to use compared with their current method and 70% (n = 37) also said they would prefer its use over current devices for all injectable fertility medications. All nurses considered the redesigned pen easy to learn and believed it would be easy to teach patients how to use. Eighty-six percent (n = 24) of the nurses thought it was easy to teach patients to determine the remaining dose to be dialed and injected in a second pen if the initial dose was incomplete. Compared with other injection devices, 96% (n = 27) thought it was “much easier” to “as easy” to teach patients to use the redesigned pen. Based on ease of teaching, 68% (n = 19) of nurses would choose to teach the pen in preference to any other injection method. Almost all (93%, n = 26) nurses considered that having the same pen format for a range of injectable gonadotropins would facilitate teaching and learning self-injection.

Conclusion: In this market research study with infertile patients and infertility nurses, the redesigned follitropin alfa pen was perceived as easy to learn, easy to teach how to use, and well accepted.

Keywords: infertility, gonadotropin, follitropin alfa pen, prefilled pen device, recombinant human follicle-stimulating hormone

Introduction

Daily injections of urinary or recombinant gonadotropins are often used to treat infertile patients and may include human follicle-stimulating hormone with or without the addition of luteinizing hormone. These gonadotropin products are often self-injected to promote follicular development as part of the treatment plan for assisted reproductive technologies, such as ovulation induction combined with natural intercourse, intrauterine insemination, or in vitro fertilization. At the end of the controlled ovarian stimulation phase with injectable gonadotropins, a single injection of human chorionic gonadotropin may be used to promote final follicular maturation and to trigger ovulation.

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The need for daily subcutaneous injections in infertility treatment does not tend to impair treatment adherence, but there is patient anxiety surrounding whether the correct dose has been delivered and the fact that unconscious mistakes can be made.¹ To improve compliance with treatment, it is important that devices used for the administration of recombinant human gonadotropins are easy for patients to learn to use, as well as easy for nurses in charge of patient training to teach. Currently, the majority of gonadotropin products are administered via syringes or prefilled pen injection devices, which have been introduced in the last decade to try to improve patient convenience and ease of use.

A key attribute of any injection device is the number of steps required to prepare and administer the injection. Fewer and easier steps are likely to reduce injection errors and to contribute to patient confidence.

The original pen injector for administration of follitropin alfa (recombinant human follicle-stimulating hormone) was modified to include built-in, enhanced, patient-friendly features, including visually improved numbering on the dose-setting dial in a second-generation pen. The third-generation redesigned follitropin alfa pen injector used in this study is a multidose, ready-to-use prefilled pen that incorporates several new and improved features. These features include a dose display window with a magnifying glass lid to enlarge the dosing number, which shows only the selected preset dose, the return of the dose reading to zero after injection of the full prescribed dose, or information on how much residual dose is required with a second pen if the full dose has not been administered, and a fully transparent cartridge container with graduated markings, to assist the user in determining the approximate amount of product left in the pen. The pen is available in three dose presentations of follitropin alfa, ie, 300 IU, 450 IU, and 900 IU. A key feature of the pen is that it offers flexibility in individualization of treatment protocols with a wide range of dose increments, ie, 12.5–300 IU for the 300 IU pen and 12.5–450 IU for the 450 IU and 900 IU pens. Results of the dose accuracy testing of the 900 IU presentation of the redesigned follitropin alfa pen injector, performed in accordance with international standards (EN ISO 11608-1:2000), demonstrated that the pen can accurately deliver a wide range of doses.²

The objective of this market research study was to assess the ease of teaching by fertility nurses on how to use the redesigned follitropin alfa pen injector, as well as the ease of learning to use the pen by infertile patients undergoing ovarian stimulation with gonadotropins.

Materials and methods

This study was conducted in the UK in January–February 2011 (London, Birmingham, Southampton, Manchester, Glasgow, and Newcastle). Patients and nurses were recruited by Insight Research Group, London, UK, based on the criteria outlined below. All participants provided informed consent.

Study participants

Patients eligible for inclusion in this study were women of reproductive age who were either undergoing controlled ovarian stimulation or had previous experience with daily injections of gonadotropin products within the last 6 months, or were injection-naïve with no previous experience with injectable medications but were consulting with a fertility clinic and were about to start gonadotropin treatment for infertility.

Nurses working in infertility centers and responsible for teaching patients undergoing fertility treatment to use self-injection devices (syringes and pens) were also included in the study. Nurses had to teach at least 10 patients in an average month, spend 80% of their working time in infertility clinics and have 3–30 years experience of working in an infertility clinic to be eligible for inclusion.

Training procedures and study questionnaires

Patient-learning and nurse-teaching experiences when using the redesigned follitropin alfa prefilled pen (GONAL-f®/GONAL-f® Revised Formulation Female Prefilled Pen, Merck Serono SA, Geneva, Switzerland, an affiliate of Merck KGaA, Darmstadt, Germany, Figure 1) were evaluated in this market research study. Before a moderator presented and demonstrated the operation of the pen injector

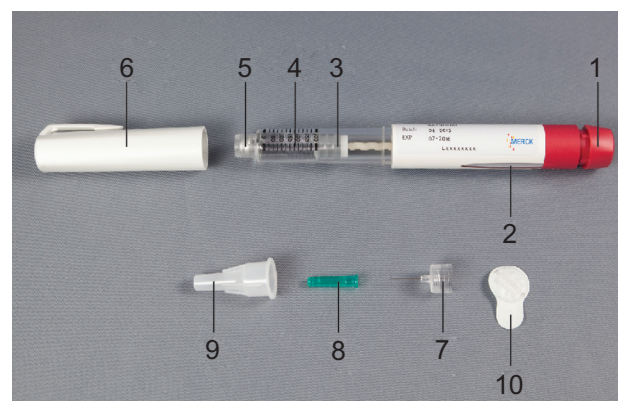


Figure 1 The components of the redesigned follitropin alfa pen injector: 1, dose-setting knob; 2, dose display; 3, plunger piston; 4, graduated reservoir holder; 5, threaded needle connector; 6, pen cap; 7, removable needle; 8, inner needle shield; 9, outer needle cap; 10, peel-off seal tab. The pen barrel and cartridge comprise sections 1–5.

