Plaquenil® Tablets

SAFETY DATA SHEET

According to Federal Register/ Vol. 77, No.58/ Mon Mar 26, 2012/Rules & Regulations

Date of Issue: November 16, 2015, Supersedes: April 24, 2013 Version 1.0

SECTION 1: Identification

1.1. Product identifier

Product form : Tablets

Product identifier : Plaquenil® Tablets

Other means of Identification: : Hydroxychloroquine sulphate tablets, USP

1.2. Recommended use of the chemical and restrictions on use

Pharmaceutical Agent. Use only as per Product Monograph as indicated for Plaquenil® (hydroxychloroquine sulphate) is indicated for the suppressive treatment and treatment of acute attacks of malaria due to *Plasmodium vivax*, *P. malariae*, *P. ovale*, and susceptible strains of *P. falciparum*. It is also indicated for the treatment of discoid and systemic lupus erythematosus, and rheumatoid arthritis (see Product Monograph for further information).

1.3. Name, address and telephone number of the chemical manufacturer, importer, or other responsible party

Concordia Pharmaceuticals Inc.
5 Canewood Industrial Park
St. Michael, Barbados BB11005

1.4. Emergency phone number

Emergency number : 1-877-370-1142 (8:30 am – 4:30 pm EST)

SECTION 2: Hazards identification

This product is a pharmaceutical as defined under the *Federal Food, Drug and Cosmetic Act*, in solid, final form for direct administration to the patient and as such it is exempt from coverage under *US GHS Hazard Communication Standard* (2012)

This SDS and classification are provided in case of the unlikely event of crushing of the tablets and release of dust from tablets.

2.1. Classification of the substance or mixture

Classification (GHS-US)

Not required; however, the classification (if applicable, would be):

Skin Irrit 2

Eye Irrit. 2A

STOT SE 3 - RI

2.2. Label elements

GHS-US labeling

Not required; however, the labelling (if applicable would be):

WARNING

Causes skin irritation

Causes serious eye irritation

May cause respiratory irritation.

PREVENTION:

Avoid breathing dust.

Wash hands thoroughly after handling.

Wear protective gloves/protective clothing/eye protection/face protection, and respiratory protection.

RESPONSE:

If on skin: Wash with plenty of water and soap.

If skin irritation occurs: Get medical advice/attention.

Take off contaminated clothing and wash it before reuse.

If in eyes: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.

If eye irritation persists: Get medical advice/attention.

If inhaled: Remove person to fresh air and keep comfortable for breathing.

Call a poison center or doctor if you feel unwell.

STORAGE:

Store locked up.

DISPOSAL:

Dispose of contents/container in accordance with local, regional, national, international regulations.

2.3. Other hazards

No additional information available

2.4. Unknown acute toxicity (GHS-US)

100% of the mixture consists of ingredient(s) of unknown acute (dermal and inhalation) toxicity.

SECTION 3: Composition/information on ingredients

3.1. Substance

Not applicable

3.2. Mixture

Name	Product identifier	%	Classification (GHS-US)
Hydroxychloroquine sulfate	(CAS No) 747-36-4	64.1	Acute Tox. 4 (Oral) Skin Irrit 2 Eye Irrit. 2A4 STOT SE 3 - RI
Magnesium stearate	(CAS No) 557-04-0	1%	Skin Irrit 2 Eye Irrit. 2A

SECTION 4: First-aid measures

4.1. Description of first aid measures

First-aid measures after inhalation : No specific first-aid measures for routine handling. Physical form suggests that risk of inhalation exposure is negligible. Dust containing drug substance could be inhaled if tablets are crushed or broken. If dust is inhaled, remove to fresh air. Seek medical attention.

First-aid measures after skin contact : Overt contamination of clothing is unlikely. However, in the event dust from broken or crushed tablets comes in contact with skin and clothing, remove contaminated clothing and wash thoroughly with running water. Use soap if available. Seek medical attention if irritation develops.

First-aid measures after eye contact : In case of contact with dust from broken or crushed tablets, flush eyes immediately for several minutes with clean and gently flowing water. Seek medical attention if irritation develops.

