Version	Revision Date:	SDS Number:	Date of last issue: 20.08.2019
4.0	12.08.2020	21218	Date of first issue: 18.07.2017

SECTION 1. PRODUCT AND COMPANY IDENTIFICATION

1.1 Product identifier

KOMBIGLYZE XR TABLETS

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

SafetyDataSheets.AlderleyPark@astrazeneca.com

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+44 (0) 1235 239 670

Alternative Names

Saxagliptin/Metformin hydrochloride extended release tablets
Saxagliptin/Metformin hydrochloride film coated extended release tablets
Metformin hydrochloride extended release tablets

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

Respiratory sensitisation : Category 1

Skin sensitisation : Category 1

GHS label elements

Hazard pictograms :

Signal word : Danger

Hazard statements : H302 Harmful if swallowed.
H317 May cause an allergic skin reaction.
H334 May cause allergy or asthma symptoms or breathing difficulties if inhaled.

Precautionary statements :

Prevention:

P261 Avoid breathing dust/ fume/ gas/ mist/ vapours/ spray.
P264 Wash skin thoroughly after handling.
P272 Contaminated work clothing should not be allowed out of the workplace.
P280 Wear protective gloves.
P285 In case of inadequate ventilation wear respiratory protection.

Response:

P301 + P312 + P330 IF SWALLOWED: Call a POISON CENTER or doctor/ physician if you feel unwell. Rinse mouth.
P302 + P352 IF ON SKIN: Wash with plenty of soap and water.
P304 + P341 IF INHALED: If breathing is difficult, remove victim to fresh air and keep at rest in a position comfortable for breathing.
P333 + P313 If skin irritation or rash occurs: Get medical advice/ attention.
P342 + P311 If experiencing respiratory symptoms: Call a POISON CENTER or doctor/ physician.

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.
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	42 -61
Celluloses	9004-34-6	< 35
Titanium dioxide	13463-67-7	< 5
Talc	14807-96-6	< 5
Saxagliptin	945667-22-1	0.1 -0.5

SECTION 4. FIRST AID MEASURES

If inhaled : Remove patient from exposure, keep warm and at rest.
OBTAIN IMMEDIATE MEDICAL ATTENTION.

In case of skin contact : Take off all contaminated clothing immediately.
After contact with skin, wash immediately with plenty of water.
Obtain immediate medical attention.

In case of eye contact : Immediately irrigate with eyewash solution or clean water, holding the eyelids apart, for at least 10 minutes.
Obtain medical attention.

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

Most important symptoms : Refer to sections 2 and 11

and effects, both acute and delayed		Harmful if swallowed. May cause an allergic skin reaction. May cause allergy or asthma symptoms or breathing difficulties if inhaled.
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	:	Avoid dispersal of dust in the air. Ensure full personal protection (including respiratory protection) during removal of spillages. See Section 8.
Environmental precautions	:	Prevent entry into drains, sewers or watercourses.
Methods and materials for containment and cleaning up	:	Moisten spillages with water. Transfer to a container for disposal. Wash the spillage area with water. See section 13.

SECTION 7. HANDLING AND STORAGE

Advice on safe handling	:	Avoid contact with skin and eyes. Do not breathe dust. Minimize dust generation and accumulation. The product may form flammable dust clouds in air, if dust from crushed tablets is allowed to accumulate. Ensure good earthing of equipment and personnel. Dust clouds may be extremely sensitive to ignition by electrostatic discharge and other ignition sources.
Conditions for safe storage	:	Store in original container. Keep container tightly closed and dry.
Recommended storage temperature	:	15 - 25 °C

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
Celluloses	9004-34-6	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	ACGIH
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
Saxagliptin	945667-22-1	TWA	10 µg/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 a self-contained breathing apparatus 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 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	:	light brown, brown, pink, pale yellow, light 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	:	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	:	Not applicable
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	:	No data available

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: 819.67 mg/kg Method: Calculation method
Acute inhalation toxicity	:	Remarks: May cause effects as described under single exposure.(STOT)
Acute dermal toxicity	:	Remarks: No information available.

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 information available.

