SECTION-1: Identification of the substance / mixture and the company / undertaking

Catalogue Number	CS-SS-26558
Product Name	Metformin Secondary standard
CAS No.	657-24-9
Category	Secondary Standards
Synonyms	"1,1-Dimethylbiguanide"
Brand	Clearsynth Labs Ltd.
Identified uses	Laboratory Chemicals
Uses advised against	Not available
Company	Clearsynth Labs Ltd. Mumbai, India
Emergency Phone #	+91-22-245045900
REACH No.	Not available

SECTION 2: Hazards identification

Disclaimer: This is sample MSDS. Please email **sales@clearsynth.com** for more details.

2.1 Classification of the substance or mixture-Regulation (EC) No 1272/2008:

Skin irritation (Category 2)
Serious eye damage/eye irritation (Category 2)
Acute toxicity (Category 4)

2.2 Label Elements

Signal Word: Warning

Hazard Statement(s)

Code	Statement
H302	Harmful if swallowed.
H315	Causes skin irritation.

H319	Causes serious eye irritation.

Precautionary Statement(s)

Code	Statement
P264	Wash hands thoroughly after handling.
P270	Not available
P301+P317	Not available
P330	Not available
P501	Dispose of contents/container in accordance with local/regional/national/international regulatio
P264+P265	Not available
P280	Wear protective gloves/protective clothing/eye protection/face protection.
P302+P352	IF ON SKIN: Wash with plenty of water and soap.
P305+P351+P338	IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if presen
P321	Specific treatment (see … on this label).
P332+P317	If skin irritation occurs: Get medical help.
P337+P317	If eye irritation persists: Get medical help.
P362+P364	Take off contaminated clothing and wash it before reuse.

SECTION 3: Composition / information on ingredients

3.1 Substance

Component : Metformin Secondary standard
CAS Number : 657-24-9
Molecular Formula : C■H■■N■
Molecular Weight : 129.16
Parent Chemical : Metformin
Synonyms : "1,1-Dimethylbiguanide"
Concentration : Not available

SECTION 4: First aid measures

SECTION 4: First-aid measures

4.1 Description of first aid measures
- General advice: Remove from exposure. Show this SDS to medical personnel if available.
- Inhalation: Move person to fresh air. If symptoms persist, get medical attention.
- Skin contact: Wash with soap and water. Remove contaminated clothing and wash before reuse. Get medical attention if irritation persists.

- Eye contact: Rinse cautiously with water for several minutes. Remove contact lenses if present and easy to do. Continue rinsing. Get medical attention if irritation persists.
- Ingestion: Rinse mouth. Do not induce vomiting unless directed by medical personnel. Get medical attention.

4.2 Most important symptoms/effects, acute and delayed
- Not available.

4.3 Indication of immediate medical attention and special treatment needed
- Treat symptomatically. No data available.

SECTION 5: Firefighting measures

SECTION 5: Fire-fighting measures

5.1 Suitable extinguishing media
- Water spray, alcohol-resistant foam, dry chemical, or carbon dioxide.

5.2 Special hazards arising from the substance or mixture
- No data available. Thermal decomposition may produce irritating and/or toxic fumes.

5.3 Advice for firefighters
- Wear self-contained breathing apparatus (SCBA) and full protective gear.
- Use water spray to cool unopened containers.

5.4 Hazardous combustion products
- Not available.

SECTION 6: Accidental release measures

SECTION 6: Accidental release measures

6.1 Personal precautions, protective equipment and emergency procedures
- Avoid dust formation and inhalation.
- Use appropriate personal protective equipment (see Section 8).
- Ensure adequate ventilation.

6.2 Environmental precautions
- Avoid release to the environment. Prevent entry into drains, surface water, or soil.

6.3 Methods and material for containment and cleaning up
- Sweep up or vacuum without generating dust; place in a suitable, closed container for disposal.
- Clean spill area with water after material pickup, as appropriate.