to the nurses, they completed part of an online nurses' questionnaire (Appendix 1) pertaining to use and perceptions of existing devices for administering fertility treatment. To ensure consistent demonstration of the pen injector, the moderator followed a script that outlined step-by-step written and diagrammatic instructions. This was also available to nurses as additional guidance in handling the pen. After receiving the verbal and written instructions, nurses were each given a new, unbranded 900 IU demonstration pen, prefilled with water for injection, and were asked to attach the needle, practice removing large air bubbles, and inject 125 IU of water into an orange as many times as required to gain familiarity with the pen injector. Nurses then completed the part of the nurses' questionnaire on ease of learning. The nurses then repeated the process, training small groups of up to five patients per nurse. The moderator ensured that an accurate demonstration of the pen injector was provided to patients.

For assessment of acceptance of the redesigned follitropin alfa pen, nurses completed the relevant questions on their questionnaire and patients completed a separate online patient questionnaire (Appendix 2). Each step of the injection process with the pen was assessed to determine both how easy it was to teach and to learn in terms of priming, attaching the needle, reading the dosing scale, setting the dose, pushing the dose setting knob when injecting, and checking that the full dose had been injected. Respondents also evaluated how easy it was to determine the remaining dose to be dialed and injected with a second pen if the initial dose was incomplete, readjust the dose if needed, and remove the needle. Nurses and treatment-experienced patients also compared the attributes of this pen injector with the self-injection devices that they currently taught or used, based on recall. The entire process of instruction, practice, and completing the questionnaire took approximately 70 minutes for nurses and 40 minutes for patients.

The redesigned prefilled follitropin alfa 900 IU demonstration pens were supplied by the manufacturer. All materials were new before assessment by each patient/nurse.

Statistical analysis

Data from nurse and patient questionnaires are presented using descriptive statistics. Scales rating key performance indicators used a 5-point scale where 5 was the best and 1 was the worst possible outcome. Questions on preferences and advantages did not use rating scales and are quoted as a percentage of participants who provided each response.

Results

Seventy-three infertile women of reproductive age and 28 nurses who had worked for 3–30 years in an infertility clinic were enrolled in this study; the numbers of patients and nurses recruited from each city are shown in Table 1.

Patients had a mean age of 35 (range 24–47) years and 8% were left-handed ($n = 6$). The baseline characteristics of the patients are summarized in Table 2; 73% ($n = 53$) of patients were treatment-experienced and 27% ($n = 20$) were treatment-naïve.

The nurses all spent at least 80% of their time working directly with patients and personally teaching women how to use injectable gonadotropins in pens or syringes/vials for fertility treatment; 7% were left-handed ($n = 2$). Injectable gonadotropin devices that nurses had taught patients to use in the previous 6 months are summarized in Table 3.

All of the patients/nurses participated in the training and completed all the sections of the questionnaires that were relevant to their experiences, ie, self-injection-naïve patients did not answer questions aimed at self-injection-experienced patients.

Patients

The specific aspects of the redesigned pen injector that patients considered easy to learn are shown in Figure 2. Eighty-eight percent ($n = 64$) of patients found the whole process easy to follow and had no trouble learning how to use the pen; 70% ($n = 51$) found it easy to learn how to set the dose and how to remove large air bubbles before use.

In the total patient population, 89% ($n = 65$) of patients were either “very” or “quite comfortable” with the zero reading on the dosing scale indicating that the full dose had been injected and 88% ($n = 64$) with pen control when injecting. The flexibility to readjust the dose, if the set dose was too high/low, was seen as an advantage in learning how to use the pen by 85% ($n = 62$) of patients.

Most (95%, $n = 69$) patients “strongly/somewhat agreed” that they were comfortable with the number of steps involved

Table 1 Number of nurses and patients recruited from each UK city

City	Nurses	Patients
Birmingham	3	7
Manchester	2	6
Newcastle	3	9
Glasgow	3	5
Southampton	5	14
London	12	32
Total	28	73

Table 2 Demographic characteristics of the study patients (n = 73)

Characteristics	
Mean (SD) age, years	35 (4.54)
Left-handed, n (%)	6 (8)
Age group, n (%)	
24–30 years	13 (18)
31–35 years	30 (41)
36–40 years	21 (29)
41–47 years	9 (12)
Fertility treatment cycles using self-injected gonadotropins undertaken in total, n (%) ^a	
0	20 (27)
1	22 (30)
2	14 (19)
3	6 (8)
4	4 (5)
5+	7 (10)
Current devices used to inject fertility medication, n (%) ^b	
None	20 (27)
Follitropin alfa pen ^c	15 (21)
Follitropin beta pen ^d	8 (11)
Syringe and vial	31 (42)

Notes: ^aPercentages do not total 100% due to rounding; ^bpercentages do not total 100% due to use/teaching of >1 device; ^cMerck Serono SA, Geneva, Switzerland; ^dMerck Sharp and Dohme Ltd, Hoddesdon, Hertfordshire, UK.

Abbreviation: SD, standard deviation.

in preparing and giving the injection, and 93% (n = 68) believed that using the new pen device would ensure that they set the correct dose and administered it in full when they self-injected at home.

