Version	Revision Date:	SDS Number:	Date of last issue: 18.07.2017
2.0	29.01.2018	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
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SafetyDataSheets.AlderleyPark@astrazeneca.com

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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.

Hazardous components which must be listed on the label:

Metformin Hydrochloride
Saxagliptin

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

Hazardous 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 and effects, both acute and delayed	:	Refer to sections 2 and 11 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.

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	:	No data available
Flash point	:	No data available
Evaporation rate	:	No data available
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	:	No data available
Relative vapour density	:	No data available
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 : No data available

Viscosity, kinematic : No data available

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 data available

Saxagliptin:

Acute oral toxicity	:	LD50 Oral (Rat): > 300 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.

Result: 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 carcinogencity 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.

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, Inhalation
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.
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	:	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	:	EC50 (Brachydanio rerio (zebrafish)): > 91 mg/l Exposure time: 96 H
Toxicity to algae	:	ErC50 (green algae): > 140 mg/l Test Type: growth rate
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 aquatic invertebrates (Chronic toxicity)	:	NOEC (Daphnia magna (Water flea)): 35 mg/l Exposure time: 21 d

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 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 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

Saxagliptin		945667-22-1
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	:	29.01.2018
Other information	:	New significant SHE information:, 8. New Occupational Exposure Limit Value, Minor changes:, 3, 8, 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.

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