Pfizer Canada Inc.
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Pointe-Claire / Dorval, Québec H9R 4V2

October 1st, 2010

Direct Healthcare Professional Communication: Synarel Nasal Spray and Cracked Pump

Dear Healthcare Professional:

Pfizer Canada Inc. would like to inform you of an issue that has arisen during the manufacture of Synarel (nafarelin acetate) and a resulting interruption in supply.

Summary

Synarel (nafarelin acetate) is an agonistic analogue of the gonadotropin releasing hormone (GnRH) which is used intranasally for hormonal management of endometriosis, including pain relief and reduction of endometriotic lesions.

During the manufacture of Synarel, Pfizer found four (4) pumps with the stem fit of the actuator head cracked. On a visual inspection of all the remaining pumps from these batches at the manufacturing site the defect rate was 0.3%. The batch numbers of the affected product distributed by Pfizer in Canada are Lot C091538 and Lot C100762. Pfizer has stopped distribution of Synarel pending resolution of this issue. This has lead to an out of stock situation.

On testing the defective pump delivered approximately a 30% greater mean dose. The potential for this additional dose with the defective pumps to have a clinically meaningful effect in a patient is unlikely.

Further information regarding safety

In Canada, the approved recommended daily dose is 400 µg, achieved by one spray (200 µg of nafarelin free base) into one nostril in the morning and one spray into the other nostril in the evening. For patients with persistent regular menstruation after 2 months of treatment, the dose of Synarel may be increased to 800 µg daily. Synarel, when used for long term treatment in adults, induces a menopause-like state. The estrogen levels while on long term treatment are comparable to those seen in menopause. The bone mineral density decline while on 400 µg and 800 µg of Synarel is very similar.

In experimental animals, a single subcutaneous administration of up to 60 times the recommended human dose (on a µg/kg basis, not adjusted for bioavailability) had no adverse effects. Bioavailability of the intranasal dose averages 2.8% (range 1.2% to 5.6%). There is no clinical experience with overdosage of nafarelin acetate.

Based on this information Pfizer believes that the potential for this additional dose with the defective pumps to have a clinically meaningful effect in a patient is unlikely.

Recommendations to Healthcare Professionals
Pfizer Canada recommends that no new patients are prescribed Synarel and that no prescriptions are filled until new unaffected stock is available.

Physicians who are using Synarel should discuss potential treatment options with their patients.

Re-supply of Synarel nasal spray by Pfizer Canada has been estimated to be no earlier than December 2010.

Reporting
As with all medical products, healthcare professionals are strongly encouraged to report any suspected adverse reaction that are associated with the use of Synarel to either Pfizer Canada Inc. by phone toll free (1-800-463-6001) or Canada Vigilance Program by phone toll-free (1-866-234-2345) or fax toll-free (1-866-678-6789).

Further information
If you have a medical inquiry regarding Synarel, please contact Pfizer Canada Inc. Medical Information at 1-800-463-6001.

Sincerely,

Bernard Prigent, MD, MBA
Vice-President and Medical Director

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