Individual Case Safety Report Form

General Information

Worldwide unique case identification number	JP-OTSUKA-2024_022334AA
Sender type	Pharmaceutical company
Sender's organisation	OTSUKA
Date report was first received from source	13/08/2024
Date of most recent information	08/11/2024
Type of report	Report from studies
Primary source country	JP
Study registration number	
Study name	Samtasu post-marketing general drug use-results survey in patients with volume overload in heart failure.
Study type	Other studies
Reporter's qualification	Other health professional, Physician
Case serious?	Yes
Medically confirmed?	Yes

Patient

Age	Age Group	Sex	Weight	Height
75 years	Elderly	Male		

Reaction / Event

MedDRA LLT	Start Date	Stop Date	Duration	Outcome	Seriousness[1]
Pneumonia aggravated				fatal	death, other
Congestive cardiac failure aggravated	13/08/2024			fatal	death, other
Drug monitoring procedure incorrectly performed	12/08/2024			unknown	
Underdose	04/08/2024			unknown	

Drug Information

Role[2]	Drug	Start Date	Stop Date	Duration	Dose	Units in Interval	Action taken
S	Tolvaptan [TOLVAPTAN SODIUM PHOSPHATE]	12/08/2024	13/08/2024	2 days	8 mg	every 1 day	Not applicable
S	Tolvaptan [TOLVAPTAN]	04/08/2024	09/08/2024	6 days			Not applicable
		10/08/2024	11/08/2024	2 days			Not applicable
C	AMINO ACIDS NOS [AMINO ACIDS]	05/08/2024	12/08/2024	8 days			
C	BAYASPIRIN [ACETYLSALICYLIC ACID]	01/08/2024	11/08/2024	11 days			
C	BEPRIDIL HYDROCHLORIDE MONOHYDRATE [BEPRIDIL HYDROCHLORIDE MONOHYDRATE]	10/08/2024	11/08/2024	2 days			
C	BISONO [BISOPROLOL]	12/08/2024	12/08/2024	1 days			
C	CODEINE PHOSPHATE [CODEINE PHOSPHATE]		06/08/2024				
C	DAYVIGO [LEMBOREXANT]	03/08/2024	11/08/2024	9 days			
C	DIART [AZOSEMIDE]		11/08/2024				
C	DILTIAZEM HYDROCHLORIDE [DILTIAZEM HYDROCHLORIDE]	10/08/2024	11/08/2024	2 days			
C	DIPHENHYDRAMINE [DIPHENHYDRAMINE]	12/08/2024	12/08/2024	1 days			
C	DOXAZOSIN MESILATE [DOXAZOSIN MESILATE]	07/08/2024	11/08/2024	5 days			
C	ENTRESTO [SACUBITRIL VALSARTAN SODIUM HYDRATE]		11/08/2024				
C	ESOMEPRAZOLE MAGNESIUM [ESOMEPRAZOLE MAGNESIUM]		06/08/2024				
C	FUROSEMIDE [FUROSEMIDE]	31/07/2024	31/07/2024	1 days			
		01/08/2024	03/08/2024	3 days			
		04/08/2024	04/08/2024	1 days			
		05/08/2024	10/08/2024	6 days			
		11/08/2024	12/08/2024	2 days			
C	GLUCONSAN K [POTASSIUM GLUCONATE]	31/07/2024	10/08/2024	11 days			
C	HEPARIN SODIUM [HEPARIN SODIUM]	10/08/2024	10/08/2024	1 days			
C	HEPARINOID [HEPARINOID]	12/08/2024	12/08/2024	1 days			

1 Seriousness: **death**=results in death; **life threat.**=life threatening; **hospital.**=requires hospitalization/prolongation of hospitalization; **disability**=results in disability/incapacity; **congen.**=congenital anomaly/birth defect; **other**=other medically important information; **(blank)**=non-serious

2 Drug role: **S**=suspect; **C**=concomitant; **I**=interacting; **N**=not administered

3 Additional Information on Drug: **1**=Counterfeit; **2**=Overdose; **3**=Drug taken by the father; **4**=Drug taken beyond expiry date; **5**=Batch and lot tested and found within specifications;**6**=Batch and lot tested and found not within specifications; **7**=Medication error; **8**=Misuse; **9**=Abuse; **10**=Occupational exposure; **11**=Off label use; **(blank)**=no additional information

