For the use of a Registered Medical Practitioner or Hospital or a Laboratory only

SARSDG 2.34 g

1. Generic Name

2-Deoxy-D-Glucose oral powder 2.34 g

2. Qualitative and quantitative Composition:

Each Sachet contains:

2-Deoxy-D-Glucose……..2.34 g

3. Dosage form and strength

Dosage form: Powder for oral use

Strength: 2.34 g

4. Clinical particulars

4.1 Therapeutic indication

SARSDG is indicated as an adjunct therapy only in moderate to severe Covid-19 patients.

4.2 Posology and method of administration

The recommended total daily dosage of SARSDG is 90 mg/kg bodyweight/given orally in two equally divided doses with an Interval of at least 12 hours between doses. To prepare one dose, the entire contents of one sachet of SARSDG should be completely dissolved in 100 ml of drinking water. Based on patient's body weight, the required quantity of the SARSDG solution should be measured out and administered. SARSDG doses should be taken twice daily for 10 consecutive days or until discharge (if discharge happens earlier than 1days).

SARSDG should be taken on an empty stomach if possible. Patients are required to be fasting preferably for all east 3 hours prior to SARSDG administration, as far as is possible.

Method of Administration:

Dissolve entire content in 100 ml of drinking water and administer to patient as per body weight and instruction provided.

4.3 Contraindications

Patients with known hypersensitivity to SARSDG or any of its analogs such as fluoroDeoxy glucose should not take SARSDG. Other contraindications include Pregnancy and lactation.

4.4 Special warnings and precautions for use

Hyperglycaemia

The blood glucose level have been observed to increase after SARSDG administration, in reported clinical trials. The blood glucose level returned to normal within 4 to 6 hours post administration, as observed in reported phase III clinical trial in patients with Glioblastoma Multiform. Hence. Caution should be exercised while administering SARSDG in diabetic patients and anti-diabetic medication may need adjustment. Daily random blood sugar monitoring is recommended as long as patient receives SARSDG.

Patients with Hepatic or Renal Impairment

In reported Phase III clinical trial in patients with Glioblastoma Multiform, a few patients had altered levels of AST (SGOT) and ALT (SGPT) though not clinically significant. There were no cases with abnormal values in serum creatinine and serum urea. . II is advisable lo exercise caution while administering SARSDG to patients with hepatic or renal impairment.

Pregnancy and Lactation

Safety of SARSDG administration in pregnant and lactating women has not been established. Therefore, SARSDG is not indicated for use in pregnant and lactating women.

4.5 Drugs interactions

Insufficient data available to conclude on drug-drug interactions of SARSDG with other drugs

4.6 Use in special populations (such as pregnant women, lactating women, pediatric patients, geriatric patients etc.)

Pediatric use

The safety and efficacy of SARSDG in children have not been demonstrated.

Pregnancy and lactation

Safety of SARSDG administration in pregnant and lactating women has not been established. Therefore, SARSDG is not indicated for use in pregnant and lactating women.

4.7 Effects on ability to drive and use machines

Not Applicable

4.8 Undesirable effects

Summary of the safety profile

A total of 176 subject with moderate to severe COVID -19 have been exposed to SARSDG in phase II and phase III clinical trials and there were no significant safety issue reported in both phase II and phase III trials in COVID -19. No related SAEs to SARSDG were reported in both trials

During treatment with SARSDG in COVI D-19 patients, adverse events like nausea, vomiting, swatting, dizziness, tiredness, confusion, tremors, tachycardia, hyperglycemia, abdominal pain, diarrhea and fatigue have been observed as side effects during clinical studies.

Nausea, fatigue, hyperglycemia have been reported in Phase II clinical trial. The details of all adverse events with an incidence of 1 %°'more.