Among the injection-experienced patients, 66% (n = 35) considered that the redesigned follitropin alfa pen was easier to learn to use than their current injection method; the pen performance was rated as “very high” or “high” by 83% (n = 44) of patients for ease of learning to remove a

Table 3 Injectable gonadotropin devices that nurses (n = 28) had taught patients to use in the previous six months

Device	n (%) ^a
Follitropin alfa pen ^b	24 (86)
Follitropin alfa syringe/vial ^b	13 (46)
Lutropin alfa syringe/vial ^b	3 (11)
Chorionic gonadotropin prefilled syringe ^b	26 (93)
Follitropin beta pen ^c	9 (32)
Follitropin beta syringe/vial ^c	2 (7)
Chorionic gonadotropin syringe/vial ^d	14 (50)
Menotropins syringe/vial ^d	25 (89)
Menotropins syringe/vial ^e	6 (21)
Urofollitropin syringe/vial ^e	7 (25)
Chorionic gonadotropin syringe/vial ^d	2 (7)

Notes: ^aPercentages do not total 100% due to teaching of >1 device; ^bMerck Serono SA, Geneva, Switzerland; ^cMerck Sharp and Dohme Ltd, Hoddesdon, Hertfordshire, UK; ^dFerring International Center SA, Saint-Prex, Switzerland; ^eBBSA Institut Biochimique SA, Lugano, Switzerland.

large air bubble, by 81% (n = 43) for attaching the needle onto the pen, by 79% (n = 42) for reading the dosing scale, and by 74% (n = 39) for reading the graduated markings on the reservoir holder. Eighty-seven percent (n = 46) of the injection-experienced patients found it easy to learn how to set the dose, 89% (n = 47) to push the dose setting knob when injecting, 89% (n = 47) to check that the full dose had been injected, 72% (n = 32) to detach and discard the needle, and 81% (n = 43) to determine any remaining dose required with a second pen if the initial dose administered was incomplete. Of these injection-experienced patients, 70% (n = 37) claimed they would prefer to use the redesigned follitropin alfa pen over their current injection device in the future for all their injectable fertility medications (Figure 3).

The number of patients with previous experience of the Puregon[®] pen was small (n = 8), reflecting the low number of Puregon pen users in the UK and, therefore, is insufficient to draw any specific conclusions regarding device preference.

Nurses

All nurses agreed that it was easy to learn how to use the redesigned pen and believed it would be easy to teach patients how to use it. Based on ease of teaching, 68% (n = 19) of the nurses would choose to teach the redesigned pen in preference to any other pen or syringe/vial currently available (Figure 4).

Regarding aspects of the pen that were easy to teach, 93% (n = 26) of nurses thought it was “very” or “somewhat” easy to teach patients the overall process of self-administering a dose (Figure 5). Compared with other pen injectors, 96% (n = 27) of nurses thought it was “much easier” to “as easy” to teach patients to use the redesigned follitropin alfa pen; 46% (n = 13) thought it was “much” or “somewhat” easier to teach patients to use the redesigned follitropin alfa pen, and 50% (n = 14) considered it was neither easier nor harder. Almost all (96%, n = 27) nurses rated as “very” or “quite” high, the range of possible doses that could be administered (due to a greater number of dosing increments), and 79% (n = 22) were confident that the patient would be able to calculate correctly any remaining dose needed with a second pen if an incomplete dose was injected with the first pen.

It was “strongly” or “somewhat” agreed by 93% (n = 26) of nurses that having the same pen format for a range of injectable gonadotropins would make it easier for them to teach patients to self-inject and for patients to learn how to self-inject; 86% (n = 24) of nurses agreed that the redesigned pen would significantly reduce their teaching time with patients, 89% (n = 25) thought it would reduce mistakes when patients

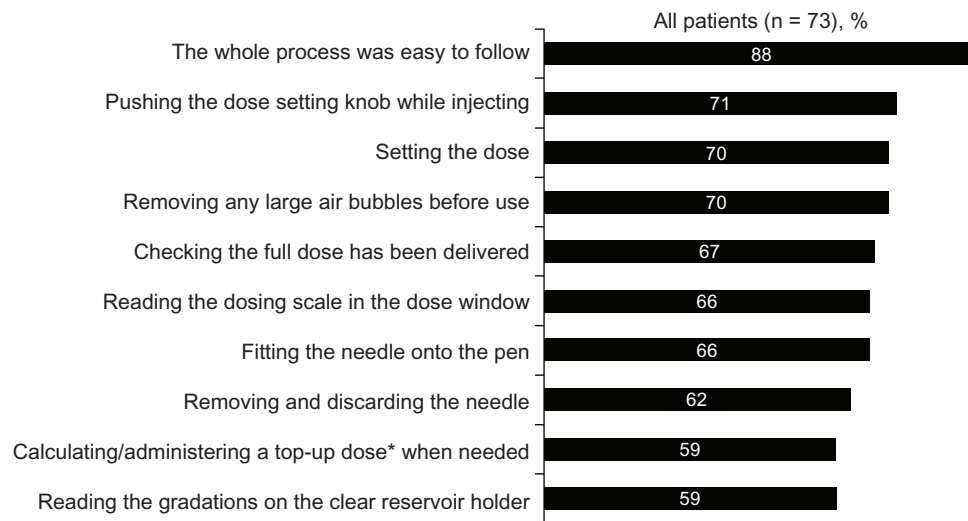


Figure 2 Aspects of the redesigned follitropin alfa pen that patients found easy to learn.
Note: *Top-up dose; remainder of dose to be dialed and injected in a second pen.

self-administered at home, and 96% (n = 27) believed that, given a choice, patients would prefer the same pen format for administering all their injectable gonadotropin products.

Discussion

This is the first study to report patient and nurse opinions on the redesigned follitropin alfa pen for infertility treatment. Patients with infertility, who currently require numerous administration devices to deliver the full spectrum of gonadotropins during infertility treatment,³ found the pen injector easy to use and most patients found the training on use easy to follow. Among the attributes of the redesigned

pen, patients rated highly the ease of checking that the full dose had been injected and the flexibility to readjust the set dose. Self-injection-experienced patients generally preferred the redesigned pen over their existing injection devices.

