

- Fatal cases where a causal relationship with XEPLION is unknown have been reported during the period of early phase pharmacovigilance.

As of April 15th 2014, 14 fatal cases have been granted permission to disclose by the reporting physicians as follows.

No	ADR (MedDRA PT)	Age	Gender	Pre-administration of Paliperidone or Risperidone/Dose	XEPLION Dose (At first injection)	Latency	Medical history	Concomitant antipsychotic(s)
1	<u>Death</u>	50s	F	Risperidone sustained-release suspension for injection/50mg	100 mg	3 days	Constipation	Aripiprazole tablet, Quetiapine fumarate tablet
2	<u>Pulmonary embolism</u> <u>Right ventricular failure</u> Rhabdomyolysis Psychiatric symptom	50s	M	Risperidone sustained-release suspension for injection/50mg	150 mg	41 days	Hyperuricaemia, Hepatic steatosis	Olanzapine tablet
3	<u>Death</u>	60s	M	Risperidone sustained-release suspension for injection/25mg	25 mg	14 days	Unknown	Quetiapine fumarate tablet
4	<u>Death</u>	50s	M	Risperidone sustained-release suspension for injection/25mg	75 mg	40 days	Hepatitis C, Hypertension, Abnormal hepatic function	Zotepine tablet
5	<u>Acute myocardial infarction</u>	30s	M	Risperidone oral solution /4mg	150 mg	4 days	Hyperuricaemia, Obesity	Aripiprazole tablet, Olanzapine tablet
6	<u>Death</u> , Palpitations Dyspnoea, Dysarthria	50s	M	None	50 mg	13 days	Hyperglycaemia, Asthma, Back pain	Olanzapine tablet
7	<u>Hypothermia</u> <u>Stress fracture</u>	40s	M	Risperidone sustained-release suspension for injection/25mg	50 mg	42 days	Hyperuricaemia	Risperidone tablet
8	<u>Death</u>	30s	M	None	150 mg	14 days	Mild mental retardation	Haloperidol decanoate injection, Olanzapine tablet, Blonanserin tablet
9	<u>Myocardial infarction</u>	60s	F	Risperidone sustained-release suspension for injection/50mg	150 mg	34 days	Hypotension, Arrhythmia	Olanzapine tablet, Quetiapine fumarate tablet, Levomepromazine maleate tablet
10	<u>Asphyxia</u> , Vomiting Cerebrovascular accident	50s	F	None	150 mg	19 days	Insomnia, Restlessness, Diabetes mellitus	Risperidone oral solution
11	<u>Death</u>	50s	M	Risperidone tablet/9mg, Paliperidone extended-release tablet/12mg (continued after start of XEPLION)	150 mg	43 days	Hypertension, Obesity, Diabetes mellitus, Extrapyramidal disorder	Paliperidone extended-release tablet, Risperidone tablet
12	<u>Death</u>	40s	M	Risperidone (Unknown formulation)	150 mg	77 days	Aspiration pneumonia	None
13	<u>Multi-organ failure</u> Abnormal hepatic function	50s	F	None	150 mg	107 days	Pneumonia, Ileus	None
14	<u>Pneumonia</u>	70s	M	Risperidone oral solution/2mg (as needed basis)	150 mg	36 days	None	Risperidone oral solution, Haloperidol injection, Haloperidol oral solution, Olanzapine tablet

Underline: events leading to outcome of death

■ Death case details

<Death>

Patient		Daily dose (number of doses)	Adverse drug reaction	
Gender/Age	Indication (Medical history)		Clinical course and treatment	
M/40s	Schizophrenia (Aspiration Pneumonia)	150 mg (once) 100 mg (once) 50 mg (twice)	<p>History of present illness and past medical history of diabetes mellitus: None</p> <p>Approximately 1 year before administration</p> <p>Start of administration</p> <p>7 days after</p> <p>35 days after</p> <p>36 days after</p> <p>63 days after</p> <p>77 days after (onset)</p>	<p>Since around this time, the patient had experienced repeated episodes of aspiration pneumonia and had been hospitalized for aggravated aspiration pneumonia. The patient's physical condition was poor. Risperidone had been administered in the previous treatment.</p> <p>The patient was transferred from another hospital to the reporter's hospital for the aspiration pneumonia. Treatment with XEPLION 150 mg was started because the patient was unable to take oral drugs.</p> <p>Treatment with XEPLION 100 mg was administered.</p> <p>Treatment with XEPLION 50 mg was administered.</p> <p>Abnormal blood sugar level developed. The laboratory data were unknown. The patient received 20% glucose solution.</p> <p>Treatment with XEPLION 50 mg was administered. No extrapyramidal symptom (EPS) developed after XEPLION had been initiated.</p> <p>The patient died. Cause of death: Unknown. Autopsy: Not performed. Electrocardiogram: No abnormalities. Renal function, hepatic function, and cardiac function: No abnormalities. Drug dependence: None.</p>
Concomitant drug(s): Sodium valproate, Flunitrazepam				

<Multi-organ failure, Abnormal hepatic function>

Patient		Daily dose (number of doses)	Adverse drug reaction	
Gender/Age	Indication (Medical history)		Clinical course and treatment	
F/50s	Schizophrenia (Pneumonia, Ileus)	150 mg (4 times) 100 mg (once)	<p>The patient did not have chronic hepatitis.</p> <p>Unknown</p> <p>Start of administration</p> <p>7 days after</p> <p>35 days after</p> <p>63 days after</p> <p>Unknown</p> <p>Unknown</p> <p>91 days after</p> <p>100 days after</p> <p>107 days after (onset)</p>	<p>The patient was transferred from another hospital to the reporter's hospital for ileus. The patient's condition had been complicated by pneumonia.</p> <p>Treatment with XEPLION 150 mg was started.</p> <p>XEPLION 100 mg was administered.</p> <p>XEPLION 150 mg was administered.</p> <p>XEPLION 150 mg was administered.</p> <p>Pedal oedema was observed during treatment with XEPLION.</p> <p>The pedal oedema improved with diuretic drugs.</p> <p>XEPLION 150 mg was administered.</p> <p>No EPS developed after XEPLION had been initiated.</p> <p>Abnormal hepatic function developed. GOT: 1890 IU/L GPT: 1330 IU/L</p> <p>The patient died of multi-organ failure during the hospitalization. Renal function and cardiac function: No abnormalities Autopsy: Not performed.</p>
Concomitant drug(s): Piperacillin sodium, Pantethine, Lansoprazole, Cefotiam hydrochloride, Kampo products				