Safety Data Sheet

1. IDENTIFICATION	
Product identifier	Rexulti® 3-mg, 4-mg Tablets
Synonyms	Brexpiprazole; OPC-34712
Identified uses	Drug Products
Supplier's details	Otsuka Pharmaceutical Co., Ltd. 2-9 Kanda-Tsukasamachi, Chiyoda-ku Tokyo 101-8535, Japan (Also see section 16)
Emergency telephone number	Telephone: +81-88-672-6080 (Monday/Friday, 8:00/17:00, JPT) Telefax: +81-88-637-5520
Contact E-mail	Kawano.Daiki@otsuka.jp, yamane@otsuka.jp

2. HAZARDS IDENTIFICATION	
Classification of the substance or mixture	
CLP/GHS	Hazardous to the aquatic environment - Category Chronic 2
Label elements	
Pictogram(s)	
Signal word	Warning
Hazard statement	H411: Toxic to aquatic life with long lasting effects.
Precautionary statement	P273: Avoid release to environment. P391: Collect spillage. P501: Dispose of contents/container in accordance with local/regional/national/international regulations.
Other Hazards	
Eye	Not irritating.
Skin	Not irritating.
Ingestion	May be harmful
Inhalation	Not irritating

3. COMPOSITION & INFORMATION ON INGREDIENTS

Component	CAS#	% (by wt)
Brexpiprazole	913611-97-9	3.2-4.3%
Microcrystalline cellulose	9004-34-6	< 11%
Other Ingredients (Non-Hazardous Ingredient)	--	< 80%

4. FIRST AID MEASURES

Eye Contact	Rinse immediately with plenty of water for at least 15 minutes. Keep eye wide open while rinsing. If exposed or concerned: Get medical attention/advice.
Skin Contact	Take off contaminated clothing and shoes immediately. Wash off immediately with plenty of water for at least 15 minutes. Discard contaminated clothing or wash before re-use. If exposed or concerned: Get medical attention/advice.
Ingestion	Do NOT induce vomiting. Never give anything by mouth to an unconscious person. If exposed or concerned: Get medical attention/advice.
Inhalation	Move to fresh air. Oxygen or artificial respiration if needed. If exposed or concerned: Get medical attention/advice.
Most Important symptoms and effects, both acute and delayed	Suicidal thoughts or actions. Stroke. Neuroleptic Malignant Syndrome: hyperpyrexia, muscle rigidity, altered mental status and evidence of autonomic instability (irregular pulse or blood pressure, tachycardia, diaphoresis and cardiac dysrhythmia). Additional signs may include elevated creatine phosphokinase, myoglobinuria (rhabdomyolysis), and acute renal failure. Uncontrolled body movements (tardive dyskinesia): Problems with metabolism: high blood sugar (hyperglycemia) or diabetic ketoacidosis: feel very thirsty, need to urinate more than usual, feel very hungry, diabetic coma, increased blood fat levels (cholesterol and triglycerides). Low white blood cell, neutrophil, granulocyte counts Epileptic seizures (convulsions) Difficulty swallowing Abnormal blood prolactin level
Indication of immediate medical attention and special treatment needed	Pay close attention to deterioration of clinical status and appearance of suicidal thoughts or actions. Oral activated charcoal and sorbitol (50 g/240 mL), administered one hour after ingesting oral brexpiprazole, decreased brexpiprazole Cmax and area under the curve (AUC) by approximately 5% to 23% and 31% to 39%, respectively, charcoal and sorbitol should be considered as the treatment of overdose. Although there is no information on the effect of hemodialysis in treating an overdose with brexpiprazole,

	hemodialysis is unlikely to be useful in overdose management since brexpiprazole is highly bound to plasma proteins. Gastric lavage and treatment with an emetic may be useful immediately after overdose. Stay at adequate room temperature, cool, and drink plenty of water if fever and dehydration are observed. Monitor body temperature. Show this SDS to the physician. Management of overdose should concentrate on supportive therapy, maintaining an adequate airway, oxygenation and ventilation, and management of symptoms. Therefore cardiovascular monitoring should be started immediately and should include continuous electrocardiographic monitoring to detect possible arrhythmias. Otherwise, close medical supervision and monitoring should continue until the patient recovers. Complete blood counts, triglyceride, prolactin and creatinine kinase levels in the blood might be monitored.