There are several reports that infertile patients find pen injectors simpler and easier to use than other administration methods.^{1,4-7} In a study of nurse-led training on administration of follicle-stimulating hormone, 123 participants attended training and completed a questionnaire. Of the patients who expressed a preference, 94% preferred a pen device to a reconstitution and conventional needle and syringe method. The most common reasons given for selection of a prefilled

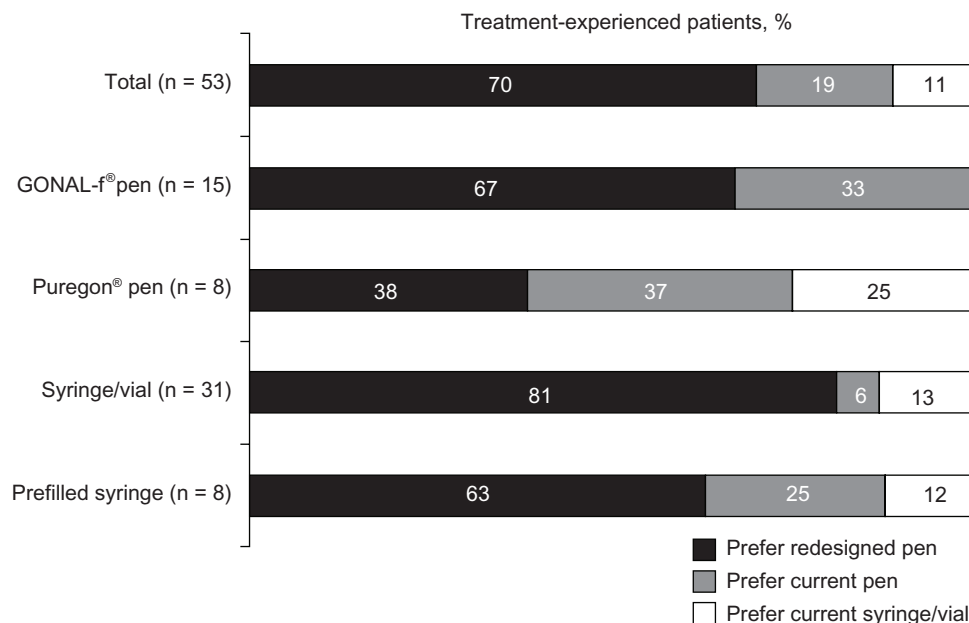


Figure 3 Summary of device preferences by injection-experienced patients.

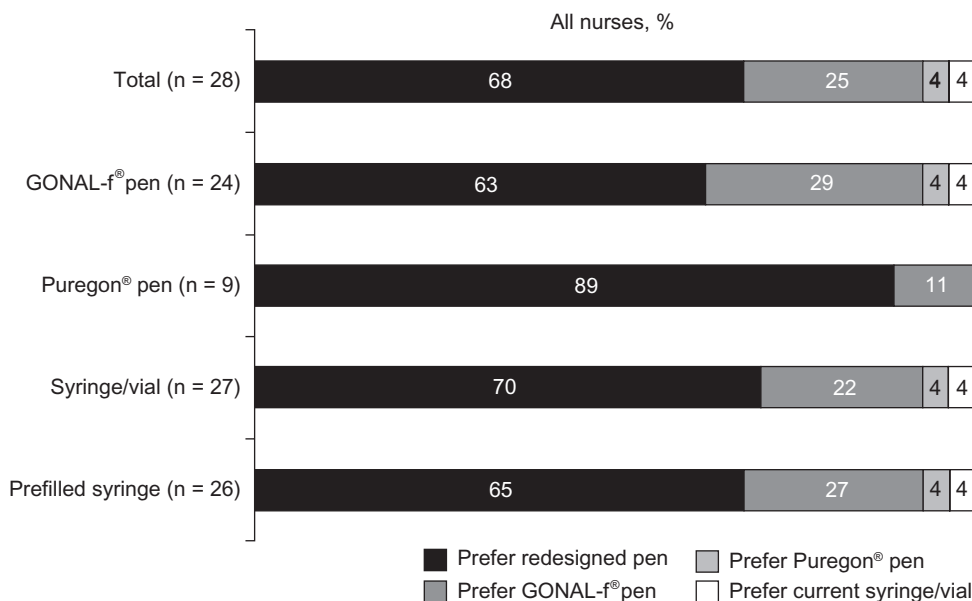


Figure 4 Summary of device preference by infertility nurses teaching patients to self-inject.

pen were that it was considered to be easy to use, had a simple and reliable dosing mechanism, and minimized the chance of making a dosing error.¹

Prefilled disposable insulin pen injectors have received positive ratings for intuitiveness, instruction time, ease of use, and acceptance in patient surveys.^{8,9} Among patients with rheumatoid arthritis, a pen injector for a monoclonal antibody scored well compared with a prefilled syringe in

terms of pain and time to inject and was perceived to be easier to use and more convenient.¹⁰

All the infertility nurses in this study found the pen injector easy to learn to use and believed that it would be easy to teach patients to use. Most nurses considered that having the same device for a range of injectable gonadotropins would facilitate teaching patients to self-inject and would reduce teaching time. These results are in agreement with those from