6.4 Reference to other sections
- See Section 8 for exposure controls/personal protection and Section 13 for disposal considerations.

SECTION-7: Handling and storage

SECTION 7: Handling and storage

7.1 Precautions for safe handling
- Handle in accordance with good industrial hygiene and safety practice.
- Avoid contact with eyes, skin, and clothing.

- Avoid breathing dust. Use with adequate ventilation.
- Keep container tightly closed when not in use.

7.2 Conditions for safe storage, including any incompatibilities
- Store in a cool, dry, well-ventilated place.
- Protect from moisture.
- Incompatibilities: Not available.

7.3 Specific end use(s)
- Laboratory/research use as a secondary standard. Not for food, drug, or household use.

SECTION 8: Exposure controls / personal protection

SECTION 8: Exposure controls/personal protection

8.1 Control parameters
- Occupational exposure limits: Not available.
- Biological limit values: Not available.

8.2 Exposure controls
- Engineering controls: Provide adequate ventilation. Use local exhaust where dust may be generated.
- Personal protective equipment (PPE):
- Eye/face protection: Safety glasses with side shields or chemical splash goggles.
- Skin protection: Protective gloves. Wear lab coat or suitable protective clothing.
- Respiratory protection: If ventilation is inadequate or dust is generated, use a suitable particulate respirator per applicable standards.
- Hygiene measures: Wash hands after handling. Do not eat, drink, or smoke when using this product.

SECTION 9: Physical and chemical properties

9.1 Information on basic physical and chemical properties

Test	Result
Appearance	No data available
IR spectrum	No data available
pH	No data available
Solubility	No data available

Property	Value
a) Physical State	No data available
b) Color	No data available
c) Odor	No data available

Property	Value
d) pH	2.7
e) Vapour Pressure	No data available
f) Viscosity	No data available
g) Initial Boiling Point and boiling range	No data available
h) Melting Point / Freezing Point	No data available
i) Auto Ignition Temperature	No data available
j) Flash Point	No data available
k) Explosion Limit, Lower	No data available
l) Explosion Limit, Upper	No data available
m) Decomposition Temperature	No data available
n) Loss on Drying	No data available
o) Relative Density	No data available
p) Solubility (in DMSO)	No data available
q) Oxidizing Properties	No data available