5. FIRE FIGHTING MEASURES

Fire Fighting Extinguishing Media	Suitable extinguishing media: Carbon dioxide, Dry chemical, Water spray, Foam Unsuitable extinguishing media: Do NOT use water jet.
Fire Fighting Instructions	Use personal protective equipment. In the event of fire, wear self-contained breathing apparatus. Stay on the side from which the wind comes. Make sure the personnel are away from the fumes. Avoid releasing of extinguishing water into the environment.
Hazardous Combustion Products	COx NOx SOx gas can form flammable or explosive mixture with alcohol or metals. In the event of fire and/or explosion do not breathe fumes.

6. ACCIDENTIAL RELEASE MEASURES

Personal precautions	Refer to protective measures listed in sections 7 and 8. Use personal protective equipment. Examples include tightly fitting safety goggles, lab coat and impervious gloves. Wear respiratory protection. Depending on the nature of the spill (quantity and extent of spill) additional protective clothing and equipment such as a self-contained breathing apparatus may be needed.
Emergency procedure	Use personal protective apparatus if exposed to vapors/dust/aerosol.
Environmental protection	Prevent release to drains and waterways. Prevent release to the environment.
Containment Method	Wet down any dust to prevent generation of aerosols, if appropriate. Cover with suitable material.

Methods for cleaning up	Contain and collect spillage and place in container for disposal according to local regulations (see Section 13). Handle waste materials, including gloves, protective clothing, contaminated spill cleanup material, etc., as appropriate for chemically and pharmacologically similar materials.

7. HANDLING AND STORAGE	
Safe Handling	Avoid exposure - obtain special instructions before use. Avoid formation of dust and aerosols. When handling broken or crushed tablets, ensure worker exposure is below the recommended exposure limit. Keep away from heat and sources of ignition. Prevent release to drains and waterways.
Storage Condition	Store under between 20ºC - 25ºC. Excursion permitted between 15ºC - 30ºC. Protect against light. Keep away from heat, sparks and flames. Store locked up.
Container Requirement	Store in the original primary packaging as provided.

8. EXPOSURE CONTROL / PERSONAL PROTECTION	
ACGIH TLV-TWA	10 mg/m^3 TWA - Corn Starch, Microcrystalline Cellulose, Magnesium Stearate **Company Guideline** 2 µg/m^3 8 hour TWA- Brexpiprazole (API)
ACGIH TLV-STEL	Not available
OSHA PEL-TWA	Not available
JSOH PEL-TWA	Not available
Engineering Control	When handling small quantities in a clinical setting, good room ventilation is desirable. Specific engineering controls should not be needed. When handling broken or crushed tablets, ensure worker exposure is below the recommended exposure limit. If significant dust is generated, use process enclosures, containment technology, or other engineering controls to keep airborne levels below recommended exposure limit. Ensure adequate ventilation, especially in confined areas.
Personal Protection	
Respiratory Protection	Normally not required for handling a small number of tablets. Use the indicated respiratory protection if the occupational exposure limit is exceeded and/or in case of product release (dust). Use and selection of respiratory protection is based upon engineering controls in use and potential for aerosol generation.
Hand Protection	Impervious nitrile, rubber and latex gloves are recommended (EN 420, EN 374). Please note that employees who are allergic to natural rubber latex should use nitrile gloves.

Eye Protection	Glasses or chemical splash resistant goggles are recommended if eye contact is possible.
Skin and body Protection	Choose body protection in relation to its type, amount, and to the specific work-place.
Airborne Exposure limits	This formulation contains an active pharmaceutical ingredient (API) with the company guideline limit noted above. To keep the API below the recommended guideline, the material as supplied should be controlled during handling to limit total airborne aerosol exposure to: 46.5 µg/m³.
Contaminated Items	Mentioned in section 13

9. PHSYCAL AND CHEMICAL PROPERTIES	
Appearance	solid, tablet
Color	Purple (3-mg), white (4-mg)
Odour/Odour Threshold	Odorless
pH	Not applicable
Melting Point/freezing point	No data available
Initial Boiling Point/Boiling Point	No data available
Flash Point	No data available
Evaporate Rate	Not applicable
Flammability	Not highly flammable
Explosive Limit	No data available
Vapor Pressure	Not Applicable
Vapor Density	Not applicable
Relative density	No data available
Solubility	No data available
Partition coefficient : n-octanol/water	Not applicable
Auto-ignition temperature	No data available
Decomposition Temperature	No data available
Viscosity coefficient	Not applicable