First-aid measures after ingestion : Induction of vomiting is not a recommended first-aid procedure. In the event of occupational ingestion, seek immediate medical attention or contact the Poison Control Center for further instructions. Do not attempt to give any solid or liquid by mouth if the exposed subject is unconscious or semi-conscious. Wash out the mouth with water.

4.2. Most important symptoms and effects, both acute and delayed

Symptoms/injuries after inhalation : Inhaling airborne dust may cause respiratory tract irritation. Effects may be presumed to be similar to those which may occur following ingestion.

Symptoms/injuries after skin contact : Itching, skin and membrane pigmentation, skin eruptions have been reported following ingestion. Dermatitis has also been reported. The dust from crushed or broken tablets may be irritating to the skin.

Symptoms/injuries after eye contact : Dust from crushed or broken tablets may cause eye irritation (e.g., tearing and redness).

Symptoms/injuries after ingestion : Very rapidly and completely absorbed after ingestion. In accidental overdose, or rarely with lower doses toxic symptoms may occur within 30 minutes. Symptoms include headache, drowsiness, visual disturbances, cardiovascular collapse, and convulsions. These effects may be followed by sudden respiratory and cardiac arrest. A number of fatalities have been reported in children following accidental ingestion, sometimes in relatively small doses. Other effects include irritability, nervousness, muscle weakness, emotional changes, nightmares, headache, dizziness, vertigo, loss of coordination/imbalance, ringing in the ears, and convulsions. May produce bleaching of hair, and hair loss. Blood effects can include aplastic anemia, and changes in blood cell counts. Nausea, vomiting, diarrhea, and abdominal cramps are also possible. Irreversible damage to the retina in the eyes has occurred in patients who received long-term or high dose therapy. Can also produce reversible changes to the cornea, and visual disturbances. Crosses the placenta. Taking this product orally may produce allergic reactions, but this is not anticipated to be an issue for small accidental ingestion in a workplace, except in previously sensitized individuals.

4.3. Indication of any immediate medical attention and special treatment needed

No additional information available.

SECTION 5: Fire-fighting measures

5.1. Extinguishing media

Suitable extinguishing media : Water, carbon dioxide or chemical dry powder.

Unsuitable extinguishing media : No known unsuitable extinguishing media.

5.2. Special hazards arising from the chemical

Fire hazard : May emit hydrogen chloride, nitrogen oxide and sulfur oxides under fire conditions.

If the product tablets are crushed during handling, dust/powdered material may be released. In such situations the material may pose a Combustible Dust hazard. Do not use clean up methods that result in dust clouds as a spark may result in an explosion and fire.

5.3. Advice for fire-fighters

Protection during fire-fighting : For single units (packages): No special requirements needed. For larger amounts (multiple packages/pallets) of product: Since toxic, corrosive or flammable vapors might be evolved from fires involving this material and associate packaging, do not enter fire area without proper breathing apparatus and full protective equipment. Move containers from the fire area if possible without increased personal risk. If possible, contain and collect fire-fighting water for later disposal.

SECTION 6: Accidental release measures

6.1. Personal precautions, protective equipment and emergency procedures

General measures (Spills) : No special requirements for spills from single containers. If the tablets are crushed or broken dust containing drug substance may be released. Minimize dust generation and accumulation. Do not breathe dust.
For large spills, take precautions to prevent entry into waterways, sewers or surface drainage systems. Use protective clothing during clean-up prior to disposal of spilled material. See Section 8 for appropriate PPE.

6.1.1. For non-emergency personnel

Emergency procedures : See Section 8 for appropriate PPE. Avoid unnecessary contact, especially with dust.

6.1.2. For emergency responders

Protective equipment : Use protective clothing during clean-up prior to disposal. See Section 8 for appropriate PPE. Avoid unnecessary contact, especially with dust.

6.2. Environmental precautions

Prevent entry to sewers and public waters. Notify authorities if product enters sewers or public waters.

6.3. Methods and material for containment and cleaning up

For containment : Recover the product by vacuuming, shoveling or sweeping. Minimize dust generation and accumulation.