SECTION 10: Stability and reactivity

SECTION 10: Stability and reactivity

10.1 Reactivity
- No data available.

10.2 Chemical stability
- Stable under recommended storage conditions.

10.3 Possibility of hazardous reactions
- No data available.

10.4 Conditions to avoid
- Avoid dust generation. Avoid moisture exposure. Other conditions: Not available.

10.5 Incompatible materials
- Not available.

10.6 Hazardous decomposition products
- Not available.

SECTION 11: Toxicological information

11.1 Information on toxicological effects

- Acute toxicity: IDENTIFICATION AND USE: Metformin is antihyperglycemic, not hypoglycemic agent. It does not cause insulin release from the pancreas and does not cause hypoglycemia, even in large doses. HUMAN EXPOSURE AND TOXICITY: Metformin is believed to work by inhibiting hepatic glucose production and increasing the sensitivity of peripheral tissue to insulin. It does not stimulate insulin secretion, which explains the absence of hypoglycemia. Metformin also has beneficial effects on the plasma lipid concentrations and promotes weight loss. Accumulation of metformin may occur in patients with renal impairment, and such accumulation rarely can result in lactic acidosis, a serious, potentially fatal metabolic disease. Lactic acidosis constitutes a medical emergency requiring immediate hospitalization and treatment; lactic acidosis is characterized by elevated blood lactate concentrations, decreased blood pH, electrolyte disturbances with an increased anion gap, and an increased lactate/pyruvate ratio. Lactic acidosis also may occur in association with a variety of pathophysiologic conditions, including diabetes mellitus, and whenever substantial tissue hypoperfusion and hypoxemia exist. Approximately 50% of cases of metformin-associated lactic acidosis have been reported to be fatal. No evidence of mutagenicity or chromosomal damage was observed in in vitro test systems, including human lymphocytes assay. ANIMAL STUDIES: No evidence of carcinogenic potential was seen in a 104-week study in male and female rats receiving metformin hydrochloride dosages up to and including 900 mg/kg daily or in a 91-week study in male and female mice receiving metformin hydrochloride at dosages up to and including 1500 mg/kg daily. Cancer preventive effect of metformin (MF) has been studied in mice, rats and hamsters. In the majority of cases metformin treatment leads to inhibition of carcinogenesis. No evidence of impaired fertility was observed in rats following administration of metformin hydrochloride dosages of 600 mg/kg daily. Reproduction studies in rats and rabbits given metformin hydrochloride dosages of 600 mg/kg daily have not revealed teratogenicity. No evidence of mutagenicity or chromosomal damage was observed in vivo in a micronucleus test in mice or in in vitro test systems, including microbial (Ames test) and mammalian (mouse lymphoma) assays. Pretreatment of rat cerebellar granule neurons with metformin greatly enhanced cell viability against glutamate-induced neurotoxicity. In aged male mice fed high-fat diet supplemented with metformin for 6 months, metformin decreased body fat composition and attenuated declines in motor function induced by a high fat diet. Performance in the Morris water maze test of hippocampal based memory function, showed that metformin prevented impairment of spatial reference memory associated with the high fat diet. ECOTOXICITY STUDIES: Adult fathead minnows (Pimephales promelas) were chronically exposed to metformin for 4 wk, at 40 ug/L. Metformin treatment induced significant up-regulation of messenger ribonucleic acid (mRNA) encoding the egg-protein vitellogenin in male fish, an indication of endocrine disruption. Metformin overdose is associated with hypoglycemia and lactic acidosis. If the clinicians suspect lactic acidosis due to toxic metformin levels, they immediately recommend discontinuing the medication and initiating hemodialysis. Metformin is easily dialyzable owing to its small molecular weight and minimal protein binding. In cases of metformin toxicity, treatment primarily involves supportive care, as no specific antidote is available yet.
- Skin corrosion/irritation: No data available.
- Serious eye damage/eye irritation: No data available.
- Respiratory or skin sensitization: No data available.
- Germ cell mutagenicity: IDENTIFICATION AND USE: Metformin is antihyperglycemic, not hypoglycemic agent. It does not cause insulin release from the pancreas and does not cause hypoglycemia, even in large doses. HUMAN EXPOSURE AND TOXICITY: Metformin is believed to work by inhibiting hepatic glucose production and increasing the sensitivity of peripheral tissue to insulin. It does not stimulate insulin secretion, which explains the absence of hypoglycemia. Metformin also has beneficial effects on the plasma lipid concentrations and promotes weight loss. Accumulation of metformin may occur in patients with renal impairment, and such accumulation rarely can result in lactic acidosis, a serious, potentially fatal metabolic disease. Lactic acidosis constitutes a medical emergency requiring immediate hospitalization and treatment; lactic acidosis is characterized by elevated blood lactate concentrations, decreased blood pH, electrolyte disturbances with an increased anion gap, and an increased lactate/pyruvate ratio. Lactic acidosis also may occur in association with a variety of pathophysiologic conditions,