Role[2]	Drug	Start Date	Stop Date	Duration	Dose	Units in Interval	Action taken
C	IRRIBOW [RAMOSETRON HYDROCHLORIDE]	07/08/2024	11/08/2024	5 days			
C	ISOZOL [THIAMYLAL SODIUM]	10/08/2024	10/08/2024	1 days			
C	LEVOFLOXACIN HEMIHYDRATE [LEVOFLOXACIN HEMIHYDRATE]	02/08/2024	12/08/2024	11 days			
C	LOXOPROFEN SODIUM [LOXOPROFEN SODIUM]		11/08/2024				
C	MAINTATE [BISOPROLOL FUMARATE]		11/08/2024				
C	MEROPENEM TRIHYDRATE [MEROPENEM TRIHYDRATE]	12/08/2024	13/08/2024	2 days			
C	MINNEBRO [ESAXERENONE]	02/08/2024	11/08/2024	10 days			
C	MOSAPRIDE CITRATE [MOSAPRIDE CITRATE]		06/08/2024				
C	NIFEDIPINE [NIFEDIPINE]	01/08/2024	11/08/2024	11 days			
C	NOREPINEPHRINE [NOREPINEPHRINE]	13/08/2024	13/08/2024	1 days			
C	POTASSIUM CHLORIDE [POTASSIUM CHLORIDE]	10/08/2024	11/08/2024	2 days			
C	PRIMPERAN [METOCLOPRAMIDE HYDROCHLORIDE]	09/08/2024	12/08/2024	4 days			
C	RINDERON-VG [BETAMETHASONE VALERATE, GENTAMICIN SULFATE]	12/08/2024	12/08/2024	1 days			
C	ROSUVASTATIN CALCIUM [ROSUVASTATIN CALCIUM]	01/08/2024	11/08/2024	11 days			
C	SERENACE [HALOPERIDOL]	13/08/2024	13/08/2024	1 days			
C	SOLDACTONE [POTASSIUM CANRENOATE]	12/08/2024	13/08/2024	2 days			
C	SOLU MEDROL [METHYLPREDNISOLONE SODIUM SUCCINATE]	02/08/2024	05/08/2024	4 days			
C	TRAZENTA [LINAGLIPTIN]	07/08/2024	11/08/2024	5 days			
C	URIEF [SILODOSIN]		11/08/2024				
C	VEEN D [CALCIUM CHLORIDE DIHYDRATE, GLUCOSE, POTASSIUM CHLORIDE, SODIUM ACETATE, SODIUM CHLORIDE]	04/08/2024	07/08/2024	4 days			
C	VERAPAMIL HYDROCHLORIDE [VERAPAMIL HYDROCHLORIDE]	09/08/2024	10/08/2024	2 days			
C	VITAMEDIN INTRAVENOUS [CYANOCOBALAMIN, PYRIDOXINE HYDROCHLORIDE, THIAMINE DISULFIDE]	03/08/2024	13/08/2024	11 days			

Drug Information *(cont.)*

Info[3]	Drug	Indication	Cumul. dose to 1st Reaction	Pharm. Form	Route of Admin.	Batch / Lot #
	Tolvaptan [TOLVAPTAN SODIUM PHOSPHATE]	Cardiac failure, Fluid retention	16 mg	Intravenous infusion	Intravenous use	
	Tolvaptan [TOLVAPTAN]	Fluid retention, Cardiac failure		Tablet	Oral use	
	AMINO ACIDS NOS [AMINO ACIDS]	Amino acid supplementation		Injection	Other	
	BAYASPIRIN [ACETYLSALICYLIC ACID]	Cardiac failure, Product used for unknown indication			Oral use	
	BEPRIDIL HYDROCHLORIDE MONOHYDRATE [BEPRIDIL HYDROCHLORIDE MONOHYDRATE]	Product used for unknown indication			Oral use	
	BISONO [BISOPROLOL]	Product used for unknown indication		Transdermal patch	Transdermal use	
	CODEINE PHOSPHATE [CODEINE PHOSPHATE]	Product used for unknown indication			Oral use	
	DAYVIGO [LEMBOREXANT]	Product used for unknown indication			Oral use	
	DIART [AZOSEMIDE]	Product used for unknown indication			Oral use	
	DILTIAZEM HYDROCHLORIDE [DILTIAZEM HYDROCHLORIDE]	Product used for unknown indication			Oral use	
	DIPHENHYDRAMINE [DIPHENHYDRAMINE]	Product used for unknown indication		Cream	Transdermal use	
	DOXAZOSIN MESILATE [DOXAZOSIN MESILATE]	Product used for unknown indication			Oral use	
	ENTRESTO [SACUBITRIL VALSARTAN SODIUM HYDRATE]	Cardiac failure			Oral use	
	ESOMEPRAZOLE MAGNESIUM [ESOMEPRAZOLE MAGNESIUM]	Product used for unknown indication		Capsule	Oral use	