Number (%) of Patients with Adverse Events

SARSDG	90mg+soc		SARSDG1 26mg + SOC		soc	
	N=22		N=22		N=22	
System organ class preferred team n (%)	Number of events n (%)		Number of events n (%)		Number of events n (%)	
	22	8 (36.4)	6	5 (23.8)	9	5 (22.7)
Number of patients with at least one Af.	3	3 (13.6)	1	1 (4.8)	0	0
cardiac disorders	2	2 (9.1)	0	0	0	0

Palpitations	1	1 (4.5)	1	1 (4.8)	0	0
Sinus tachycardia	5	3 (13.6)	0	0	0	0
Gastrointestinal disorders	1	1 (4.5)	0	0	0	0
Abdominal pain	2	2 (9 1)	0	0	0	0
Diarrhoea	2	2 (9 1)	0	0	0	0
Nausea	4	2 (9 1)	0	0	0	0
General disorders and administration site conditions	3	2 (9 1)	0	0	0	0
Fatigue	1	1 (4.5)	0	0	0	0
Pain	2	2 (9 1)	1	1 (4.8)	0	0
Investigations	1	1 (4.5)	1	1 (4.8)	0	0
Electrocardiogram OT prolonged	1	1 (4.5)	0		0	0
Electrocardiogram T wave inversion	1	1 (4.5)	0		0	0
Metabolism and nutrition disorders	1	1 (4.5)	2	2(9.5)	5	4 (18.2)
Hyperglycaemia	1	1 (4.5)	2	2(9.5)	5	4 (18.2)
Musculoskeletal and connective tissue disorders	0	0	0	0	1	4 (18.2)
Limb discomfort	0	0	0	0	1	4 (18.2)
Nervous system disorders	4	3 (13.6)	0	0	1	4 (18.2)
Ageusia	1	1 (4.5)	0	0	0	0
Dizziness	3	2 (9 1)	0	0	0	0
Headache	0	0	0	0	1	4 (18.2)
Respiratory, thoracic and mediastinal disorders	3	3 (13.6)	0	0	2	4 (18.2)
Acute respiratory distress syndrome	1	1 (4.5)	0	0	0	0
Cough	2	2 (9 1)	0	0	0	0
Hypoxia	0	0	0	0	1	4 (18.2)
Nasal congestion	0	0	0	0	1	4 (18.2)

Skin and subcutaneous tissue disorder	0	0	2	1(4.8)	0	0
Hyperhidrosis	0	0	2	1(4.8)	0	0

N=Total number of patient in the specified system group.

n: number of patient with at lest one TEAE in the specified field

Subjects are counted only once within each preferred term and system preferred class

Percentage are based on the total number of patients in the specified treatment group under safety analysis.

Adverse event will be coded using the medical dictionary of regulatory activities (medDRA version 23.0)

Analysis dataset: ADAE

There was no significance difference in the number of patients who developed adverse event between SARSDG+ standard of care in reported phase II clinical trials.

Tabulated list of adverse reactions

Description of adverse reactions

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via any point of contact of Torrent Pharma available at:
https://www.torrentpharma.com/index.php/site/info/adverse_event_reporting
By reporting side effects, you can help provide more information on the safety of this medicine.

4.9 Overdose

Doses up to 300 mg/kg body weight of SARSDG have been evaluated clinically to assess tolerance and toxicities, in dose-escalation studies in glioblastoma multiform cancer patient and it has been found to be well tolerated without any acute side effects. The symptoms of over dosage may include hyperglycemia, thirst, drowsiness, nausea, vomiting, sweating and giddiness. In clinical studies, patients who developed nausea and vomiting were managed conservatively with intravenous fluid, parenteral antiemetic's and antiedema measures. In the event of over dosage, appropriate treatment and supportive measures should be instituted.

In reported clinical trials COVID-19 patients, patients were exposed to maximum 126mg/kg/day, and it has been found to be well tolerated without any acute side effects.

5 Pharmacological properties

5.1 Mechanism of Action

The mechanism of action of SARSDG in the treatment of COVID-19 is unknown Enhanced glycolysis is basic need for viral replication in host cells. Based on these fact, intervention at the level of virus induced host cells metabolism is a promising target to inhibit the viral reproduction and progression of disease. SARSDG is a synthetic analogue of glucose, which blocks glycolysis at the initial stage ad cause depletion of ATP as well as glucose derivatives required for protein glycosylation. It also inhibits anabolic reprogramming of host cells, which is essentially required for fast viral multiplication. SARSDG induced inhibition of viral

envelope biosynthesis and virion assembly due to blocked glycosylation of membrane protein also appear to be the alternate mechanism for virus attenuation. Moreover, this molecule selectively accumulates more in virally infected cells due to high glucose demand of these cells.