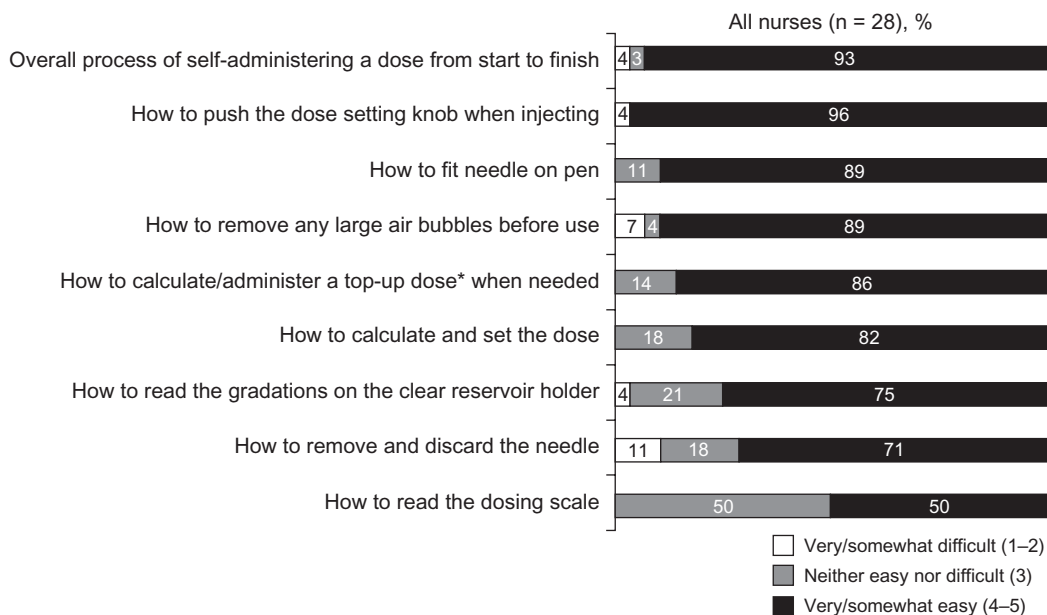


Figure 5 Fertility nurses' opinion of ease of teaching for each of the functions of the redesigned follitropin alfa pen. Note: *Top-up dose; remainder of dose to be dialed and injected in a second pen.

another study in which pen injectors have been reported to be well received by nurses.¹¹

Patients may use several different administration devices to deliver the full spectrum of gonadotropins during infertility treatment, so there is a need to harmonize the administration devices for infertility. A device that could be used to administer the full range of gonadotropins would have advantages for nurses in terms of teaching time and for patients in terms of learning time. The use of a common device is also likely to reduce administration errors.

A limitation of the present study was that only the redesigned follitropin alfa pen was tested and the answers about the devices that were used currently were based on recall. However, 73% of patients interviewed were self-injection-experienced and had received fertility treatment with injectable gonadotropins in the previous six months. Thus, it is considered that results based on patient recall were unlikely to have biased the patients' answers. In addition, the study was performed in a viewing facility, was open-label and uncontrolled, and assessed perceived ease of learning and ease of teaching of the pen device rather than use in an actual fertility treatment cycle. Further studies are needed to confirm the findings in clinical practice.

Conclusion

In this market research study with infertile patients and infertility nurses, the redesigned follitropin alfa pen was perceived as easy to learn and easy to teach how to use, and was well-accepted. There was also a high level of confidence among participants that the full dose of gonadotropin had been injected properly and that it was easy to learn how to check that the correct dose had been delivered. Moreover, most nurses considered that a single platform for delivery of the full spectrum of infertility medications that a patient might require during treatment would have advantages for teaching and learning use for administration.

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Disclosure

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Appendix I

Nurse questionnaire. Duration sections 1 and 2, approximately five minutes; section 3, approximately 15 minutes.

Section I

Usage and perception of existing devices.

1A. Are you left or right-handed? (Ask all, single code only.)

Left-handed	1	Go to Q1B
Right-handed	2	Go to Q1B
Both	3	Go to Q1B

1B. Which of the following injectable gonadotropin injection devices have you taught your patients to use in the last six months? Please tick all which apply. (Ask all, multicode allowed.)

GONAL-f® pen (follitropin alfa)	1	Go to Q2A
GONAL-f® syringe/vial (follitropin alfa)	2	Go to Q2C
Luveris® syringe/vial (lutropin alfa)	3	Go to Q2C
Ovitrelle® prefilled syringe (choriogonadotropin alfa)	4	Go to Q2C
Puregon® pen (follitropin beta)	5	Go to Q2B
Puregon® syringe/vial (follitropin beta)	6	Go to Q2C
Pregnyl® syringe/vial (chorionic gonadotropin)	7	Go to Q2C
Bravelle® syringe/vial (urofollitropin)	8	Go to Q2C
Menopur® syringe/vial (menotropin)	9	Go to Q2C
Merional® syringe/vial (menotropin)	10	Go to Q2C
Fostimon® syringe/vial (urofollitropin)	11	Go to Q2C
Choragon® syringe/vial (chorionic gonadotropin)	12	Go to Q2C
Others (write in)	13	Go to Q2C

2A. The following is a list of attributes relating to the current GONAL-f® pen. Please rate its performance on the following scale. (Randomize order of 2A, 2B, and 2C. Ask Q2A if code 01 (GONAL-f® pen) coded at Q1B. Single code per statement.)

1. Very low
2. Quite low
3. Neither low nor high
4. Quite high
5. Very high

Range of possible doses which can be prescribed (due to permitted dose increments)	1
Ease for the nurse to learn how to use	2
Ease for the nurse to teach patients how to use	3
Your confidence that the patient understands how to remove any large air bubbles before use	4
Ease for patient to fit needle onto pen	5
Ease for patient to read the dosing scale	6
Your confidence in the patient's ability to calculate and set the correct dose	7
Ease for patient to pull up and prime the injection button	8
Ease for patient to push the injection button when injecting	9
Ease for patient to administer the injection	10
Ease for patient to check that the full dose has been injected	11
Your confidence that the full dose has been injected when patients self-administer at home	12
Ease of removing and discarding the needle	13
Your confidence that the patient is able to correctly calculate any top-up dose needed after injection	14
Patient's satisfaction with the number of steps involved in preparing/giving the injection	15
Your confidence that the patient understands how to use the pen properly	16

2B. The following is a list of attributes relating to the current Puregon® pen. Please rate its performance on the following scale. (Ask Q2B if code 05 (Puregon® pen) coded at Q1B. Single code per statement.)