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- Carcinogenicity: IDENTIFICATION AND USE: Metformin is antihyperglycemic, not hypoglycemic agent. It does not cause insulin release from the pancreas and does not cause hypoglycemia, even in large doses. HUMAN EXPOSURE AND TOXICITY: Metformin is believed to work by inhibiting hepatic glucose production and increasing the sensitivity of peripheral tissue to insulin. It does not stimulate insulin secretion, which explains the absence of hypoglycemia. Metformin also has beneficial effects on the plasma lipid concentrations and promotes weight loss. Accumulation of metformin may occur in patients with renal impairment, and such accumulation rarely can result in lactic acidosis, a serious, potentially fatal metabolic disease. Lactic acidosis constitutes a medical emergency requiring immediate hospitalization and treatment; lactic acidosis is characterized by elevated blood lactate concentrations, decreased blood pH, electrolyte disturbances with an increased anion gap, and an increased lactate/pyruvate ratio. Lactic acidosis also may occur in association with a variety of pathophysiologic conditions, including diabetes mellitus, and whenever substantial tissue hypoperfusion and hypoxemia exist. Approximately 50% of cases of metformin-associated lactic acidosis have been reported to be fatal. No evidence of mutagenicity or chromosomal damage was observed in in vitro test systems, including human lymphocytes assay. ANIMAL STUDIES: No evidence of carcinogenic potential was seen in a 104-week study in male and female rats receiving metformin hydrochloride dosages up to and including 900 mg/kg daily or in a 91-week study in male and female mice receiving metformin hydrochloride at dosages up to and including 1500 mg/kg daily. Cancer preventive effect of metformin (MF) has been studied in mice, rats and hamsters. In the majority of cases metformin treatment leads to inhibition of carcinogenesis. No evidence of impaired fertility was observed in rats following administration of metformin hydrochloride dosages of 600 mg/kg daily. Reproduction studies in rats and rabbits given metformin hydrochloride dosages of 600 mg/kg daily have not revealed teratogenicity. No evidence of mutagenicity or chromosomal damage was observed in vivo in a micronucleus test in mice or in in vitro test systems, including microbial (Ames test) and mammalian (mouse lymphoma) assays. Pretreatment of rat cerebellar granule neurons with metformin greatly enhanced cell viability against glutamate-induced neurotoxicity. In aged male mice fed high-fat diet supplemented with metformin for 6 months, metformin decreased body fat composition and attenuated declines in motor function induced by a high fat diet. Performance in the Morris water maze test of hippocampal based memory function, showed that metformin prevented impairment of spatial reference memory associated with the high fat diet. ECOTOXICITY STUDIES: Adult fathead minnows (Pimephales promelas) were chronically

