

Version 7.0 Revision Date: 22.11.2019 SDS Number: 11653 Date of last issue: 08.02.2018
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 Emergency Telephone
PO Box 131 +44 (0) 1235 239 670
66 Talavera Rd, North Ryde
NSW 2113
AUSTRALIA
+61 2 9978 3500

SafetyDataSheets.AlderleyPark@astrazeneca.com

Alternative Names

Dapagliflozin and metformin hydrochloride tablets
Dapagliflozin and Metformin Hydrochloride IR Tablets 2,5/850 mg, 2,5/1000 mg, 5/850 mg, 5/1000 mg
Dapagliflozin and Metformin Hydrochloride XR Tablets 5/500 mg, 5/1000 mg, 10/500 mg, 10/1000 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.

Version 7.0 Revision Date: 22.11.2019 SDS Number: 11653 Date of last issue: 08.02.2018
Date of first issue: 31.08.2017

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.

Other hazards which do not result in classification

May cause nausea, vomiting, severe abdominal pain and diarrhoea.

May cause hypoglycemia.

See Section 11.

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

Components

| Chemical name | CAS-No. | Concentration (% w/w) |
|-------------------------|-------------|-----------------------|
| Metformin Hydrochloride | 1115-70-4 | 36 -68 |
| Celluloses | 9004-34-6 | 20 -54 |
| Dapagliflozin | 960404-48-2 | 0.2 -0.9 |

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.

SAFETY DATA SHEET



Version 7.0 Revision Date: 22.11.2019 SDS Number: 11653 Date of last issue: 08.02.2018
Date of first issue: 31.08.2017

- 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.
See Section 8.
- 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/m ³ | COM; HYG |
| Celluloses | 9004-34-6 | TWA | 10 mg/m ³ | AU OEL |
| | Further information: This value is for inhalable dust containing no asbestos and < 1% crystalline silica | | | |
| | | TWA | 10 mg/m ³ | ACGIH |
| Dapagliflozin | 960404-48-2 | TWA | 0.01 mg/m ³ | 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

| | | | |
|---------|----------------|-------------|---------------------------------|
| Version | Revision Date: | SDS Number: | Date of last issue: 08.02.2018 |
| 7.0 | 22.11.2019 | 11653 | Date of first issue: 31.08.2017 |

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 : Xiduo IR tablets:, 2,5/850 mg - white; 2,5/1000 mg - orange; 5/850 mg - brown; 5/1000 mg - yellow, Xigudo XR tablets:, 5/500 mg - orange; 5/1000 mg - pink; 10/500 - pink; 10/1000 - yellow
- Odour : No data available

SAFETY DATA SHEET



Version 7.0 Revision Date: 22.11.2019 SDS Number: 11653 Date of last issue: 08.02.2018
Date of first issue: 31.08.2017

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 : Not applicable

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 : Not explosive

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 : None known.

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|---------|----------------|-------------|---------------------------------|
| Version | Revision Date: | SDS Number: | Date of last issue: 08.02.2018 |
| 7.0 | 22.11.2019 | 11653 | Date of first issue: 31.08.2017 |

reactions

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 in vivo.

Version 7.0 Revision Date: 22.11.2019 SDS Number: 11653 Date of last issue: 08.02.2018
Date of first issue: 31.08.2017

11.3 Serious eye damage/eye irritation

Not classified based on available information.

Components:

Metformin Hydrochloride:

Remarks : May cause slight eye irritation.

Dapagliflozin:

Result : Irritating to eyes.

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 carcinogenicity in animal studies.

| | | | |
|---------|----------------|-------------|---------------------------------|
| Version | Revision Date: | SDS Number: | Date of last issue: 08.02.2018 |
| 7.0 | 22.11.2019 | 11653 | Date of first issue: 31.08.2017 |

Dapagliflozin:

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

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.

| | | | |
|---------|----------------|-------------|---------------------------------|
| Version | Revision Date: | SDS Number: | Date of last issue: 08.02.2018 |
| 7.0 | 22.11.2019 | 11653 | Date of first issue: 31.08.2017 |

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/aquatic plants | : | 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 |
|---|---|---|

