Version	Revision Date:	SDS Number:	Date of last issue: 31.08.2017
6.0	08.02.2018	11653	Date of first issue: 31.08.2017

SECTION 1. PRODUCT AND COMPANY IDENTIFICATION

1.1 Product identifier

XIGDUO TABLETS

Details of the supplier of the safety data sheet : ASTRAZENECA PTY LTD
PO Box 131
66 Talavera Rd, North Ryde
NSW 2113
AUSTRALIA
+61 2 9978 3500

SafetyDataSheets.AlderleyPark@astrazeneca.com

Emergency Telephone
+44 (0) 1235 239 670

Alternative Names

Dapagliflozin and metformin hydrochloride tablets
Dapagliflozin and Metformin Hydrochloride Tablets 2,5/850 mg, 2,5/1000 mg, 5/850 mg, 5/1000 mg
Xigduo IR
Xigduo XR

CAS No. : Not applicable

1.2 Relevant identified uses of the substance or mixture and uses advised against

Use of the Substance/Mixture : Treatment of Type II Diabetes

SECTION 2. HAZARDS IDENTIFICATION

GHS Classification

Acute toxicity (Oral) : Category 4

Reproductive toxicity : Category 1B

Effects on or via lactation

GHS label elements

Hazard pictograms :

Signal word : Danger

Hazard statements : H302 Harmful if swallowed.
H360 May damage fertility or the unborn child.
H362 May cause harm to breast-fed children.

Precautionary statements :

Prevention:

P201 Obtain special instructions before use.
P202 Do not handle until all safety precautions have been read and understood.
P260 Do not breathe dust or mist.
P264 Wash skin thoroughly after handling.
P281 Use personal protective equipment as required.

Response:

P301 + P312 + P330 IF SWALLOWED: Call a POISON CENTER or doctor/ physician if you feel unwell. Rinse mouth.
P308 + P313 IF exposed or concerned: Get medical advice/ attention.

Disposal:

P501 Dispose of contents/ container to an approved waste disposal plant.

Hazardous components which must be listed on the label:

Metformin Hydrochloride
Dapagliflozin

Other hazards which do not result in classification

See Section 11.
May cause nausea, vomiting, severe abdominal pain and diarrhoea.
May cause hypoglycemia.
The product may form flammable dust clouds in air, if dust from crushed tablets is allowed to accumulate.

SECTION 3. COMPOSITION/INFORMATION ON INGREDIENTS

Substance / Mixture : Mixture

Hazardous components

Chemical name	CAS-No.	Concentration (% w/w)
Metformin Hydrochloride	1115-70-4	67 -68
Titanium dioxide	13463-67-7	0.1 -1
Talc	14807-96-6	1
Dapagliflozin	960404-48-2	0.1 -0.5

SECTION 4. FIRST AID MEASURES

If inhaled : Remove patient from exposure.
Obtain medical attention if ill effects occur.

In case of skin contact : Wash skin with soap and water.

In case of eye contact : Irrigate with eyewash solution or clean water, holding the eyelids apart, for at least 10 minutes.
Obtain medical attention if ill effects remain.

If swallowed : Wash out mouth with water and give 200-300ml of water to drink.
Obtain medical attention if ill effects occur.
Do NOT induce vomiting as a First-Aid measure.

Most important symptoms and effects, both acute and delayed : Refer to sections 2 and 11
Harmful if swallowed.
May damage fertility or the unborn child.
May cause harm to breast-fed children.

Notes to physician : Symptomatic treatment and supportive therapy as indicated.
For further detail consult the prescribing information.

SECTION 5. FIREFIGHTING MEASURES

Suitable extinguishing media : water spray, foam, dry powder or CO2.

Unsuitable extinguishing media : Avoid high pressure media which could cause the formation of a potentially explosible dust-air mixture.

Specific hazards during firefighting : If involved in a fire, it may burn and emit noxious and toxic fumes.

Special protective equipment for firefighters : A self contained breathing apparatus and suitable protective clothing should be worn in fire conditions.

SECTION 6. ACCIDENTAL RELEASE MEASURES

Personal precautions, protective equipment and emergency procedures : Ensure suitable personal protection during removal of spillages.
Avoid dispersal of dust in the air.

