Case Details

Case 1 (Intracranial venous sinus thrombosis)

Patient		Daily dose Duration	Adverse reactions	
Gender /Age	Reason for use	1 tablet	Clinical course and Treatment	Outcome
Female 20s	Dysmenorrhea, Acne, irregular menstruation	7 days	BMI, 17.3; Non-smoker; Family history, Grandfather Cerebral infarction; No prior medication; Nulliparity 10 days before prescription The patient visited hospital A for the first time. Hormone test showed normal level. Day of prescription YAZ was prescribed at hospital A. Day 1 of treatment Treatment initiated(1 tablet/day). Day 2 of treatment Headache occurred. Day 6 of prescription* The patient visited an internal medicine department in Hospital B due to physical deconditioning. She complained of headache, queasy, and palpitations from the morning. Blood pressure was 105/68. Electrocardiogram and blood test showed normal. Anaemia was serious. Intravenous drip was administered. She was treated with Domperidone, Rebamipide, and Biodiastase. No convulsion in lower extremities. No paralysis. Day 9 after prescription The patient visited an internal medicine department in hospital B again. She had headache. Blood pressure was 103/70. No abnormal findings. Clotiazepam was prescribed to be taken as needed. She was advised to visit gynecologist because of serious anaemia. The patient visited hospital A again. She complained of feeling sick. She had queasy and impaired appetite. Vital signs were normal. Urine ketone body test showed negative. She complained of headache after fluid replacement was performed, therefore, the prescriber advised her to see a cerebral surgeon. (Total dose of YAZ was 7 tablets. Administration was immediately discontinued.) The patient visited a cerebral surgery department in Hospital C. At the time of visiting, no obvious symptoms such as paralysis were seen. The patient made an appointment for examination and went back home. She vomited and had difficulty in walking. Day 10 after prescription Difficulty in movement occurred. Day 11 after prescription In the morning, mother of the patient found her incontinent on the bed. The patient was transferred to hospital D. CT and MRI were conducted. She was immediately referred to hospital E. On the way to hospital E, level of consciousness was JSC III-300 and convulsion was observed. Deep cerebral venous sinus thrombosis was diagnosed with CT findings. She was immediately admitted to hospital E on the day, and started to receive treatment with heparin. Day 12 after prescription Hydrocephalus was aggravated and respiratory failure occurred. Endotracheal intubation was performed. Antiphospholipid antibody: (-). ANCA (Anti-Neutrophil Cytoplasmic Antibody): (-). Day 13 after prescription The Patient passed away. An autopsy was conducted on the same day. No marked traumatic injury was observed. There were no findings suggesting myocardial infarction or congenital anomaly.	Death
Medical History	Concomitant Disease			
None	Anemia			
Concomitant drug: clotiazepam				

* Clinical course and Treatment were described with “Day after prescription” instead of “Day of treatment” because Day of treatment was unknown.

Case 2 (Pulmonary artery embolism)

Patient		Daily dose Duration	Adverse reactions	
Gender /Age	Reason for use	1 tablet 526 days	Clinical course and Treatment	Outcome
Female late teen	Dysmenorrhea, Endometriosis		BMI, 22.7; Non-smoker; No Family history. No thrombus-related factor was identified with a medical interview (no measurement of fibrinolytic or coagulation system marker), no prior medication, nulliparity Day 1 of treatment YAZ was prescribed at a hospital and treatment initiated (1 tablet/day) for dysmenorrhea and endometriosis. Loxoprofen sodium hydrate and Rebamipide were prescribed (7days). Day 499 of treatment: Last YAZ (2 sheets: 56T) was prescribed at a hospital. Day 526 of treatment: After going out, she came back to her lodging at around 21:00. The contact was lost. Day 529 of treatment A janitor, who tried to confirm the safety, detected her lying in the room (the same clothes when she went out on Day 526). YAZ (36T) was left. Autopsy result Estimated date of death: Day 526 Cause of death: pulmonary artery embolism (Thrombosis in pulmonary artery trunk was observed. No macroscopic thrombosis was found in lower extremities.) Concomitant medications: None Medical history: None Smoking: None No alcohol was detected. No malformation and traumatic injury were observed. Although she had been dead for 5 days or more, no remarkable finding was observed in blood test and Postmortem CT.	Death
Medical History	Concomitant Disease			
None	None			
Concomitant drug: loxoprofen sodium hydrate, Rebamipide (only seven days from prescription)				