exposed to metformin for 4 wk, at 40 ug/L. Metformin treatment induced significant up-regulation of messenger ribonucleic acid (mRNA) encoding the egg-protein vitellogenin in male fish, an indication of endocrine disruption. /LABORATORY ANIMALS: Chronic Exposure or Carcinogenicity/ Long-term use of anti-diabetic agents has become commonplace as rates of obesity, metabolic syndrome and diabetes continue to escalate. Metformin, a commonly used anti-diabetic drug, has been shown to have many beneficial effects outside of its therapeutic regulation of glucose metabolism and insulin sensitivity. Studies on metformin's effects on the central nervous system are limited and predominantly consist of in vitro studies and a few in vivo studies with short-term treatment in relatively young animals; some provide support for metformin as a neuroprotective agent while others show evidence that metformin may be deleterious to neuronal survival. In this study, we examined the effect of long-term metformin treatment on brain neurotrophins and cognition in aged male C57Bl/6 mice. Mice were fed control (C), high-fat (HF) or a high-fat diet supplemented with metformin (HFM) for 6 months. Metformin decreased body fat composition and attenuated declines in motor function induced by a HF diet. Performance in the Morris water maze test of hippocampal based memory function, showed that metformin prevented impairment of spatial reference memory associated with the HF diet. Quantitative RT-PCR on brain homogenates revealed decreased transcription of BDNF, NGF and NTF3; however protein levels were not altered. Metformin treatment also decreased expression of the antioxidant pathway regulator, Nrf2. The decrease in transcription of neurotrophic factors and Nrf2 with chronic metformin intake, cautions of the possibility that extended metformin use may alter brain biochemistry in a manner that creates a vulnerable brain environment and warrants further investigation.
- Reproductive toxicity: IDENTIFICATION AND USE: Metformin is antihyperglycemic, not hypoglycemic agent. It does not cause insulin release from the pancreas and does not cause hypoglycemia, even in large doses. HUMAN EXPOSURE AND TOXICITY: Metformin is believed to work by inhibiting hepatic glucose production and increasing the sensitivity of peripheral tissue to insulin. It does not stimulate insulin secretion, which explains the absence of hypoglycemia. Metformin also has beneficial effects on the plasma lipid concentrations and promotes weight loss. Accumulation of metformin may occur in patients with renal impairment, and such accumulation rarely can result in lactic acidosis, a serious, potentially fatal metabolic disease. Lactic acidosis constitutes a medical emergency requiring immediate hospitalization and treatment; lactic acidosis is characterized by elevated blood lactate concentrations, decreased blood pH, electrolyte disturbances with an increased anion gap, and an increased lactate/pyruvate ratio. Lactic acidosis also may occur in association with a variety of pathophysiologic conditions, including diabetes mellitus, and whenever substantial tissue hypoperfusion and hypoxemia exist. Approximately 50% of cases of metformin-associated lactic acidosis have been reported to be fatal. No evidence of mutagenicity or chromosomal damage was observed in in vitro test systems, including human lymphocytes assay. ANIMAL STUDIES: No evidence of carcinogenic potential was seen in a 104-week study in male and female rats receiving metformin hydrochloride dosages up to and including 900 mg/kg daily or in a 91-week study in male and female mice receiving metformin hydrochloride at dosages up to and including 1500 mg/kg daily. Cancer preventive effect of metformin (MF) has been studied in mice, rats and hamsters. In the majority of cases metformin treatment leads to inhibition of carcinogenesis. No evidence of impaired fertility was observed in rats following administration of metformin hydrochloride dosages of 600 mg/kg daily. Reproduction studies in rats and rabbits given metformin hydrochloride dosages of 600 mg/kg daily have not revealed teratogenicity. No evidence of mutagenicity or chromosomal damage was observed in vivo in a micronucleus test in mice or in in vitro test systems, including microbial (Ames test) and mammalian (mouse lymphoma) assays. Pretreatment of rat cerebellar granule neurons with metformin greatly enhanced cell viability against glutamate-induced neurotoxicity. In aged male mice fed high-fat diet supplemented with metformin for 6 months, metformin decreased body fat composition and attenuated declines in motor function induced by a high fat diet. Performance in the Morris water maze test of hippocampal based memory function, showed that metformin prevented impairment of spatial reference memory associated with the high fat diet. ECOTOXICITY STUDIES: Adult fathead minnows (Pimephales promelas) were chronically exposed to metformin for 4 wk, at 40 ug/L. Metformin treatment induced significant up-regulation of messenger