Environmental precautions : Prevent entry into drains.

Methods and materials for containment and cleaning up : Avoid dust generation.
Transfer spilled tablets to a suitable container for disposal.
Wash the spillage area with water.

SECTION 7. HANDLING AND STORAGE

Advice on safe handling : Avoid contact with skin and eyes.
Wash hands after use.
Minimize dust generation and accumulation.
The product may form flammable dust clouds in air, if dust from crushed tablets is allowed to accumulate.

Conditions for safe storage : Keep container tightly closed.
Protect from light.
Store at room temperature.

SECTION 8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Components with workplace control parameters

Components	CAS-No.	Value type (Form of exposure)	Control parameters / Permissible concentration	Basis
Metformin Hydrochloride	1115-70-4	TWA	5 mg/m3	COM; HYG
Titanium dioxide	13463-67-7	TWA	10 mg/m3	AU OEL
	Further information: This value is for inhalable dust containing no asbestos and < 1% crystalline silica			

		TWA	10 mg/m3 (Titanium dioxide)	ACGIH
Talc	14807-96-6	TWA	2.5 mg/m3	AU OEL
		TWA	0.1 fibres per cubic centimeter	ACGIH
		TWA (Respirable fraction)	2 mg/m3	ACGIH
Dapagliflozin	960404-48-2	TWA	0.01 mg/m3	COM

Engineering measures : The specific controls will depend on local circumstances and should be based on the risk assessment. Appropriate controls to reduce exposure may include engineering controls, for example ventilation, procedural controls and the use of personal protection equipment.

Prevent entry into drains, sewers or watercourses.

Personal protective equipment

Respiratory protection : Use an air fed hood if the risk assessment does not support the selection of other protection.

Eye protection : Use safety glasses to protect against direct contact with the product if the risk assessment does not support the selection of other protection.

Skin and body protection : Use impervious clothing to protect against direct contact with the product or for repeated, excessive handling use full chemical protective suit if the risk assessment does not support the selection of other protection. Use impervious protective gloves to protect against direct contact with the product. If the product is dissolved or wetted use a glove material that is resistant to the solvent/liquid.

Protective measures : Decisions about whether the use of personal protective equipment (PPE) is appropriate as part of the control strategy should be based on the workplace risk assessment and should take account of local legislative requirements for selection and use. There are multiple factors that will affect the specific requirements such as amount and concentration of the material, duration of exposure, frequency of exposure, external environmental conditions, the task, the user etc.
All the information above should not be used in isolation and should be considered in the context of the workplace risk assessment on a case by case basis.

The recommended personal protective equipment (PPE) is based on preventing the potential adverse health effects from exposure to the active pharmaceutical ingredient (API). The risk of exposure to the API in the formulation/product needs to be taken into consideration.

SECTION 9. PHYSICAL AND CHEMICAL PROPERTIES

Appearance	:	film-coated tablets
Colour	:	2,5/850 mg - white; 2,5/1000 mg - orange; 5/850 mg - brown; 5/1000 mg - yellow
Odour	:	No data available
Odour Threshold	:	No data available
pH	:	No data available
Melting point/range	:	No data available
Initial boiling point and boiling range	:	Not applicable
Flash point	:	No data available
Evaporation rate	:	Not applicable
Flammability (solid, gas)	:	No data available
Upper explosion limit / Upper flammability limit	:	No data available
Lower explosion limit / Lower flammability limit	:	No data available
Vapour pressure	:	Not applicable
Relative vapour density	:	Not applicable
Relative density	:	No data available
Solubility(ies)		
Water solubility	:	No data available
Solubility in other solvents	:	No data available
Partition coefficient: n-octanol/water	:	No data available
Auto-ignition temperature	:	No data available
Decomposition temperature	:	No data available
Viscosity		
Viscosity, dynamic	:	Not applicable
Viscosity, kinematic	:	Not applicable
Explosive properties	:	No data available
Oxidizing properties	:	Not applicable

SECTION 10. STABILITY AND REACTIVITY

Reactivity	:	No known reactivity hazard under normal conditions.
Chemical stability	:	Stable under normal conditions.
Possibility of hazardous reactions	:	None known.
Conditions to avoid	:	No conditions producing hazardous situations known.
Incompatible materials	:	None known.
Hazardous decomposition products	:	No hazardous decomposition products are known.