5.2 Pharmacodynamics properties

Clinical Trial Data

In reported phase II clinical trials in moderate to severe COVID- 19 patients, the median time to first negative conversion of SARS-COV-2 on RT-PCR assay of a respiratory tract sample was 4.0 days for patients in 90mg SARSDG +SoC group. The median time to first negative conversion of SARS-COV-2 on RT-PCR assay of a respiratory tract sample was 7 days for patients in the SoC2 group.

Preliminary read-out of partial data from the reported phase III study shows higher proportion of subjects in SARSDG + SoC arm improved from a baseline clinical score of 5 (hospitalized, on oxygen) on the WHO-10-point ordinal scale of clinical status to a score of 4 'hospitalized, no oxygen therapy required') (42% vs 31%) and 3 (11% Vs 6%) on WHO scale on Day-3-in comparison with SOC, indicating an early recovery from oxygen dependence. This improvement in oxygen dependence was observed to similar extent in the patients aged 65 years or above. At the discharge, 9% more patients turned RT-PCR negative in SARSDG arm (85% patients) as compared to SoC.(76%patients)

5.3 Pharmacokinetic properties

In a reported phase I/II clinical trial in patients with glioblastoma multiform, blood 2-deoxy-D-glucose levels showed a maximum at I hour after administration and thereafter decrease exponentially with an average half-life of 89 ± 17 min, by 24 h, detectable amount of 2-Deoxy-D-glucose were not found in the blood. Blood glucose levels gradually increased following SARSDG administration, reaching a maximum value (3 to 4 times the basal level of 5.0 ± 0.8 Mm) at about 3h after administration. The levels subsequently decreased and reached the basal value by 24h, the ratio of 2-Deoxy-D-glucose to glucose in the blood was found to be the highest (6.0-1.0) 1 hour after SARSDG administration and decreased rapidly reaching an insignificant value (<0.02) by 6 hours.

6 Nonclinical properties

6.1 Animal Toxicology or Pharmacology

Acute toxicity

Acute toxicity studied were conducted by administrating 2-Deoxy-D-glucose orally to mice and rats at doses of 1000mg, 2000mg, 4000mg, and 8000mg/kg body weight. Additionally acute toxicity studies were performed in mice by administering 2-Deoxy-D-glucose at the above doses and at 16000mg/kg dose. Treated animal were observed for 14 days after the treatment. There was no mortality during the reported study period of 14 days after oral administration. The median lethal dose (LD50) after oral administration as a single dose of mice and rats was found to be >8000mg/kg bodyweight. The median lethal dose after intravenous administration as a single dose in mice was found to be >8000mg/kg bodyweight (confidence limits 5100-12600mg/kg body weight).

Cardio-respiratory effects

In the cardio respiratory effects studies were conducted by administrating 2-Deoxy-D-glucose was administrated intravenously to rats. It did not show any dose dependent changes in mean arterial pressure, heart rate, respiratory rate, neuromuscular transmission

and rectal temperature. Reportedly, similar study conducted in guinea pigs showed no effect on mean arterial pressure and minute ventilation.

A reported study was carried out to find the effects of 2-Deoxy-D-glucose on respiratory variables in rats and mice. 2-Deoxy-D-glucose was given orally at doses of 500, 1000 and 2000g/kg. Respiratory variables were recorded for a period of 4 hours after administration. 2-Deoxy-D-glucose effects on Respiratory variables like frequency, tidal volume, and respiratory flow, inspiratory and expiratory time were minimal.

