2 SYNOPSIS

Name of Sponsor/Company: Name of Finished Product: Name of Active Ingredient(s):	Individual Study Table Referring to Part of the Dossier Volume: Page:	*(For national authority use only)*
Title of study: Diphereline Post Marketing Surveillance Study Study number: A-38-52014-118		
Investigators: PPD		
Study centre(s): 12 centers in Korea		
Publication (reference): none		
Studied period (years): one year Date of first enrolment: 01 December 2004 Date of last completed: 28 December 2005		Phase of development: IV
Objectives: The objective of the study was to assess the safety and efficacy of Diphereline 3.75 mg in gynaecology use such as Endometriosis and Fibromyoma		
Methodology: This is an open, non-comparative, multi-center, phase IV study.		
Number of patients (planned and analysed): Planned: 300 patients Enrolled: 245		
Diagnosis and criteria for inclusion: Inclusion criteria: • Patients who suffer from Endometriosis or Fibromyoma • Patients who need GnRH agonist after laparoscopy diagnosis of Endometriosis • Patients who need GnRH agonist to facilitate or modify a Fibromyoma related surgical technique		

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- Fibromyoma patients with associated anemia (hemoglobin less than or equal to 8 g/dL)

Exclusion criteria:

- Pregnant or breast-feeding women
- Hypersensitivity to GnRH analogues or to one of its excipients
- Patients who were recently (< 6 months) administered triptorelin or another GnRH analogue

Test product, dose and mode of administration:

Diphereline 3.75mg (Triptorelin actate), injection for intramuscular administration

Duration of treatment:

Diphereline 3.75mg was administrated strictly intramuscular every 4 weeks. The maximum duration of treatment was 6 months

Criteria for evaluation:

<u>Effectiveness</u>:

Efficacy of treatment was to be assessed according to the following criteria:

- Physical examination, and patients' symptom reports.
- Hormonal responses, in particular the levels of estradiol, LH, and FSH
- If necessary, vaginal ultrasonography or laparoscopy

The overall evaluation was classified according to the following criteria:

1= notably improved

2= improved

3= not changed

4= little worsened

5= worsened

6= not available (record to be taken to describe why an evaluation was not available)

<u>Safety</u>:

All AEs, regardless of drug relationship, were to be recorded for all patients whom investigators assessed at least once after the administration of Diphereline 3.75 mg.

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Statistical methods:

Effectiveness

An overall evaluation for efficacy was performed. The subjects included in the overall evaluation analysis were all patients who received at least one dose of study medication. The proportions of patients with notably improved, improved, not changed, little worsened, worsened, and not available conditions were determined. All proportions were presented with a corresponding 95% confidence interval.

Safety

Safety was evaluated in relation to the number of AE events and the number of cases with abnormal results in relevant laboratory tests.

Summary - conclusions:

The study included 245 valid cases from 12 investigational sites. Data that were duplicated or that could not be confirmed by the investigators were excluded.

No protocol deviations were reported.

Effectiveness results:

In the present study, treatment administration was the same in all patients, regardless of the disease. The efficacy of the study drug was judged using subjective clinical measures, because GnRH agonists are usually used to treat symptomatic disease. Patients were asked to score their clinical symptoms before and after the injection and an overall evaluation of the changes observed during the treatment was made.

227 / 232 patients (97.8%) were improved or notably improved after at least 1 dose of Diphereline 3.75 mg. None of the patients' symptoms worsened during the study. Symptoms were unchanged in only 1 patient.

Safety results:

No AEs were reported during the study period.

Conclusion:

In conclusion, the use of Diphereline 3.75 mg appeared to have beneficial effects and to be well tolerated in patients suffering from endometriosis and uterine fibromyomas.

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<tr><td colspan="3">Diphereline 3.75 mg can be considered as a treatment to reduce the severity of disease-associated symptoms while minimising the incidence of hypoestrogenic symptoms and eventually improving the Quality of life in these patients.

Date of report: 15 December 2014</td></tr>
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