SAFETY DATA SHEET



Version 7.0 Revision Date: 22.11.2019 SDS Number: 11653 Date of last issue: 08.02.2018
Date of first issue: 31.08.2017

- NOEC (*Daphnia magna* (Water flea)): 120 mg/l
Exposure time: 48 h
Method: OECD Test Guideline 202
- Toxicity to algae/aquatic plants : ErC50 (green algae): 120 mg/l
Exposure time: 72 h
Method: OECD Test Guideline 201
- 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
- NOEC (*Chironomus riparius* (harlequin fly)): 150 mg/l
Exposure time: 28 d
Method: OECD Test Guideline 218
- Toxicity to microorganisms : EC50 (Sewage sludge organisms): > 200 mg/l
Exposure time: 3 h
Test Type: Respiration inhibition
Method: OECD Test Guideline 209
- NOEC (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 %
Exposure time: 28 d
Method: OECD Test Guideline 301F
Remarks: Not rapidly degradable.
The substance is not significantly hydrolyzed in water.

Version 7.0 Revision Date: 22.11.2019 SDS Number: 11653 Date of last issue: 08.02.2018
Date of first issue: 31.08.2017

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 \geq 1 mg/l.

Distribution among environmental compartments : Remarks: No information available.

Dapagliflozin:

Mobility : Remarks: Water solubility \geq 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.
Dispose of contents/ container to an approved incineration plant.

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.

| | | | |
|---------|----------------|-------------|---------------------------------|
| Version | Revision Date: | SDS Number: | Date of last issue: 08.02.2018 |
| 7.0 | 22.11.2019 | 11653 | Date of first issue: 31.08.2017 |

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:

| | | |
|-------|---|---|
| TCSI | : | Not listed |
| TSCA | : | Substance(s) not listed on TSCA inventory |
| AICS | : | Not listed |
| DSL | : | This product contains the following components that are not on the Canadian DSL nor NDSL. Metformin Hydrochloride Dapagliflozin |
| ENCS | : | Not listed |
| ISHL | : | Not listed |
| KECI | : | Not listed |
| IECSC | : | Not listed |
| CHINV | : | Not in compliance with the inventory |
| REACH | : | Not in compliance with the inventory |
| TRINV | : | Not in compliance with the inventory |

SECTION 16. OTHER INFORMATION**Further information**

Revision Date : 22.11.2019

SAFETY DATA SHEET



Version 7.0 Revision Date: 22.11.2019 SDS Number: 11653 Date of last issue: 08.02.2018
Date of first issue: 31.08.2017

Other information : New significant SHE information:
3. Composition/information on ingredients
8. Occupational Exposure Limit Value
Minor changes:
1
2
3
9
11
12
13
15
16

Date format : dd.mm.yyyy

Full text of other abbreviations

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

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; CHINV - China Inventory; CMR - Carcinogen, Mutagen or Reproductive Toxicant; COM - In-house occupational exposure limit; CPR - Controlled Products Regulations; 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; HYG - Analytical method for occupational exposure monitoring; IARC - International Agency for Research on Cancer; IATA - International Air Transport Association; 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; LC50 - Lethal Concentration to 50 % of a test population; LD50 - Lethal Dose to 50% of a test population (Median Lethal Dose); 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; OECD - Organization for Economic Co-operation and Development; OPPTS - Office of Chemical Safety and Pollution Prevention; PBT - Persistent, Bioaccumulative and Toxic substance; (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; Sen - Capable of causing respiratory sensitization; Sk - Can be absorbed through skin, thus contributing to systemic effects; STEL - Short-term exposure limit 15-minutes time-weighted average; TLV - Threshold Limit Value (ACGIH); TLV-C - Threshold Limit Value Ceiling limit (ACGIH); TRINV - Turkey Inventory; TSCA - Toxic Substances Control Act (United States); TWA - Long-term exposure limit 8h time-weighted average; 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

SAFETY DATA SHEET



| | | | |
|---------|----------------|-------------|---------------------------------|
| Version | Revision Date: | SDS Number: | Date of last issue: 08.02.2018 |
| 7.0 | 22.11.2019 | 11653 | Date of first issue: 31.08.2017 |

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