1. Very low
2. Quite low
3. Neither low nor high
4. Quite high
5. Very high

Range of possible doses which can be prescribed (due to permitted dose increments)	1
Ease for the nurse to learn how to use	2
Ease for the nurse to teach patients how to use	3
Your confidence that the patient understands how to remove any large air bubbles before use	4
Ease for patient to assemble the pen (insert treatment cartridge)	5
Ease for patient to fit needle onto pen	6
Ease for patient to read the dosing scale	7
Your confidence in the patient's ability to calculate and set the correct dose	8
Ease for patient to push the injection button when injecting	9
Ease for patient to administer the injection	10
Ease for patient to check that the full dose has been injected	11
Your confidence that the full dose has been injected when patients self-administer at home	12
Ease of removing and discarding the needle	13
Your confidence that the patient is able to correctly calculate any top-up dose needed after injection	14
Patient's satisfaction with the number of steps involved in preparing/giving the injection	15
Your confidence that the patient understands how to use the pen properly	16

2C. The following is a list of attributes relating to current syringes and vials. Please rate their performance on the following scale. (Ask Q2C if codes 02, 03, 04, 06, 07, 08, 09, 10, 11, and 12 (syringes and vials) coded at Q1B. Single code per statement.)

1. Very low
2. Quite low
3. Neither low nor high
4. Quite high
5. Very high

Range of possible doses which can be prescribed (due to permitted dose increments)	1
Ease for the nurse to learn how to use	2
Ease for the nurse to teach patients how to use	3
Your confidence that the patient understands how to remove any large air bubbles before use	4
Ease for patient to fit needle onto syringe	5
Ease for patient to read the dosing scale	6
Ease for patient to mix the treatment in the vial	7
Ease for patient to read the gradations on the clear reservoir holder	8
Your confidence in the patient's ability to calculate and set the correct dose	9
Ease for patient to administer the injection	10
Ease for patient to check that the full dose has been injected	11
Your confidence that the full dose has been injected when patients self-administer at home	12
Ease of removing and discarding the needle	13
Your confidence that the patient is able to correctly calculate any top-up dose needed after injection	14
Patient's satisfaction with the number of steps involved in preparing/giving the injection	15
Your confidence that the patient understands how to use the syringe properly	16

Section 2

Reactions to pen demonstration, to be completed after the training session. (Section divider, introduction to be shown to respondent.) Now, you will be shown a demonstration on how to use the new pen.* You will have the opportunity to try the new pen after the demonstration. Please click NEXT after you had a chance to try the new pen.

3. Below is a list of statements that you may or may not agree with. Please tick all that you agree with having had your training session. (Ask all, multicode allowed.)

I found it easy to learn to use the pen	1	Go to Q4
I believe this new pen would be easy for me to teach my patients to use	2	Go to Q4
It will take me less time to teach my patients to use this new pen compared with current pens	3	Go to Q4
It is easy to remove large air bubbles from the new pen	4	Go to Q4
It is easier to read the dosing scale on this new pen compared with other pens/syringes	5	Go to Q4
There are fewer steps involved in preparing the pen for injection compared with current pens	6	Go to Q4
I believe my patients will be able to prepare and inject in a shorter period of time using this pen compared with current pens	7	Go to Q4
There is less room for error when setting/adjusting the dose with this new pen compared with current pens	8	Go to Q4
I am confident my patients will be able to regularly administer treatment at the correct dose using this pen	9	Go to Q4
I believe my patients will be more confident in using this new pen than other pens/syringes	10	Go to Q4

4. How comfortable are you with each of the following? (Ask all, single code per statement.) For each attribute please indicate whether you are:

5. Very comfortable
4. Quite comfortable
3. Neutral
2. Quite uncomfortable
1. Very uncomfortable

The comfort of holding the pen whilst injecting	1	Go to Q5
Pushing the dose setting knob when injecting	2	Go to Q5
The soft click sound when injecting	3	Go to Q5
Pressure required from thumb when injecting	4	Go to Q5
The zero reading on the dosing scale following injection, indicating the full dose has been injected	5	Go to Q5
The control of the pen whilst injecting	6	Go to Q5

5. Please rate the new pen on each of the following attributes. (Ask all, single code per statement.)

5. Very high
4. Quite high
3. Neither low nor high
2. Quite low
1. Very low

Range of possible doses which can be prescribed (due to permitted dose increments)	1	Go to Q6
Ease for the nurse to learn how to use	2	Go to Q6
Ease for the nurse to teach patients how to use	3	Go to Q6
Your confidence that the patient understands how to remove any large air bubbles before use	4	Go to Q6
Ease for patient to fit needle onto pen	5	Go to Q6
Ease for patient to read the dosing scale	6	Go to Q6
Ease for patients to read the gradations on the clear reservoir holder	7	Go to Q6
Your confidence in the patient's ability to calculate and set the correct dose	8	Go to Q6

(Continued)

*The term "new pen" refers to the "redesigned follitropin alfa pen."

(Continued)

Ease for patient to push the dose setting knob when injecting	9	Go to Q6
Ease for patient to administer the injection	10	Go to Q6
Ease for patient to check that the full dose has been injected	11	Go to Q6
Your confidence that the full dose has been injected when patients self-administer at home	12	Go to Q6
Ease of removing and discarding the needle	13	Go to Q6
Your confidence that the patient is able to correctly calculate any top-up dose needed after injection	14	Go to Q6
Patient's satisfaction with the number of steps involved in preparing/giving the injection	15	Go to Q6
Your confidence that the patient understands how to use the pen properly	16	Go to Q6

6. Please rank the importance of the following attributes if recommending any injection device for gonadotropins to a fellow fertility nurse like yourself. (Ask all, provide a ranking ladder that respondent can drag and drop each attribute onto.)

