

A MULTI-DOSE, PREFILLED PEN INJECTOR FOR THE ADMINISTRATION OF FOLLITROPIN ALFA WITH A DOSE INCREMENT OF 5 IU

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Problem statement: Patients undergoing treatment for infertility are often prescribed subcutaneous injections of follicle-stimulating hormone (FSH), which is to be administered with precise and convenient pen injectors. Nomograms for the precise calculation of the FSH starting dose were developed based on factors such as antral follicle count and serum anti-mullerian hormone. New pen injectors are needed to allow for the accurate self-administration of FSH in a wide range of starting doses with a dose increment lower than that of existing injectors. The new follitropin alfa pen injector is designed with a dose range of 0 to 300 international units (IU) and a dose increment of 5 IU.

Methods: In this study, 48 pen injectors, three dose dial settings - minimum (5 IU), midrange (150 IU), and maximum (300 IU) – were tested in compliance with ISO 11608-1:2014(E) for each pen injector.

Study results:

1. Testing the 48 pen injectors produced the following results which are consistent with the ISO 11608-1:2014(E) requirements of dose accuracy:

Target dose, IU	Target dose, ml	Mean value of the dispensed volume, ml	SD, ml	Coefficient Ktar (95% 2-sided CI, p=0.975)	Coefficient Kact	Ktar < Kact
5	0,0083	0,0081	± 0,0006	2.736	9,94	passed
150	0,2499	0,2478	± 0,0030		3,45	passed
300	0,4990	0,4941	± 0,0062		3,24	passed

2. The described pen injector was used in the clinical study of the equivalence between two recombinant follitropins in women undergoing IVF/ICSI (NCT 03088137) with the following primary end-point results in terms of aspirated oocytes:

Population	Primapur® group (with a new pen-injector), N=55 Mean±SD	Gonal-f® group, N=55 Mean±SD	Mean difference Mean±SD	P-value of equivalence	95% 2-sided CI of mean difference	
					Lower limit	Upper limit
ITT (n=110)	12,16±7,28	11,62±6,29	0,546±1,297	0,002	-2,026	3,116

Conclusion: The personalized approach to the follitropin alfa starting dose selection (based on individually-estimated physiological parameters) and the minimum dose adjustment increment of 5 IU may help achieve an accurate adjustment of the required dose of follitropin alfa for ovarian hyperstimulation and ovulation induction protocols.