SECTION 11. TOXICOLOGICAL INFORMATION

11.1 Acute toxicity

Harmful if swallowed.

Product:

Acute oral toxicity	:	Acute toxicity estimate: 735.29 mg/kg Method: Calculation method

Components:

Metformin Hydrochloride:

Acute oral toxicity	:	LD50 Oral (Rat): 1,000 - 1,770 mg/kg Assessment: The component/mixture is moderately toxic after single ingestion.
Acute inhalation toxicity	:	Remarks: May cause effects as described under single exposure.(STOT)
Acute dermal toxicity	:	Remarks: No data available

Dapagliflozin:

Acute oral toxicity	:	Evident toxicity with mortality in rats at a dose of: 750 mg/kg Assessment: The component/mixture is moderately toxic after single ingestion.
Acute inhalation toxicity	:	Remarks: No information available on acute toxicity. May cause effects as described under repeated exposure.(STOT)
Acute dermal toxicity	:	Remarks: No data available

11.2 Skin corrosion/irritation

Not classified based on available information.

Components:

Metformin Hydrochloride:

Remarks: May cause slight skin irritation.

Dapagliflozin:

Remarks: Non-irritant.

11.3 Serious eye damage/eye irritation

Not classified based on available information.

Components:

Metformin Hydrochloride:

Remarks: May cause slight eye irritation.

Dapagliflozin:

Result: Eye irritation

11.4 Respiratory or skin sensitisation

Skin sensitisation

Not classified based on available information.

Respiratory sensitisation

Not classified based on available information.

Components:

Metformin Hydrochloride:

Remarks: No information available.

Dapagliflozin:

Remarks: It is not a skin sensitiser in vivo.
Unlikely to cause skin sensitisation.

Chronic toxicity

11.5 Germ cell mutagenicity

Not classified based on available information.

Components:

Metformin Hydrochloride:

Germ cell mutagenicity - Assessment : There is no evidence of genotoxic potential in in vitro and in vivo tests.

Dapagliflozin:

Germ cell mutagenicity - Assessment : The substance is not considered to be genotoxic.

11.6 Carcinogenicity

Not classified based on available information.

Components:

Metformin Hydrochloride:

Carcinogenicity - Assessment : No evidence of carcinogencity in animal studies.

Dapagliflozin:

Carcinogenicity - Assessment : Studies in animals have shown that chronic exposures produce no carcinogenic effects.

11.7 Reproductive toxicity

May damage fertility or the unborn child.
May cause harm to breast-fed children.

Components:

Metformin Hydrochloride:

Reproductive toxicity - Assessment : There is no evidence of reprotoxicity in animal tests.

Dapagliflozin:

Reproductive toxicity - Assessment : Clear evidence of adverse effects on development, based on animal experiments.
Effects on or via lactation

11.8 STOT - single exposure

Not classified based on available information.

Components:

Metformin Hydrochloride:

Exposure routes: Oral, Inhalation
Remarks: Based on human experience.
May cause nausea, vomiting, severe abdominal pain and diarrhoea.

Dapagliflozin:

Remarks: May cause effects as described under repeated exposure.(STOT)

11.9 STOT - repeated exposure

Not classified based on available information.

Components:

Metformin Hydrochloride:

Exposure routes: Oral, Inhalation
Remarks: May cause effects as described under single exposure.(STOT)
Repeated exposure may cause anorexia.
Repeated exposure may produce adverse effects on the testes, uterus and kidneys.

Dapagliflozin:

Exposure routes: Oral
Target Organs: Kidney, Bone
Assessment: Causes damage to organs through prolonged or repeated exposure.
Remarks: These effects are derived from studies in animals.

Remarks: Repeated exposure may cause diarrhea, nausea, gastrointestinal discomfort, weakness, headache, dizziness, sweating, paleness, rash, dermatitis, swelling, blurred vision, abdominal pain, flank pain, changes in clinical chemistry parameters, and lowered blood pressure.
Increased risk of urinary tract infection and fungal infection.
May cause hypoglycemia.
It may produce diuretic effects.