Range of possible doses which can be prescribed (due to permitted dose increments)	1	Go to Q7
Ease for the nurse to learn how to use	2	Go to Q7
Ease for the nurse to teach patients how to use	3	Go to Q7
Your confidence that the patient understands how to remove any large air bubbles before use	4	Go to Q7
Ease for patient to fit needle onto pen	5	Go to Q7
Ease for patient to read the dosing scale	6	Go to Q7
Ease for patients to read the gradations on the clear reservoir holder	7	Go to Q7
Your confidence in the patient's ability to calculate and set the correct dose	8	Go to Q7
Ease for patient to push the dose setting knob when injecting	9	Go to Q7
Ease for patient to administer the injection	10	Go to Q7
Ease for patient to check that the full dose has been injected	11	Go to Q7
Your confidence that the full dose has been injected when patients self-administer at home	12	Go to Q7
Ease of removing and discarding the needle	13	Go to Q7
Your confidence that the patient is able to correctly calculate any top-up dose needed after injection	14	Go to Q7
Patient's satisfaction with the number of steps involved in preparing/giving the injection	15	Go to Q7
Your confidence that the patient understands how to use the device properly	16	Go to Q7

7. (Ask all, single code per statement.) Overall, how easy do you think it will be to teach patients how to use the new pen compared with:

5. Much easier to teach
4. Somewhat easier to teach
3. No better nor worse
2. Somewhat harder to teach
1. Much harder to teach

The current GONAL-f® pen?	1	Go to Q8	Only show this option if code
The current Puregon® pen?	2	Go to Q8	
Current syringes and vials?	3	Go to Q8	

8. How confident are you in teaching patients how to use the new pen after your training? (Ask all, single code only.)

5. Very confident
4. Quite confident
3. Neutral
2. Not very confident
1. Not at all confident

9. Which of the following aspects of the new pen, if any, do you see as advantages over current injection methods. Please tick all that apply. (Ask all, multicode.)

Transparent (clear) reservoir holder	1	Go to Q10
Gradations on the reservoir holder	2	Go to Q10
Needle attachment and removal	3	Go to Q10
Flexibility to readjust dose (if set dose is too high/low)	4	Go to Q10
Single press release for injection	5	Go to Q10
The soft click sound when injecting	6	Go to Q10
Pressure required from thumb when injecting	7	Go to Q10
Visibility of dosing window	8	Go to Q10
Ability to see any top-up dose needed after injection	9	Go to Q10
The zero reading on the dosing scale following injection, indicating the full dose has been injected	10	Go to Q10
Additional confidence that the full dose has been injected compared with current pens/syringes	11	Go to Q10

Section 3

Evaluation of the pen and how easy it was to train patients to use it – to be completed after the nurses train the patients to use the pen. (Section divider, introduction to be shown to respondent.) Now, you will have the opportunity to demonstrate and train some patients on how to use the new pen. Please click NEXT after you have trained the patients on how to use the new pen.

10. On a scale of 1–5, how easy has it been to teach patients to perform each of the following functions of the new pen? (Ask all, single code per statement.)

5. Very easy
4. Somewhat easy
3. Neither easy nor difficult
2. Somewhat difficult
1. Very difficult

How to remove any large air bubbles before use	1	Go to Q11
How to fit needle on pen	2	Go to Q11
How to read the gradations on the clear reservoir holder	3	Go to Q11
How to read the dosing scale	4	Go to Q11
How to calculate and set the dose	5	Go to Q11
How to push the dose setting knob when injecting	6	Go to Q11
How to calculate/administer a top-up dose when needed	7	Go to Q11
How to remove and discard the needle	8	Go to Q11
Overall process of self-administering a dose from start to finish	9	Go to Q11
Others (please state)	10	Go to Q11

11. Based on your experience with the new pen today, to what extent would you be likely to recommend it to a fellow fertility nurse like yourself? (Ask all, single code only.)

5. Very likely
4. Likely
3. Neither likely nor unlikely
2. Unlikely
1. Very unlikely

12. Now that you have trained some patients to use the new pen, to what extent do you agree with the following statements? (Ask Q12 if code 01 and/or code 05 (pens) coded at Q1B.)

5. Strongly agree
4. Somewhat agree

Appendix 2

Patient questionnaire. Approximate duration 15 minutes.

Section 1

Evaluation of previously used devices.

1A. Are you left or right-handed? (Ask all, single code only.)

Left-handed	1	Go to Q1B
Right-handed	2	Go to Q1B
Both	3	Go to Q1B

1B. Do you currently use, or have you ever used in the past, a self-administered injectable medication for fertility treatment? (Ask all, single code only.)

Yes	1	Go to Q1C	(Code as “injection experienced”)
No	2	Go to Q2	(Code as “injection naive”)

1C. Which of the following fertility treatments have you used in the past six months? Please tick all which apply. (Ask all, multicode allowed.)

GONAL-f® pen (follitropin alfa)	1	Go to Q1D
GONAL-f® syringe/vial (follitropin alfa)	2	Go to Q1D
Luveris® syringe/vial (lutropin alfa)	3	Go to Q1D
Ovitrelle® prefilled syringe (choriogonadotropin alfa)	4	Go to Q1D
Puregon® pen (follitropin beta)	5	Go to Q1D
Puregon® syringe/vial (follitropin beta)	6	Go to Q1D
Pregnyl® syringe/vial (chorionic gonadotropin)	7	Go to Q1D
Bravelle® syringe/vial (urofollitropin)	8	Go to Q1D
Menopur® syringe/vial (menotropin)	9	Go to Q1D
Merional® syringe/vial (menotropin)	10	Go to Q1D
Fostimon® syringe/vial (urofollitropin)	11	Go to Q1D
Choragon® syringe/vial (chorionic gonadotropin)	12	Go to Q1D
Others (write in)	13	Go to Q1D

1D. Which of the following injection methods do you currently use to inject your fertility medication? Please tick all which apply. (Ask all, multicode allowed.)