Case 3 (Pulmonary embolism, Deep vein thrombosis)

Patient		Daily dose Duration	Adverse reactions	
Gender /Age	Reason for use	1 tablet	Clinical course and Treatment	Outcome
Female 40s	Dysmenorrhea	Ca. 1 year	BMI, 23.6; No Family history; Non-smoker; Para 2. No thrombus-related factor and history of thrombosis were identified with a medical interview (no measurement of fibrinolytic or coagulation system marker), No prior medication. Cervical cytology: NILM (Negative for intra epithelial lesion or malignancy). A myoma 4.5 cm in size was present. Prescriber proposed the Patient about treatment of Yaz in case she has no anaemia by uterine myoma. Diclofenac sodium was prescribed. Day 1 of Prescription* No anaemia was found, then Yaz was prescribed for dysmenorrhea (1 tablet/day). Diclofenac sodium and teprenone were prescribed. Day 46 after prescription 3 sheets of Yaz were prescribed as no complaint was made by the patient about adverse event. Day 126 after prescription 3 sheets of Yaz, diclofenac sodium and teprenone were prescribed. Day 207 after prescription The patient complained of right leg cramps, but no tenderness when her leg was grasped by hand. Transvaginal ultrasound was performed as follow-up examination. The size of myoma was slightly increased to about 7 cm. Prescriber informed her that it is advisable to receive a treatment with surgery to improve the symptoms, but she was not so keen to have it. Yaz (3 sheets), diclofenac sodium and teprenone were prescribed. Solifenacin succinate was prescribed for pollakiuria. Day 222 after prescription Solifenacin succinate was prescribed. Day 254 after prescription Solifenacin succinate was prescribed. Day 294 after prescription No increase of myoma was seen with transvaginal ultrasound. 3 sheets of Yaz were prescribed. 2 or 3 weeks before the day of withdrawal The patient complained pain and swelling of her right leg and saw an orthopedist. Day 369 after prescription (Withdrawal date) Difficulty of breathing developed and the patient was transferred to an emergency department. Depressed level of consciousness (Japan Coma Scale: I-3), Tachypnoea and difficulty of breathing were observed. Blood pressure, 94/74; HR, 126; SpO2, 100% under giving oxygen. When the patient was transferred into the ambulance, kinking of upper limbs, extension of lower limbs and ankylosis were observed. Cardio-respiratory arrest developed in the ambulance. After the ambulance reached the hospital, heart beating restarted. After this, 2 times of cardiac arrest occurred and she was resuscitated each time, but consciousness did not come back. Although body temperature decreased to 34 C-degrees by therapeutic hypothermia for protection of brain, bleeding developed remarkablely so the therapy was stopped. RCC: 7 units and FFP: 8 units were transfused. Day 1 of withdrawal RCC: 3 units were transfused. Contrast-enhanced CT revealed pulmonary embolism and deep vein thrombosis as well as pleural effusion. Treatment with heparin and warfarin was started. Day 6 of withdrawal Renal failure was gradually advanced. Urine output decreased was observed. Treatment with frusemide was made. Day 7 of withdrawal Continuous hemodiafiltration was initiated. Drainage of bilateral pleural effusion was made. Day 9 of withdrawal Pupils dilated and Blood pressure rapidly increased appeared. Intracranial pressure increased caused by brain ischemia were considered and treatment with concentrated glycerin/fructose was made. Day 16 of withdrawal The patient was in a condition which can be judged as brain death	Death
Medical History	Concomitant Disease			
None	Uterine myoma			

			without any discrepancy. Day 19 of withdrawal Cardiac arrest and respiratory arrest were observed. Mydriasis and pupillary light reflex lost were seen. It was confirmed that the patient passed away.	
Concomitant drug: diclofenac sodium, teprenone, solifenacin succinate				

* Clinical course and Treatment were described with “Day after prescription” instead of “Day of treatment” because Day of treatment was unknown.