Objective: The aim of this study was to investigate the effect of a combination of vaginal gestrinone in Pentravan™ with oral pinus pinaster extract and resveratrol on the pain scores of patients with deep endometriosis. Patient and Methods: Twenty-five patients with deep endometriosis, ovarian endometriotic cysts and severe pain refractory to previous hormonal treatment were enrolled. Pain scores were evaluated at baseline and 1, 2 and 6 months after the beginning of treatment using a visual analogic scale. The patients were treated with a combination of 5 mg of vaginal gestrinone in Pentravan™ (Fagron, the Netherlands) three times a week and 100 mg of oral pinus pinaster extract (Fagron) and 30 mg of resveratrol (Fagron) daily. Vaginal ultrasonography and blood analysis were performed at baseline and after 2 months of treatment. Results: Mean pain score was 9 prior to treatment, reducing significantly to 1 (p=0.0001) in the second month of treatment. After six months, all patients were pain-free. Amenorrhea rates were 80% in the second month, reaching 100% during the remainder of the treatment. Uterine and ovarian cyst volume decreased from 200 to 140 cm³ and from 35 to 15 cm³ respectively after the second month (p=0.04). There were no statistically significant changes in total cholesterol, baseline FSH, LH and estradiol levels, although ovulation was suppressed in all patients. There was a small but significant decrease in HDL-cholesterol, triglycerides and total testosterone. Liver enzymes were not significantly affected. SHBG levels decreased significantly from 100 to 10 nmol/l (p=0.04). Side effects such as leg pain, headaches and weight gain occurred in less than 20% of cases. Conclusion: The combination of vaginal gestrinone in Pentravan™ with oral pinus pinaster extract and resveratrol is very effective for the treatment of endometriosis-related pain.