ribonucleic acid (mRNA) encoding the egg-protein vitellogenin in male fish, an indication of endocrine disruption. /LABORATORY ANIMALS: Developmental or Reproductive Toxicity/ Maternal obesity may program the fetus and increase the susceptibility of the offspring to adult diseases. Metformin crosses the placenta and has been associated with decreased inflammation and reversal of fatty liver in obese leptin-deficient mice. We investigated the effects of metformin on maternal and fetal lipid metabolism and hepatic inflammation using a rat model of diet-induced obesity during pregnancy. Female Wistar rats (6-7 weeks old) were fed normal or high calorie diets for 5 weeks. After mating with normal-diet fed males, half of the high calorie-fed dams received metformin (300 mg/kg, daily); dams (8 per group) continued diets through gestational day 19. Maternal and fetal livers and fetal brains were analyzed for fatty acids and for fatty acid metabolism-related gene expression. Data were analyzed by ANOVA followed by Dunnett's post hoc testing. When compared to control-lean maternal livers, obesogenic-diet-exposed maternal livers showed significantly higher saturated fatty acids (14:0 and 16:0) and monounsaturated fatty acids (16:1n7 and 18:1n9) and lower polyunsaturated (18:2n6 and 20:4n6 [arachidonic acid]) and anti-inflammatory n3 polyunsaturated fatty acids (18:3n3 and 22:6n3 [docosahexaenoic acid]) ($p<0.05$). Metformin did not affect diet-induced changes in maternal livers. Fetal livers exposed to the high calorie diet showed significantly increased saturated fatty acids (18:0) and monounsaturated fatty acids (18:1n9 and 18:1n7) and decreased polyunsaturated fatty acids (18:2n6, 20:4n6 and 22:6n3) and anti-inflammatory n3 polyunsaturated fatty acids, along with increased gene expression of fatty acid metabolism markers (Fasn, D5d, D6d, Scd1, Lxra). Metformin significantly attenuated diet-induced inflammation and 18:1n9 and 22:6n3 in fetal livers, as well as n3 fatty acids ($p<0.05$). Prenatal obesogenic diet exposure significantly increased fetal liver IFNgamma levels ($p<0.05$), which was reversed by maternal metformin treatment ($p<0.05$). Consumption of a high calorie diet significantly affected maternal and fetal fatty acid metabolism. It reduced anti-inflammatory polyunsaturated fatty acids in maternal and fetal livers, altered gene expression of fatty acid metabolism markers, and induced inflammation in the fetal livers. Prenatal metformin attenuated some diet-induced fatty acid changes and inflammation in the fetal livers without affecting maternal livers, suggesting that maternal metformin may impact fetal/neonatal fatty acid/lipid metabolism.

- STOT-single exposure: No data available.
- STOT-repeated exposure: IDENTIFICATION AND USE: Metformin is antihyperglycemic, not hypoglycemic agent. It does not cause insulin release from the pancreas and does not cause hypoglycemia, even in large doses. HUMAN EXPOSURE AND TOXICITY: Metformin is believed to work by inhibiting hepatic glucose production and increasing the sensitivity of peripheral tissue to insulin. It does not stimulate insulin secretion, which explains the absence of hypoglycemia. Metformin also has beneficial effects on the plasma lipid concentrations and promotes weight loss. Accumulation of metformin may occur in patients with renal impairment, and such accumulation rarely can result in lactic acidosis, a serious, potentially fatal metabolic disease. Lactic acidosis constitutes a medical emergency requiring immediate hospitalization and treatment; lactic acidosis is characterized by elevated blood lactate concentrations, decreased blood pH, electrolyte disturbances with an increased anion gap, and an increased lactate/pyruvate ratio. Lactic acidosis also may occur in association with a variety of pathophysiologic conditions, including diabetes mellitus, and whenever substantial tissue hypoperfusion and hypoxemia exist. Approximately 50% of cases of metformin-associated lactic acidosis have been reported to be fatal. No evidence of mutagenicity or chromosomal damage was observed in in vitro test systems, including human lymphocytes assay. ANIMAL STUDIES: No evidence of carcinogenic potential was seen in a 104-week study in male and female rats receiving metformin hydrochloride dosages up to and including 900 mg/kg daily or in a 91-week study in male and female mice receiving metformin hydrochloride at dosages up to and including 1500 mg/kg daily. Cancer preventive effect of metformin (MF) has been studied in mice, rats and hamsters. In the majority of cases metformin treatment leads to inhibition of carcinogenesis. No evidence of impaired fertility was observed in rats following administration of metformin hydrochloride dosages of 600 mg/kg daily. Reproduction studies in rats and rabbits given metformin hydrochloride dosages of 600 mg/kg daily have not revealed teratogenicity. No evidence of mutagenicity or chromosomal damage was observed in vivo in a micronucleus test in mice or in in vitro test systems, including