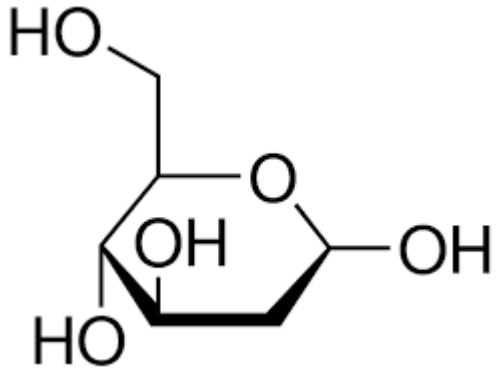
Sub-acute oral toxicity

2-Deoxy-D-glucose administered orally once a day for 28 days of mice and rats, at doses of 250mg, 500mg and 1000mg/kg showed no mortality, no clinical signs of toxicity, and no adverse effect on body weight gain, food intake, hematological and biochemical parameter and on organs in gross pathology and histology.

7 Description

The active ingredient in SARSDG powder is 2-Deoxy-D-glucose, which is a synthetic glucose analog. The molecular formula is $C_6H_{12}O_5$ and molecular weight 164.2. It is a white to off white powder.

Structure of 2 Deoxy-D Glucose



8 Pharmaceutical particulars

8.1 Incompatibilities

Not applicable. It is an oral drug and no excipient involved in manufacturing of SARSDG.

8.2 Shelf-life

Do not use later than date of expiry.

8.3 Packaging information

SARSDG is available in sachets of 2.34g.

8.4 Storage and handing instructions

Store below 30'C, Protect from moisture.

Keep the medicine out of reach of children.

9 Patient Counselling Information

Package leaflet: Information for the user

SARSDG

2-Deoxy-D-Glucose oral powder 2.34 g

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet.

What is in this leaflet

9.1 What SARSDG is and what it is used for

SARSDG is an antimetabolite drug and is used as adjunct therapy in the acute treatment of patient with moderate to severe COVID-19 disease, in the hospital setting. SARSDG was shown in the reported clinical trial to improve the symptoms and fasten the recovery in COVID-19 patients.

SARSDG is approved for "restricted emergency use" for the treatment of moderate to severe COVID-19 disease.

9.2 What you need to know before you take SARSDG

Do not take SARSDG

If you have any allergies

Tell your healthcare provider about all of your medical conditions, including

If you have kidney or liver problem

If you are pregnant or plan to become pregnant

If you are breastfeed or plan to breastfeed

Pregnancy, breast-feeding and fertility (pregnancy and lactation)

Safety of SARSDG administration in pregnant and lactating women has not been established. Therefore, SARSDG is not indicated for use in pregnant and lactating women.

9.3 How to take SARSDG / how to use SARSDG

The recommended total daily dosage of SARSDG is 90mg/kg body weight/given orally in two equal divided doses with an interval of at least 12hours between doses. Please refer to "instructions for use"

If you forget to take SARSDG

Do not take a double dose to make up for the forgotten dose. Take your next, normal dose, the next day, at your usual time.
If you have any further questions on the use of this medicine ask your doctor or pharmacist.

If you stop taking SARSDG

Should your doctor decide to stop your SARSDG treatment, he/she will instruct you about the gradual withdrawal of SARSDG.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

9.4 Possible side effects

Like all medicines, SARSDG can cause side effects, although not everybody gets them.

- Nausea, vomiting, sweating, dizziness, tiredness, confusion, tremors, tachycardia
- Hyperglycemia (increase in blood glucose level)
- Abdomen pain and diarrhea
- Fatigue

9.5 How to store SARSDG

Store below 30'C, Protect from moisture.

9.6 Contents of the pack and other information

The active ingredient in SARSDG is 2-Deoxy-D-Glucose.

It is available in sachet of 2.34g

10. Details of manufacturer

Manufactured by:
Bajaj Healthcare Ltd.
(Unit-3) (Formulation Division)
R.S.NO 1818, Manjusar-Savli rd., At & Post- Manjusar, Tal. Savli,
Dist. Vadodra-391775, Gujarat, INDIA.

11. Details of permission or license number with date

Mfg Lic No. G/25/1811 issued on 03.09.2021

12. Date of revision

Not Applicable

MARKETED BY

TORRENT PHARMACEUTICALS LTD.

IN/SARSDG 2.34g/DEC-21/01/PI