SYNOPSIS STUDY EDI09/01

SPONSOR:	OM Pharma SA, 22, rue du Bois-du-Lan, P.O. Box 88, 1217 Meyrin 2/Geneva, Switzerland
TITLE OF THE STUDY:	**A Multicentre, Double-blind, Placebo-Controlled, Parallel Group Study of the Effect of Oral Etamsylate (Dicynone®) in Patients with Menorrhagia (HMB)**
STUDY REFERENCE:	EDI09/01
STUDY DIRECTOR:	Professor Anne Gompel; Paris, France
INDICATION:	Heavy Menstrual Bleedings (HMB) with regular menstrual cycles
STUDY PHASE:	III
OBJECTIVE:	To assess the effect of etamsylate when compared with placebo on the reduction of menstrual blood loss in patients with HMB
STUDY DESIGN:	Multicentre, double-blind, placebo-controlled, parallel group, randomised clinical study
STUDY CENTRES:	20 to 30 sites in Bulgaria, Czech Republic, France and Portugal
NUMBER OF PATIENTS:	N = 230 including dropouts
MAIN INCLUSION CRITERIA:	Females aged ≥ 18 to ≤ 50, with excessive menstrual blood loss of ≥ 80 to ≤ 250 mL per menstruation and regular menstrual cycle
MAIN EXCLUSION CRITERIA:	Patients with systemic pathology which can influence haemostasis, patients with complex hyperplasia with or w/o atypia, endometrial carcinoma, severe adenomyosis or with submucous fibroids, patients with uterine cavity > 10 weeks of pregnancy size, patients pregnant or lactating and unreliable patients
TREATMENT	Patients will be treated with 1 capsule three times a day. Treatment lasts 10 days and starts 5 days before the expected onset of menses. Patients will be administered study medication for 3 menstrual cycles. Patients will be randomised after cycle 0 provided that menstrual blood loss is ≥ 80 to ≤ 250mL.
TIME SCHEDULE:	Study duration per patient: 6 months

	• Visit 1 (Screening) - Day -21 to Day -7 of Cycle S1 • Visit 2 (Screening) - 2nd to 3rd week of Cycle S1 (Day+8 to Day +21) • Visit 3 - 2nd week of Cycle S2 (Day +8 to Day +14) • Visit 4 - Day -10 to Day -7 of Cycle 1 • Visit 5 - 3rd week of Cycle1 (Day +14 to Day +21) • Visit 6 - 3rd week of Cycle 2 (Day +14 to Day +21) • Visit 7 - 2nd week of Cycle 3 (Day +8 to Day +14)
PRIMARY EFFICACY VARIABLE:	Menstrual blood loss (MBL) during the 3rd treatment cycle, measured by the alkaline haematin method
SECONDARY EFFICACY VARIABLES:	• Menstrual blood loss during treatment cycles 1 and 2, measured by the alkaline haematin method. • Number of days of menstrual flow for the 3 cycles • Blood haemoglobin, S-ferritin, TSAT • Type and duration of prescribed concomitant treatment(s) • Global assessment of efficacy and quality of life by patient and investigator
SAFETY VARIABLES:	• Physical examination • Vital signs • Safety laboratory • Adverse events and serious adverse events
STATISTICAL ANALYSIS:	A multiple test procedure with a-priori ordered hypotheses will be carried out for the primary variable and selected secondary variables (closed test principle): • The experiment wise error rate is stipulated to α = 5%. • The first null hypothesis will be tested by means of a two-sided t-test (level of significance α = 5%). If this leads to a significant result, then: • The three elementary hypotheses will be tested by means of a t-test (2a) and Mann-Whitney-Wilcoxon tests (2b and 2c) at the same level of significance (closed test procedure). This procedure controls the experiment wise error rate. Furthermore, the mean treatment differences and corresponding 95% confidence intervals will be estimated.
RESULTS	This study was discontinued prematurely on March 31st 2011 before any subject received their first dose owing to difficulties in subject accrual following changes requested by Competent Authorities and Ethics Review Boards. Following the numerous requests by competent authorities to modify the inclusion and exclusion criteria of the study (e.g. removal of patients wearing an intrauterine device) and reducing the eligible population, the feasibility of the study was re-evaluated as well as the strategy concerning

	the product, and made the decision to stop this study prematurely. Only one patient in France was randomized on 28/03/2011 but she did not take the treatment and left the study because her menstrual blood loss was less than 80 ml. For the other countries involved, Portugal, the Czech Republic and Bulgaria, the study had not already started.