microbial (Ames test) and mammalian (mouse lymphoma) assays. Pretreatment of rat cerebellar granule neurons with metformin greatly enhanced cell viability against glutamate-induced neurotoxicity. In aged male mice fed high-fat diet supplemented with metformin for 6 months, metformin decreased body fat composition and attenuated declines in motor function induced by a high fat diet. Performance in the Morris water maze test of hippocampal based memory function, showed that metformin prevented impairment of spatial reference memory associated with the high fat diet. ECOTOXICITY STUDIES: Adult fathead minnows (Pimephales promelas) were chronically exposed to metformin for 4 wk, at 40 ug/L. Metformin treatment induced significant up-regulation of messenger ribonucleic acid (mRNA) encoding the egg-protein vitellogenin in male fish, an indication of endocrine disruption. /HUMAN EXPOSURE STUDIES/ The link between metformin and lactic acidosis in metformin therapy may be causal, associated or coincidental. Our objective was to investigate this link by studying and analyzing published reports of so-called 'metformin-associated lactic acidosis'. Systematically searched in the BIOSIS, DERWENT, EMBASE, MEDLINE, and PASCAL databases of the English language and non-English language literature for all reports of so-called 'metformin-associated lactic acidosis' published from May 1995 through January 2000. Reports related to metformin overdose or contrast media-induced renal failure /were not included/. Metformin accumulation and concurrent pathologies were critically reviewed as precipitating factors for metformin-associated lactic acidosis. Metformin accumulation was assessed in terms of the recorded measurement of metformin concentration in plasma or, if not available, by the presence of primary renal failure, i.e. renal failure that was not secondary to a shock syndrome. We found 21 reports describing a total of 26 patients. Criteria of lactic acidosis (lactate > 5 mmol/L, pH <or= 7.35) were not met in four patients. In the remaining 22 patients, plasma metformin concentration was determined in only four, of whom one had a normal value. In the 18 patients with lactic acidosis where plasma metformin concentration data was not available, the presence of primary renal failure was absent or unlikely in six patients, uncertain in two, and likely or proven in 14. With regard to these 14 patients, the precipitating factor was metformin in 12 patients (in the context of renal failure either chronic or acute) and intercurrent pathologies in two others. Overall, lactic acidosis was either absent (n = 4), precipitated by concurrent pathology (n = 8), precipitated by metformin without apparent associated pathology (n = 12) or of uncertain origin (n = 2). Death occurred 10 times but only once in the 12 patients with metformin-induced lactic acidosis and this was not related to metformin. While the term 'metformin-associated lactic acidosis' is commonly used to depict all situations of lactic acidosis in metformin therapy, true metformin-associated lactic acidosis, i.e. one which refers to metformin and concurrent pathologies as co-precipitating factors, was never observed in the studied reports ... /Salt not specified/
- Aspiration hazard: No data available.

Likely routes of exposure
- /SIGNS AND SYMPTOMS/ Overdose of metformin hydrochloride has occurred, including ingestion of amounts greater than 50 grams. Hypoglycemia was reported in approximately 10% of cases, but no causal association with metformin hydrochloride has been established. Lactic acidosis has been reported in approximately 32% of metformin overdose cases.

Symptoms related to the physical, chemical and toxicological characteristics
- IDENTIFICATION AND USE: Metformin is antihyperglycemic, not hypoglycemic agent. It does not cause insulin release from the pancreas and does not cause hypoglycemia, even in large doses. HUMAN EXPOSURE AND TOXICITY: Metformin is believed to work by inhibiting hepatic glucose production and increasing the sensitivity of peripheral tissue to insulin. It does not stimulate insulin secretion, which explains the absence of hypoglycemia. Metformin also has beneficial effects on the plasma lipid concentrations and promotes weight loss. Accumulation of metformin may occur in patients with renal impairment, and such accumulation rarely can result in lactic acidosis, a serious, potentially fatal metabolic disease. Lactic acidosis constitutes a medical emergency requiring immediate hospitalization and treatment; lactic acidosis is characterized by elevated blood lactate concentrations, decreased blood pH, electrolyte disturbances with an increased anion gap, and an increased lactate/pyruvate ratio. Lactic