10. STABILITY AND REACTIVITY	
Reactivity	No data available
Stability	Stable under normal conditions.
Possibility of hazardous reaction	Nothing in particular
Conditions to Avoid	Overheating and dehydration
Incompatible Materials	Oxidizing agent
Hazardous Decomposition Products	COx NOx SOx

11. TOXICOLOGICAL INFORMATION	
Acute Toxicity	Brexpiprazole Oral approximate lethal dose 1000mg/kg (rat)
Respiratory Sensitization	No data available
Skin Corrosion/Irritation	Not irritating
Serious Eye Damage/Irritation	Not irritating

Germ Cell Mutagenicity	Brexpiprazole Negative: (in vitro; bacteria) Positive: (in vitro; mouse cells) 50μmol/L
Carcinogenicity	Brexpiprazole No adverse effect level (NOAEL) oral (mouse): 5mg/kg in male & 2mg/kg in female Adenoma in mammary and pituitary gland: 5mg/kg in female, but negative (oral) rat 10mg/kg in male & 30mg/kg in female
Reproductive Toxicity	Brexpiprazole Non-toxic dose(oral): 0.3mg/kg (rat) Decrease in fertility index (oral): 3mg/kg (rat) Increased in pre-implantation loss (oral): 30mg/kg(rat)
STOT-Single Exposure	Not available
STOT-Repeated Exposure	Not available
Aspiration Hazard	Not available

12. ECOLOGICAL INFORMATION

Ecotoxicity	Brexpiprazole **Chronic toxicity to fish** Early-life Stage NOEC 0.056 mg/L (zebra fish (Danio rerio)) **Chronic toxicity to Crustacea** NOEC 0.13 mg/L (Daphnia magna) (survival and reproduction) **Chronic toxicity to Algae** EC_{50} (72h) > 0.13 mg/kg (Pseudokirchneriella subcapitata) NOEC 0.011 mg/L (Daphnia magna) (Pseudokirchneriella subcapitata)
Persistence and Degradability	Brexpiprazole Biodegradation Ready biodegradation (28D): -6.0%; Not Biodegradable - unlikely to undergo rapid biodegradation in the environment
Bioaccumulative Potential	Brexpiprazole Kinetic bioconcentration factor (BCF_K): >1000 (rainbow trout)
Mobility in Soil	Brexpiprazole Log Octanol/Water Partition Coefficient [log Kow]: 2.41 (pH 5.0), 4.27 (pH 7.0), 4.86 (pH 9.0)
PBT and vPvB assessment	No data available

13. DISPOSAL CONSIDERATIONS

Disposal Information	Disposal should be in accordance with applicable regional, national and local laws and regulations. Local regulations may be more stringent than regional or national requirements. This information presented only applies to the material as supplied.

14. TRANSPORT INFORMATION

Transport Route and Regulations	Ground	Air	Marine	Other
	ADR、RID	ICAO/IATA	IMDG	-
UN number	UN3077			
Proper Shipping Name	Environmentally hazardous substance, solid, n.o.s (Brexpiprazole mixture)			
Transport hazard class	9			
Packing group	III			
Environmental hazards	Yes			
Transport in bulk according to Annex II of MARPOL73/78 and the IBC code	Not applicable			
Special precautions for user	**IMDG** MeS:F-A,S-F **Transportation Classification for All Modes:** Marine pollutant			

15. REGULATORY INFORMATION

Safety, health and environmental regulations	313 Toxic Release Inventory No components listed on the SARA 313 inventory. TSCA Inventory Not listed. Food, drug and cosmetic products are exempt from TSCA.

16. OTHER INFORMATION

Details of the supplier of the safety data sheet	**Prepared by:** **Manufacturing Process Development Depratment (Pharmaceutical Products)** Otsuka Pharmaceutical Co. Ltd. Tokushima Itano Factory Matsutani Itano-cho, Itano-gun Tokushima 779-0195, Japan

End of Safety Data Sheet