Saxagliptin:

Acute oral toxicity : LD50 Oral (Rat): > 2,000 mg/kg
Assessment: The substance or mixture has no acute oral toxicity

Acute inhalation toxicity : Remarks: May cause effects as described under sensitisation.

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.

Saxagliptin:

Remarks : Unlikely to cause skin irritation.

11.3 Serious eye damage/eye irritation

Not classified based on available information.

Components:

Metformin Hydrochloride:

Remarks : May cause slight eye irritation.

Saxagliptin:

Remarks : Unlikely to cause eye irritation.

11.4 Respiratory or skin sensitisation

Skin sensitisation

May cause an allergic skin reaction.

Respiratory sensitisation

May cause allergy or asthma symptoms or breathing difficulties if inhaled.

Components:

Metformin Hydrochloride:

Remarks : No information available.

Saxagliptin:

Result : The product is a skin sensitiser, sub-category 1A.

: The product is a respiratory sensitiser, sub-category 1A.

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.

Saxagliptin:

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

11.6 Carcinogenicity

Not classified based on available information.

Components:

Metformin Hydrochloride:

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

Saxagliptin:

Carcinogenicity - Assessment : Studies in animals have shown that repeated doses produce no carcinogenic effects.

11.7 Reproductive toxicity

Not classified based on available information.

Components:

Metformin Hydrochloride:

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

Saxagliptin:

Reproductive toxicity - Assessment : Some evidence of adverse effects on sexual function and fertility, based on animal experiments., Some evidence of adverse effects on development, based on animal experiments., Studies in animals have shown that high doses produce adverse reproductive effects in the presence of maternal toxicity.

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.

Saxagliptin:

Exposure routes : Oral
Remarks : High exposure effects include hyperactivity and increased respiration.
May cause effects as described under sensitisation.

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.

Saxagliptin:

Exposure routes : Oral
Target Organs : Endocrine system, Immune system, Skin
Assessment : Causes damage to organs through prolonged or repeated exposure.
Remarks : Studies in animals have shown that repeated doses produce adverse effects on the heart, kidneys and liver.
Ingestion studies in animals have shown that repeated doses produce adverse effects on the gastrointestinal tract.
Based on human experience.
May cause headache, nausea, vomiting, diarrhoea and skin rash.
May cause a decreased white blood cell count.

11.10 Aspiration toxicity

Not classified based on available information.

Components:

Metformin Hydrochloride:

No information available.

Saxagliptin:

No information available.

Further information

Product:

Remarks : This health hazard assessment is based on a consideration of the composition of this product.

SECTION 12. ECOLOGICAL INFORMATION

Ecotoxicity

Product:

Ecotoxicology Assessment

Chronic aquatic toxicity : This product has no known ecotoxicological effects.

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

Saxagliptin:

Toxicity to fish : LC50 (Brachydanio rerio (zebrafish)): > 91 mg/l
Exposure time: 96 h
Method: OECD Test Guideline 203

Toxicity to algae/aquatic plants : ErC50 (green algae): > 140 mg/l
Exposure time: 72 h
Test Type: growth rate
Method: OECD Test Guideline 201

Toxicity to fish (Chronic toxicity) : NOEC (Pimephales promelas (fathead minnow)): 9.5 mg/l
Exposure time: 32 d
Method: OECD Test Guideline 210

Toxicity to daphnia and other : NOEC (Daphnia magna (Water flea)): 35 mg/l

aquatic invertebrates (Chronic toxicity)		Exposure time: 21 d Method: OECD Test Guideline 211
Toxicity to microorganisms	:	NOEC (Sewage sludge organisms): 821 mg/l Exposure time: 3 h 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

Saxagliptin:

Biodegradability	:	aerobic Result: Not readily biodegradable. Biodegradation: 5.9 % Exposure time: 28 d Method: OECD Test Guideline 310 Remarks: Carbon dioxide evolution

Bioaccumulative potential

Components:

Metformin Hydrochloride:

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

Saxagliptin:

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.

Saxagliptin:

Mobility	:	Remarks: The substance has high mobility in soil. Hydrolysed by water.
Distribution among	:	Remarks: No information available.

environmental compartments

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 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:

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 Saxagliptin
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	:	12.08.2020
Other information	:	Full Review - minor changes 6 9 11 15
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

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.

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