acidosis also may occur in association with a variety of pathophysiologic conditions, including diabetes mellitus, and whenever substantial tissue hypoperfusion and hypoxemia exist. Approximately 50% of cases of metformin-associated lactic acidosis have been reported to be fatal. No evidence of mutagenicity or chromosomal damage was observed in in vitro test systems, including human lymphocytes assay. ANIMAL STUDIES: No evidence of carcinogenic potential was seen in a 104-week study in male and female rats receiving metformin hydrochloride dosages up to and including 900 mg/kg daily or in a 91-week study in male and female mice receiving metformin hydrochloride at dosages up to and including 1500 mg/kg daily. Cancer preventive effect of metformin (MF) has been studied in mice, rats and hamsters. In the majority of cases metformin treatment leads to inhibition of carcinogenesis. No evidence of impaired fertility was observed in rats following administration of metformin hydrochloride dosages of 600 mg/kg daily. Reproduction studies in rats and rabbits given metformin hydrochloride dosages of 600 mg/kg daily have not revealed teratogenicity. No evidence of mutagenicity or chromosomal damage was observed in vivo in a micronucleus test in mice or in in vitro test systems, including microbial (Ames test) and mammalian (mouse lymphoma) assays. Pretreatment of rat cerebellar granule neurons with metformin greatly enhanced cell viability against glutamate-induced neurotoxicity. In aged male mice fed high-fat diet supplemented with metformin for 6 months, metformin decreased body fat composition and attenuated declines in motor function induced by a high fat diet. Performance in the Morris water maze test of hippocampal based memory function, showed that metformin prevented impairment of spatial reference memory associated with the high fat diet. ECOTOXICITY STUDIES: Adult fathead minnows (Pimephales promelas) were chronically exposed to metformin for 4 wk, at 40 ug/L. Metformin treatment induced significant up-regulation of messenger ribonucleic acid (mRNA) encoding the egg-protein vitellogenin in male fish, an indication of endocrine disruption.

SECTION 12: Ecological information

SECTION 12: Ecological information

12.1 Toxicity
- Not available.

12.2 Persistence and degradability
- Not available.

12.3 Bioaccumulative potential
- Not available.

12.4 Mobility in soil
- Not available.

12.5 Results of PBT and vPvB assessment
- Not available.

12.6 Endocrine disrupting properties
- Not available.

12.7 Other adverse effects
- Not available.

SECTION 13: Disposal considerations

SECTION 13: Disposal considerations

13.1 Waste treatment methods
- Dispose of contents/container in accordance with local/regional/national/international regulations.
- Do not discharge to drains.
- Contaminated packaging: Dispose of as unused product or according to local requirements.

Waste codes
- Not available.

SECTION 14: Transport information

SECTION 14: Transport information

- UN number: Not available.
- UN proper shipping name: Not available.
- Transport hazard class(es): Not available.
- Packing group: Not available.
- Environmental hazards: Not available.
- Special precautions for user: Not available.

Transport in bulk according to IMO instruments
- Not available.

SECTION 15: Regulatory information

SECTION 15: Regulatory information

15.1 Safety, health and environmental regulations/legislation specific for the substance or mixture
- Not available.

15.2 Chemical safety assessment
- Not available.

SECTION 16: Other information

SECTION 16: Other information

- Product name: Metformin Secondary standard
- Catalog no.: CS-SS-26558
- CAS no.: 657-24-9
- Synonyms: 1,1-Dimethylbiguanide
- Supplier: Clearsynth Labs Ltd., Mumbai, India
- Emergency phone: +91-22-245045900

Disclaimer
- The information provided is believed to be accurate based on available data, but no warranty is expressed or implied. Users are responsible for determining suitability for their particular application and for compliance with applicable laws and regulations.

Revision information
- Not available.

DISCLAIMER

This MSDS is system-generated. Please verify and confirm all data, statements, and values with the Support Team before use or distribution.