Info[3]	Drug	Indication	Cumul. dose to 1st Reaction	Pharm. Form	Route of Admin.	Batch / Lot #
	FUROSEMIDE [FUROSEMIDE]	Product used for unknown indication			Other	
	GLUCONSAN K [POTASSIUM GLUCONATE]	Product used for unknown indication			Oral use	
	HEPARIN SODIUM [HEPARIN SODIUM]	Thromboembolism prophylaxis, Prophylaxis			Other	
	HEPARINOID [HEPARINOID]	Product used for unknown indication		Cutaneous liquid	Transdermal use	
	IRRIBOW [RAMOSETRON HYDROCHLORIDE]	Product used for unknown indication			Oral use	
	ISOZOL [THIAMYLAL SODIUM]	Sedation procedure			Other	
	LEVOFLOXACIN HEMIHYDRATE [LEVOFLOXACIN HEMIHYDRATE]	Product used for unknown indication			Other	
	LOXOPROFEN SODIUM [LOXOPROFEN SODIUM]	Product used for unknown indication			Oral use	
	MAINTATE [BISOPROLOL FUMARATE]	Product used for unknown indication			Oral use	
	MEROPENEM TRIHYDRATE [MEROPENEM TRIHYDRATE]	Product used for unknown indication			Other	
	MINNEBRO [ESAXERENONE]	Product used for unknown indication			Oral use	
	MOSAPRIDE CITRATE [MOSAPRIDE CITRATE]	Product used for unknown indication			Oral use	
	NIFEDIPINE [NIFEDIPINE]	Product used for unknown indication			Oral use	
	NOREPINEPHRINE [NOREPINEPHRINE]	Cardiac failure			Other	
	POTASSIUM CHLORIDE [POTASSIUM CHLORIDE]	Product used for unknown indication			Oral use	
	PRIMPERAN [METOCLOPRAMIDE HYDROCHLORIDE]	Product used for unknown indication			Other	
	RINDERON-VG [BETAMETHASONE VALERATE, GENTAMICIN SULFATE]	Redness		Cream	Transdermal use	
	ROSUVASTATIN CALCIUM [ROSUVASTATIN CALCIUM]	Product used for unknown indication			Oral use	
	SERENACE [HALOPERIDOL]	Product used for unknown indication			Other	
	SOLDACTONE [POTASSIUM CANRENOATE]	Product used for unknown indication			Other	
	SOLU MEDROL [METHYLPREDNISOLONE SODIUM SUCCINATE]	Product used for unknown indication			Other	
	TRAZENTA [LINAGLIPTIN]	Product used for unknown indication			Oral use	
	URIEF [SILODOSIN]	Product used for unknown indication			Oral use	
	VEEN D [CALCIUM CHLORIDE DIHYDRATE, GLUCOSE, POTASSIUM CHLORIDE, SODIUM ACETATE, SODIUM CHLORIDE]	Nutritional supplementation		Injection	Other	
	VERAPAMIL HYDROCHLORIDE [VERAPAMIL HYDROCHLORIDE]	Product used for unknown indication			Other	
	VITAMEDIN INTRAVENOUS [CYANOCOBALAMIN, PYRIDOXINE HYDROCHLORIDE, THIAMINE DISULFIDE]	Vitamin supplementation			Other	

Time-to-Onset and Rechallenge matrix table

Reaction/Event (MedDRA LLT)	Drug	TTO	Rechallenge? / Reaction recurred?
Pneumonia aggravated	Tolvaptan [TOLVAPTAN SODIUM PHOSPHATE]	2 days	no / not applicable
	Tolvaptan [TOLVAPTAN]	-	no / not applicable
Congestive cardiac failure aggravated	Tolvaptan [TOLVAPTAN SODIUM PHOSPHATE]	1 days	no / not applicable
	Tolvaptan [TOLVAPTAN]	9 days	no / not applicable
Drug monitoring procedure incorrectly performed	Tolvaptan [TOLVAPTAN SODIUM PHOSPHATE]	0 days	no / not applicable
	Tolvaptan [TOLVAPTAN]	8 days	no / not applicable
Underdose	Tolvaptan [TOLVAPTAN SODIUM PHOSPHATE]	-8 days	no / not applicable
	Tolvaptan [TOLVAPTAN]	0 days	no / not applicable

Relevant Medical History and Concurrent Conditions

MedDRA LLT	Start Date	End Date	Continuing	Family History	Comments
Cardiac failure congestive					
Left heart failure	30/07/2024				Type of Heart failure was Left heart failure □
Fluid retention	12/08/2024				