Methods for cleaning up	:	Wet-down all dusts and soak up contents of broken tablets with an absorbent material. Carefully collect material and place in a properly labeled waste container for disposal. Wash area of spill to remove from surfaces. Wash skin thoroughly after handling. Collect and place it in a suitable, properly labelled container for recovery or disposal. Water can be used for clean-up and decontamination operations. No specific decontamination or detoxification procedures have been identified for this substance.

6.4. Reference to other sections

See Heading 8. Exposure controls and personal protection.

SECTION 7: Handling and storage30

7.1. Precautions for safe handling

Precautions for safe handling	:	Avoid breaking or crushing tablets. If tablets are crushed or broken, dust containing drug substance may be released. Avoid breathing dust and avoid contact with skin, eyes and clothing. Use local exhaust ventilation or respiratory protection for operations which generate dust. Wash thoroughly after handling. See Section 8 for appropriate PPE.

7.2. Conditions for safe storage, including any incompatibilities

Storage conditions	:	Store at room temperature up to 30 °C. Keep this and all drugs out of the reach of children. No known incompatibilities.

7.3. Specific end use(s)

Pharmaceutical agent.

SECTION 8: Exposure controls/personal protection

8.1. Control parameters

The following components have applicable exposure limits. In the event of possible dust/powder generation from these tablets, we have provided the following information to enable users to safely handle the product in that form.

Magnesium stearate (CAS# 557-04-0) (Stearates)		
ACGIH	TLV-TWA	10 mg/m^3
OSHA	PEL-TWA	None established

Starch (CAS# 9005-25-8)		
ACGIH	TLV-TWA	10 mg/m^3
OSHA	PEL-TWA	15 mg/m^3 (total dust)
		5 mg/m^3 (respirable fraction)

8.2. Exposure controls

Appropriate engineering controls	:	None required for normal handling of this material. If tablets are crushed or broken, dust containing drug substance may be released. If dust is generated, local exhaust ventilation may be required.
Hand protection	:	If tablets are crushed or broken, dust containing drug substance may be released and impervious gloves should be worn.
Eye protection	:	If tablets are crushed or broken, dust containing drug substance may be released. Wear safety glasses with side shields or goggles where risk of eye exposure exists.
Skin and body protection	:	If tablets are crushed or broken, dust containing drug substance may be released. Wear suitable working clothes.
Respiratory protection	:	If tablets are crushed or broken, dust containing drug substance may be released. Wear NIOSH approved respirator if concentrations exceed exposure limits.
Other information	:	When using, do not eat, drink or smoke.

SECTION 9: Physical and chemical properties

9.1. Information on basic physical and chemical properties

Physical state	:	Solid tablet.
Appearance	:	White film coated tablet.
Odor	:	Odorless
Odor threshold	:	No data available
pH	:	No data available

Relative evaporation rate (butyl acetate=1)	:	No data available
Melting point	:	198-240 °C
Freezing point	:	No data available
Boiling point	:	No data available
Flash point	:	No data available
Auto-ignition temperature	:	No data available
Decomposition temperature	:	No data available
Flammability (solid, gas)	:	No data available
Vapor pressure	:	No data available
Relative vapor density at 20 °C	:	No data available
Relative density	:	No data available
Solubility	:	Soluble in water, insoluble in alcohol, ether and chloroform
Log Pow	:	No data available
Log Kow	:	No data available
Viscosity, kinematic	:	No data available
Viscosity, dynamic	:	No data available
Explosive properties	:	No data available
Oxidizing properties	:	No data available
Explosive limits	:	No data available

9.2. Other information

No additional information available

SECTION 10: Stability and reactivity

10.1. Reactivity

Not expected to present a significant hazard under anticipated conditions of normal use.

10.2. Chemical stability

Anticipated to be stable under anticipated conditions of normal use.

10.3. Possibility of hazardous reactions

Not expected to present a significant hazard under anticipated conditions of normal use.

10.4. Conditions to avoid

None known.

10.5. Incompatible materials

None known.

10.6. Hazardous decomposition products

None known for normal handling of this product. Toxic, corrosive or flammable thermal decomposition products are expected when the material is exposed to fire.

SECTION 11: Toxicological information

11.1. Information on toxicological effects

INFORMATION ON LIKELY ROUTES OF EXPOSURE:

Routes of exposure may include oral, dermal, inhalation (in case of crushed tablets), or ingestion.