11.10 Aspiration toxicity

Not classified based on available information.

Components:

Metformin Hydrochloride:

No information available.

Dapagliflozin:

No data available

SECTION 12. ECOLOGICAL INFORMATION

Ecotoxicity

Components:

Metformin Hydrochloride:

Toxicity to fish	:	LC50 (Lepomis macrochirus (Bluegill sunfish)): > 982 mg/l Exposure time: 96 H LOEC (Pimephales promelas (fathead minnow)): > 10 mg/l NOEC (Pimephales promelas (fathead minnow)): 10 mg/l
Toxicity to daphnia and other aquatic invertebrates	:	EC50 (Daphnia magna (Water flea)): 130 mg/l Exposure time: 48 H
Toxicity to algae	:	EC50 (Pseudokirchneriella subcapitata (green algae)): > 100 mg/l Exposure time: 72 H NOEC (green algae): 100 mg/l Exposure time: 72 H
Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity)	:	NOEC (Daphnia magna (Water flea)): 67 mg/l Exposure time: 21 d

Dapagliflozin:

Toxicity to daphnia and other aquatic invertebrates	:	EC50 (Daphnia magna (Water flea)): > 120 mg/l Exposure time: 48 H Method: OECD Test Guideline 202
Toxicity to algae	:	ErC50 (green algae): 120 mg/l Exposure time: 72 H NOEC (green algae): 37 mg/l Exposure time: 72 H Method: OECD Test Guideline 201
Toxicity to fish (Chronic toxicity)	:	NOEC (Pimephales promelas (fathead minnow)): 1 mg/l Exposure time: 32 d Method: OECD Test Guideline 210 Remarks: Highest concentration tested (no effects).
Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity)	:	NOEC (Daphnia magna (Water flea)): 10 mg/l Exposure time: 21 d Method: OECD Test Guideline 211
Toxicity to microorganisms	:	(NOEC) Respiration inhibition (Sewage sludge organisms): 200 mg/l Exposure time: 3 H Test Type: Respiration inhibition Method: OECD Test Guideline 209

Persistence and degradability

Components:

Metformin Hydrochloride:

Biodegradability	:	aerobic Result: Not readily biodegradable. Biodegradation: 0.60 % Exposure time: 28 d Remarks: FDA 3.11

Dapagliflozin:

Biodegradability	:	Biodegradation: 11 % Method: OECD Test Guideline 301F Remarks: Not rapidly degradable. The substance is not significantly hydrolyzed in water.

Bioaccumulative potential

Components:

Metformin Hydrochloride:

Bioaccumulation	:	Remarks: The substance has low potential for bioaccumulation.

Dapagliflozin:

Bioaccumulation	:	Remarks: The substance has low potential for

bioaccumulation.

Mobility in soil

Components:

Metformin Hydrochloride:

Mobility : Remarks: Water solubility >= 1 mg/l.

Distribution among environmental compartments : Remarks: No information available.

Dapagliflozin:

Mobility : Remarks: Water solubility >= 1 mg/l.

Distribution among environmental compartments : Remarks: No information available.

Other adverse effects

No data available

SECTION 13. DISPOSAL CONSIDERATIONS

Disposal methods

Waste from residues : Disposal should be in accordance with local, state or national legislation.
Waste, even small quantities, should never be poured down drains, sewers or water courses.
Normal waste disposal is via incineration operated by an accredited disposal contractor.

Contaminated packaging : Empty container will retain product residue. Observe all hazard precautions.

SECTION 14. TRANSPORT INFORMATION

Not classified as dangerous in the meaning of transport regulations.

SECTION 15. REGULATORY INFORMATION

Safety, health and environmental regulations/legislation specific for the substance or mixture

In order to comply with legal duties it is necessary to consult local and national legislation.

Standard for the Uniform Scheduling of Medicines and Poisons	:	No poison schedule number allocated
Prohibition/Licensing Requirements	:	There is no applicable prohibition or notification/licensing requirements, including for carcinogens under Commonwealth, State or Territory legislation.