MedDRA LLT	Start Date	End Date	Continuing	Family History	Comments
Ischaemic heart disease					Underlying disease of Heart failure
Consciousness disturbed					Consciousness Level (JCS) was 1 (Almost fully conscious but not normal).
Respiration abnormal					It is difficult to manage fluid through oral fluid intake. Main reasons for difficulties.
Hospitalisation	11/08/2024				ICU・CCU・HCU
Oxygen therapy			No		
Mechanical ventilation			No		
Hypertension			Yes		
Diabetes mellitus			Yes		
Dyslipidaemia			Yes		
Cerebral infarction			Yes		
Cerebral haemorrhage			Yes		
Prostatic hypertrophy			Yes		
Reflux oesophagitis			Yes		
Chronic diarrhoea			Yes		
Rhinitis allergic			Yes		
Hypokalaemia			Yes		
Insomnia			Yes		
Pain of lower extremities			Yes		
Asteatosis			Yes		
Atrial fibrillation			Yes		
Pruritus cutaneous			Yes		
Pneumonia			Yes		
Queasy			Yes		
Renal failure chronic			Yes		
Anaemia			Yes		
Hypoalbuminaemia			Yes		
DC shock			No		

Past Drug History

Drug	Start Date	End Date	Indication	Reaction
SPIRONOLACTONE	01/08/2024	01/08/2024	Product used for unknown indication	
SITAGLIPTIN PHOSPHATE			Product used for unknown indication	
SUGLAT		31/07/2024	Product used for unknown indication	
GLIMEPIRIDE		31/07/2024	Product used for unknown indication	
EBASTEL		31/07/2024	Product used for unknown indication	
GLUCOSE 5% BRAUN	31/07/2024	31/07/2024	Product used for unknown indication	
NITROGLYCERIN	31/07/2024	02/08/2024	Product used for unknown indication	
SULBACILLIN	01/08/2024	02/08/2024	Product used for unknown indication	

Death

Date of Death	Reported Cause	Autopsy done?	Autopsy-determined Cause of Death
13/08/2024	Congestive cardiac failure aggravated [Worsening of cardiac failure congestive] Pneumonia aggravated [Pneumonia aggravated]	No	

Reporter's Comments

Not applicable.

Sender's Comments

This patient was started on Samtasu for I.V. Infusion 8 mg (Tolvaptan Sodium Phosphate) and Tolvaptan for fluid retention due to heart failure. The patient had pneumonia aggravated (pneumonia) at an unspecified duration after initiating Samtasu and Tolvaptan therapy and worsening of cardiac failure congestive (cardiac failure congestive) 2 days after initiating Samtasu therapy and 10 days after initiating therapy with Tolvaptan, and the cause of death was pneumonia aggravated and worsening of cardiac failure congestive. The events of pneumonia aggravated (pneumonia) and worsening of cardiac failure congestive (cardiac failure congestive) are assessed as serious (fatal and medically significant). In view of the nature of the event, the likely infectious etiology, and considering the patient's underlying condition of congestive heart failure as a significant confounding factor and the elderly age as a risk factor, the causality for the event of pneumonia aggravated (pneumonia) is assessed as not related to Samtasu and Tolvaptan therapy. Based on the nature of the event, the patient's underlying conditions of congestive heart failure, ischemic heart disease, hypertension, diabetes mellitus, chronic renal failure and pneumonia, and the elderly age as significant risk factors, the causality for the event of worsening of cardiac failure congestive (cardiac failure congestive) is assessed as not related to Samtasu and Tolvaptan therapy. The special situation events of drug monitoring procedure incorrectly performed (no measurement of serum sodium and serum potassium after the administration of Samtasu on the start date of Samtasu) and underdose (Tolvaptan 3.75 mg/day was administered for fluid retention due to heart failure) are assessed as non-serious and not related to Samtasu and Tolvaptan.

Laboratory Tests

Test Name	Test Date	Results	Normal High Value	Normal Low Value	Comments
BNP	09/08/2024	848 pg/mL			
Electrocardiogram	09/08/2024	(Test Result:Normal N/A;Before initiation of Samtasu administration)			
Electrocardiogram	13/08/2024	(Test Result:Abnormal (Atrial fibrillation) N/A;)			
Laboratory test		(Test Result: exacerbation of infiltrative shadows N/A;)			
Arterial oxygen saturation	11/08/2024	92 %			
Arterial oxygen saturation	12/08/2024	92 %			
Arterial oxygen saturation	12/08/2024	91 %			
Arterial oxygen saturation	12/08/2024	98 %			
Arterial oxygen saturation	12/08/2024	95 %			
Arterial oxygen saturation	12/08/2024	93 %			
Arterial oxygen saturation	12/08/2024	91 %			
Arterial oxygen saturation	12/08/2024	92 %			
Arterial oxygen saturation	13/08/2024	92 %			

Related Reports

Relation	Case Identifier
Duplicate	JP-MMM-GLTUN6CO