GONAL-f® pen	1	Go to Q2
Puregon® pen	2	Go to Q2
Syringe and vial	3	Go to Q2
Prefilled syringe	4	Go to Q2

Section 2

Evaluation of new pen* and how easy it is to learn to use. (To be completed after the patient has received the demonstration/training from the nurse and has had a chance to try the pen themselves.) All injection-experienced and injection-naive patients to answer all questions in this section. (Section divider, introduction to be shown to respondent.) Now, you will be shown a demonstration on how to use the new pen by a qualified fertility nurse. You will have the opportunity to try the new pen after the demonstration. Please click NEXT after you had a chance to try the new pen after the demonstration.

*The term “new pen” refers to the “redesigned follitropin alfa pen.”

2. Which of the following aspects of the new pen did you find easy to learn? Please select all which apply. (Ask all, multicode.)

The whole process was easy to follow and I had no trouble learning how to use the new pen	1	Go to Q3
Learning how to fit the needle onto the pen	2	Go to Q3
Learning how to remove any large air bubbles before use	3	Go to Q3
Learning how to set the dose	4	Go to Q3
Learning how to read the dosing scale in the dose window on the side of the pen	5	Go to Q3
Learning how to read the gradations on the clear reservoir holder	6	Go to Q3
Learning how to push the dose setting knob when injecting	7	Go to Q3
Learning how to check the full dose has been delivered	8	Go to Q3
Learning how to calculate/administer a top-up dose when needed	9	Go to Q3
Learning how to remove and discard the needle	10	Go to Q3
Others (write in)	11	Go to Q3

3. How comfortable are you with the following? (Ask all, single code per statement.) For each attribute please indicate whether you are:

5. Very comfortable
4. Quite comfortable
3. Neither comfortable nor uncomfortable
2. Quite uncomfortable
1. Very uncomfortable

The comfort of holding the pen whilst injecting	1	Go to Q4
Pushing the dose setting knob when injecting	2	Go to Q4
The soft click sound when injecting	3	Go to Q4
Pressure required from thumb when injecting	4	Go to Q4
The zero reading on the dosing scale following injection, indicating the full dose has been injected	5	Go to Q4
The control of the pen whilst injecting	6	Go to Q4

4. Which of the following aspects, if any, do you see as advantages when learning how to use the new pen? Please tick all that apply. (Ask all, multicode.)

Transparent (clear) reservoir holder	1	Go to Q5
Gradations on the clear reservoir holder	2	Go to Q5
Needle attachment and removal	3	Go to Q5
Flexibility to readjust dose (if set dose is too high/low)	4	Go to Q5
Single press release for injection	5	Go to Q5
Soft click sound when injecting	6	Go to Q5
Pressure required from thumb when injecting	7	Go to Q5
Visibility of dosing window	8	Go to Q5
Ability to view any top-up dose needed after injection	9	Go to Q5
The zero reading on the dosing scale following injection, indicating the full dose has been injected	10	Go to Q5
Additional confidence that the full dose has been injected, compared with your current method of injection	11	Go to Q5

Section 3

Comparison of new pen with currently used pen/syringe. Only ask for those coded 01 at Q1B. Only injection-experienced patients to answer all questions in this section.

5. The following is a list of attributes relating to the new pen and the injection pen, syringe/vial or prefilled syringe which you currently use. (Allow comparison between new pen and each device coded at Q1D, show all devices on screen to allow direct comparison.) Need to add option of prefilled syringe to link. Please rate their performance on a scale of 1–5 where:

1. Very low
2. Quite low
3. Neither low nor high
4. High
5. Very high

Easy to learn how to use	1	Go to Q6
Easy to learn how to remove any large air bubbles before use	2	Go to Q6
Easy to learn how to fit the needle onto the pen	3	Go to Q6
Easy to learn how to read the dosing scale	4	Go to Q6
Easy to learn how to read the gradations on the clear reservoir holder	5	Go to Q6 (Ask for new pen only)
Easy to learn how to calculate and set the dose	6	Go to Q6
Flexibility to readjust dose (if set dose is too high/low)	7	Go to Q6
Easy to learn how to push the dose setting knob when injecting	8	Go to Q6
Easy to learn how to administer the injection	9	Go to Q6
Easy to check that the full dose has been injected	10	Go to Q6
Easy to remove and discard the needle	11	Go to Q6
Easy to calculate any top-up dose needed after injection	12	Go to Q6
Number of steps involved in preparing/giving the injection	13	Go to Q6

6. Now that you are trained and have tried using the new pen, to what extent do you agree with the following statements? (Single code per statement.)

5. Strongly agree
4. Somewhat agree
3. Neither agree nor disagree
2. Somewhat disagree
1. Strongly disagree

It was easier to learn how to use this new pen compared with my current injection method	1	Go to Q7
It is easier to remove large air bubbles from the new pen compared with my current injection method	2	Go to Q7
It is easier to read the dosing scale on this new pen compared with my current injection method	3	Go to Q7
It takes less time for me to prepare the new pen for my injection compared to my current injection method	4	Go to Q7
There are fewer steps involved in preparing/giving the injection with the new pen compared with my current injection method	5	Go to Q7
There is less room for error in setting/adjusting the correct dose with this new pen compared with my current injection method	6	Go to Q7
I am more confident I will be able to administer the correct dose using this new pen compared with my current injection method	7	Go to Q7
I am more confident I will be able to calculate any top-up dose needed with this new pen, compared with my current injection method	8	Go to Q7
I would be more confident in using this new pen than my current injection method	9	Go to Q7
I am confident I can self-administer using this new pen without any further help from my nurse in the future	10	Go to Q7
There is less wastage of medication compared with my current injection method as I will use all the medication in the pen before starting a new pen	11	Go to Q7