The components of this product are reported in the following inventories:

REACH	:	Not listed
DSL	:	This product contains the following components that are not on the Canadian DSL nor NDSL.
Metformin Hydrochloride		1115-70-4
Dapagliflozin		960404-48-2
AICS	:	Not listed
ENCS	:	Not listed
ISHL	:	Not listed
IECSC	:	Not listed
TCSI	:	Not listed
TSCA	:	Not On TSCA Inventory

SECTION 16. OTHER INFORMATION

Full text of other abbreviations

AICS - Australian Inventory of Chemical Substances; ANTT - National Agency for Transport by Land of Brazil; ASTM - American Society for the Testing of Materials; bw - Body weight; CMR - Carcinogen, Mutagen or Reproductive Toxicant; CPR - Controlled Products Regulations; DIN - Standard of the German Institute for Standardisation; DSL - Domestic Substances List (Canada); ECx - Concentration associated with x% response; ELx - Loading rate associated with x% response; EmS - Emergency Schedule; ENCS - Existing and New Chemical Substances (Japan); ErCx - Concentration associated with x% growth rate response; ERG - Emergency Response Guide; GHS - Globally Harmonized System; GLP - Good Laboratory Practice; IARC - International Agency for Research on Cancer; IATA - International Air Transport Association; IBC - International Code for the Construction and Equipment of Ships carrying Dangerous Chemicals in Bulk; IC50 - Half maximal inhibitory concentration; ICAO - International Civil Aviation Organization; IECSC - Inventory of Existing Chemical Substances in China; IMDG - International Maritime Dangerous Goods; IMO - International Maritime Organization; ISHL - Industrial Safety and Health Law (Japan); ISO - International Organisation for Standardization; KECI - Korea Existing Chemicals Inventory; LC50 - Lethal Concentration to 50 % of a test population; LD50 - Lethal Dose to 50% of a test population (Median Lethal Dose); MARPOL - International Convention for the Prevention of Pollution from Ships; n.o.s. - Not Otherwise Specified; Nch -

Chilean Norm; NO(A)EC - No Observed (Adverse) Effect Concentration; NO(A)EL - No Observed (Adverse) Effect Level; NOELR - No Observable Effect Loading Rate; NOM - Official Mexican Norm; NTP - National Toxicology Program; NZIoC - New Zealand Inventory of Chemicals; OECD - Organization for Economic Co-operation and Development; OPPTS - Office of Chemical Safety and Pollution Prevention; PBT - Persistent, Bioaccumulative and Toxic substance; PICCS - Philippines Inventory of Chemicals and Chemical Substances; (Q)SAR - (Quantitative) Structure Activity Relationship; REACH - Regulation (EC) No 1907/2006 of the European Parliament and of the Council concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals; SADT - Self-Accelerating Decomposition Temperature; SDS - Safety Data Sheet; TCSI - Taiwan Chemical Substance Inventory; TDG - Transportation of Dangerous Goods; TSCA - Toxic Substances Control Act (United States); UN - United Nations; UNRTDG - United Nations Recommendations on the Transport of Dangerous Goods; vPvB - Very Persistent and Very Bioaccumulative; WHMIS - Workplace Hazardous Materials Information System

Further information

Revision Date	:	08.02.2018
Other information	:	New significant SHE information:, 8. New Occupational Exposure Limit Value, Minor changes:, 3, 8, 12, 15, 16
Date format	:	dd.mm.yyyy
ACGIH	:	USA. ACGIH Threshold Limit Values (TLV)
AU OEL	:	Australia. Workplace Exposure Standards for Airborne Contaminants.
ACGIH / TWA	:	8-hour, time-weighted average
AU OEL / TWA	:	Exposure standard - time weighted average

The information provided in this Safety Data Sheet is correct to the best of our knowledge, information and belief at the date of its publication. The information given is designed only as a guidance for safe handling, use, processing, storage, transportation, disposal and release and is not to be considered a warranty or quality specification. The information relates only to the specific material designated and may not be valid for such material used in combination with any other materials or in any process, unless specified in the text.

AU / EN