SYMPTOMS RELATED TO THE PHYSICAL, CHEMICAL AND TOXICOLOGICAL CHARACTERISTICS:

Potential Adverse human health effects and symptoms	:	See below
Symptoms/injuries after inhalation	:	Inhaling airborne dust may cause respiratory tract irritation. Effects may be presumed to be similar to those which may occur following ingestion.
Symptoms/injuries after skin contact	:	Itching, skin and membrane pigmentation, skin eruptions have been reported following ingestion. Dermatitis has also been reported. The dust from crushed or broken tablets may be irritating to the skin.
Symptoms/injuries after eye contact	:	Dust from crushed or broken tablets may cause eye irritation (e.g., tearing and redness).

Symptoms/injuries after ingestion	:	Very rapidly and completely absorbed after ingestion. In accidental overdose, or rarely with lower doses toxic symptoms may occur within 30 minutes. Symptoms include headache, drowsiness, visual disturbances, cardiovascular collapse, and convulsions. These effects may be followed by sudden respiratory and cardiac arrest. A number of fatalities have been reported in children following accidental ingestion, sometimes in relatively small doses. Other effects include irritability, nervousness, muscle weakness, emotional changes, nightmares, headache, dizziness, vertigo, loss of coordination/imbalance, ringing in the ears, and convulsions. May produce bleaching of hair, and hair loss. Blood effects can include aplastic anemia, and changes in blood cell counts. Nausea, vomiting, diarrhea, and abdominal cramps are also possible. Irreversible damage to the retina in the eyes has occurred in patients who received long-term or high dose therapy. Can also produce reversible changes to the cornea, and visual disturbances. Crosses the placenta. Taking this product orally may produce allergic reactions, but this is not anticipated to be an issue for small accidental ingestion in a workplace, except in previously sensitized individuals.

DELAYED AND IMMEDIATE EFFECTS AND ALSO CHRONIC EFFECTS FROM SHORT- AND LONG-TERM EXPOSURE:

Acute toxicity	:	Not classified as an acute toxin based upon available information on the product and its components.
Skin corrosion/irritation	:	If loose product comes into contact with skin this product may be irritating to skin based on the known hazards of the components.
Serious eye damage/irritation	:	If loose product comes into contact with eyes this product may be irritating to eyes based on the known hazards of the components.
Respiratory or skin sensitization	:	Based upon the known hazards of the components, this product is not anticipated to cause respiratory or skin sensitization.
Germ cell mutagenicity	:	Based upon the known hazards of the components, this product is not anticipated to cause germ cell mutagenicity.
Carcinogenicity	:	Based upon the known hazards of the components, this product is not classified as a carcinogen.
Reproductive toxicity	:	Not classified. Dietary administration to rats produced a slight retardation of growth in offspring but no other effects. In orally dosed rabbits no adverse effects on reproductive parameters and no teratogenic effects were noted. Based upon the known hazards of the components, this product is not anticipated to cause reproductive toxicity.
Specific target organ toxicity (single exposure)	:	If loose product (not intended to be formed during occupational use) is inhaled, it may cause respiratory tract irritation. No other classifiable target organ effects after single exposure are anticipated based on the known hazards of the components.
Specific target organ toxicity (repeated exposure)	:	Not classified. Plaquenil® was administered by intramuscular (2 week study) or intravenous injection (7 week study) to monkeys. A 22 day study was also conducted in guinea pigs. At intramuscular doses of 45 mg/kg in monkeys body weight gain and red blood cell parameters were decreased. Following intravenous administration of 12 mg/kg and greater deaths occurred rapidly. One monkey had evidence of liver damage and a serum liver enzyme was increased. No effects were noted in guinea pigs at doses up to 50 mg base /kg. Repeat dose oral studies were conducted in rats (21 days), dogs (90 days), and monkeys (10 months). Plaquenil® was well tolerated in dogs and monkeys. The only effect in rats was a slight depression of growth during the first 4 days.
Aspiration hazard	:	Not anticipated to be an aspiration hazard based on the nature of the material.

NUMERICAL MEASURES OF TOXICITY:

Product Data	
LD50 oral mouse	2880 - 3320 mg/kg
LD50 dermal rabbit	Not available
LC50 inhalation mouse (ppm)	Not available

Hydroxychloroquine sulfate **(747-36-4)**	
LD50 oral rat	1240 mg/kg
LD50 dermal rabbit	Not available
LC50 inhalation mouse (ppm)	Not available

Magnesium stearate **(557-04-0)**	
LD50 oral rat	>10,000 mg/kg
LD50 dermal rabbit	Not available
LC50 inhalation mouse (ppm)	Not available

SECTION 12: Ecological information

12.1. Toxicity

No additional information available

12.2. Persistence and degradability

Persistence and degradability	No additional information available.

12.3. Bioaccumulative potential

Bioaccumulative potential	No additional Information available

12.4. Mobility in soil

Mobility in Soil	No additional information available.

12.5. Other adverse effects

No additional information available

SECTION 13: Disposal considerations

13.1. Waste treatment methods

Waste disposal recommendations : Dispose of contents/container in accordance with local/regional/international regulations.

SECTION 14: Transport information

In accordance with DOT/ ADR/ RID/ ADNR/ IMDG/ ICAO/ IATA

14.1 UN Number: Not applicable.

14.2 UN Proper shipping name: Not applicable

Additional information

Other information : No supplementary information available.

Transport by sea

No additional information available

Air transport

No additional information available

SECTION 15: Regulatory information

15.1. US Federal regulations

No additional information available

15.2. International regulations

CANADA

Not determined

EU-Regulations

Not determined

Classification according to Regulation (EC) No. 1272/2008 [CLP]

Not determined

Classification according to Directive 67/548/EEC or 1999/45/EC

Not determined

15.2.2. National regulations

No additional information available

15.3. US State regulations

No additional information available

SECTION 16: Other information

References : Available upon request

Other information : None.

Full text of classifications see Section 3:

Acute Tox. 4 (Oral)	Acute Toxicity Category 4 (Oral)
Skin Irrit 2	Skin irritant Category 2
Eye Irrit 2A	Eye irritant Category 2A
STOT SE 3 - RI	Specific Target Organ Toxicity – Single Exposure – Category 3 - Respiratory Irritant

Full List of Acronyms used in SDS:

ACGIH - American Conference of Governmental Industrial Hygienists; ADNR – Regulation for the Carriage of Dangerous Substances on the Rhine (EU); ADR/RID - European Agreement Concerning the International Carriage of Dangerous Goods by Road/Rail; ATE – Acute Toxicity Estimate; CAS# - Chemical Abstract Services Number; CLP - Classification, Labelling, and Packaging of Substances and Mixtures; CNS – Central Nervous System; DNEL - Derived No Effect Level; DOT - Department of Transportation; DSL – Domestic Substances List; ECA - Exposure Control Approach; EST - Eastern Standard Time; GHS - Globally Harmonized System of Classification and Labeling of Chemicals; IARC – International Agency for Research on Cancer; IATA – International Air Transport Association; ICAO – International Civil Aviation Organization; IMDS – International Material Data System; LEC – Local Exhaust Ventilation; LOEC – Lowest Observed Effect Concentration; NOEC – No-Observed Effect Concentration; OHC: Occupational Health Categorization; OEL – Occupational Exposure Limit; OSHA -Occupational Safety and Health Administration; PEL – Permissible Exposure Limit; PPE – Personal Protective Equipment; RPE – Respiratory Protective Equipment; SARA – Species at Risk Act; SDS – Safety Data Sheet; STEL - Short Term Exposure Limit; TDG - Transportation of Dangerous Goods; TLV- TSCA - Toxic Substances Control Act; TWA - Time Weighted Average; WHMIS - Workplace Hazardous Materials Information System

Date of Preparation: Nov 16, 2015 Revision 1

SDS US (GHS HazCom 2012)

This SDS is intended to provide a brief summary of our knowledge and guidance regarding the use of this material in an industrial setting. It is not meant to be an all-inclusive document on worldwide hazard communication regulations. This information is offered in good faith. Each user of this material needs to evaluate the conditions of use and design the appropriate mechanisms to prevent employee exposures, property damage or release to the environment. Refer to Product Monograph for pharmaceutical use information.