

1 Identification

Product identifier

Trade name: RASUVO™ (methotrexate) injection

Article number: Methotrexate 50 mg/mL

Relevant identified uses of the substance or mixture and uses advised against

Relevant identified uses of the substance or mixture:

Ready-made medicinal product / pre-filled syringe (pen) with solution for injection

Function of the substance/mixture:

Cytostatic from the pharmacotherapeutic group: Antineoplastic agents/Antimetabolites/Folic acid analogues

Details of the supplier of the safety data sheet

Manufacturer/Supplier:

Manufacturer:

medac Gesellschaft für klinische Spezialpräparate mbH

Theaterstrasse 6

22880 Wedel

GERMANY

Supplier:

Medac Pharma, Inc.

29 N. Wacker Drive, Suite 704

Chicago, IL 60606

USA

Phone 312.854.0515 | Fax 312.750.1082

Information department:

Department Product Safety

k.dreesbach@medac.de

Emergency telephone number: CHEMTREC North America (24 hours): 800-424-9300

2 Hazard(s) identification

Classification of the substance or mixture



GHS08 Health hazard

Muta. 1B H340 May cause genetic defects.

Repr. 1A H360 May damage fertility or the unborn child.



GHS07

Acute Tox. 4 H302 Harmful if swallowed.

Label elements

GHS label elements The product is classified and labeled according to the Globally Harmonized System (GHS).

Hazard pictograms GHS07, GHS08

Signal word Danger

Hazard-determining components of labeling:

methotrexate

Hazard statements

Harmful if swallowed.

May cause genetic defects.

May damage fertility or the unborn child.

Precautionary statements

Obtain special instructions before use.

Dispose of contents/containers in accordance with the federal, state or local regulatory requirements.

Additional information:

Ready-made medicinal preparations are not ruled by the European chemical act, so that the submission of a Safety Data Sheet is not obligatory.

medac, however, opts for this form because the Safety Data Sheet constitutes a reliable source of information regarding the handling of hazardous substances and preparations, and because many occupational safety measures are on the Safety Data Sheet.

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Classification system

NFPA ratings (scale 0-4)

Health = 0
Fire = 0
Reactivity = 0

Other hazards

Results of PBT and vPvB assessment

PBT: Substance(s) does/do not meet the criteria for PBT according to Regulation (EC) No 1907/2006, Annex XIII.

vPvB: Substance(s) does/do not meet the criteria for vPvB according to Regulation (EC) No 1907/2006, Annex XIII.

3 Composition/information on ingredients

Chemical characterization: Mixtures

Description: Solution for injection.

Dangerous components:

CAS: 59-05-2 RTECS: MA 1225000	methotrexate	 Acute Tox. 3, H301  Muta. 1B, H340; Repr. 1A, H360  Skin Irrit. 2, H315; Eye Irrit. 2A, H319	< 5%
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OSHA IMIS Code Number: M106

SVHC Not applicable.

Additional information

For the wording of the listed hazard statements if not yet explained in Section 2.2 or mentioned otherwise please refer to Section 16.

4 First-aid measures

Description of first aid measures

After inhalation Supply fresh air; consult doctor in case of complaints.

After skin contact

Instantly remove contaminated clothes.
Instantly wash with copious amounts of water.
Seek immediate medical advice.

After eye contact

Rinse eyes cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. Seek immediate medical advice.

After swallowing

Let drink water (2 glasses maximum).
In case of disorders consult doctor.

Most important symptoms and effects, both acute and delayed

To the best of our knowledge both acute and delayed symptoms and effects due to improper handling of this preparation have not been investigated.

Information for doctor

Show Safety Data Sheet.
Treatment according to symptoms.

Indication of any immediate medical attention and special treatment needed

No further relevant information available.

5 Fire-fighting measures

Extinguishing media

Suitable extinguishing agents Product itself does not burn. Use fire fighting measures that suit the environment.

For safety reasons unsuitable extinguishing agents For this mixture no limitations of extinguishing agents are given.

Special hazards arising from the substance or mixture None known.

Advice for firefighters

Protective equipment:

Stay in the danger area only with self-contained breathing apparatus.
Prevent skin and eye contact by keeping a safe distance or by wearing suitable protective clothing.

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USA

Trade name: RASUVO™ (methotrexate) injection**Additional information**

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Collect contaminated fire fighting water separately. Care should be taken to avoid environmental release.

6 Accidental release measures**Personal precautions, protective equipment and emergency procedures**

Evacuate, cordon and mark the contaminated area as following:

"Caution cytostatic accident – do not enter"

Protection equipment for removal of unintentional contamination or in the event of rupture :

- overshoes
- liquid-proof protective long-sleeved coat with close-fitting sleeve-bands
- protective goggles with side protection shield
- protective gloves: nitrile rubber, natural rubber (latex); material thickness 0.11 mm; penetration time 240 min.
- approved air-purifying respirator with HEPA cartridge (N99 or equivalent) according to the NIOSH Guide to the Selection and Use of Particulate Respirators
Certified Under 42 CFR 84
- cut cellulose in sufficient quantity
- receptacle and waste container, shovel

Environmental precautions: Do not allow product to reach sewage system or any water course.

Methods and material for containment and cleaning up:

Clean immediately and appropriately the affected area. A further spreading of spillage on the floor with footwear has to be avoided.

Keep ready a decontamination kit.

Take-up of liquid drugs spill. Cover contaminated area carefully using disposable cloth or cellulose, so that the liquid is completely absorbed.

Take-up of dry solid matters:

Cover contaminated area carefully with several layers of cellulose over its whole surface and wet the cellulose cautiously from above.

A dispersal (draught) must be avoided.

Take-up of glass breakage:

Use of suitable means and use of an additional pair of protective gloves.

Clean thoroughly contaminated areas.

Place the whole absorbed and contaminated material in a sealable, labelled container for disposal as hazardous waste according to local regulations (see also Section 13).

Ensure adequate ventilation.

Reference to other sections

See Section 7 for information on safe handling

See Section 8 for information on personal protection equipment.

See Section 13 for disposal information.

7 Handling and storage**Precautions for safe handling**

Handle the pen with care.

Only trained persons are authorized to handle.

Information about protection against explosions and fires: No special measures required.

Conditions for safe storage, including any incompatibilities

Store as directed by product labeling. Protect from light. Do not freeze.

Storage stability: please see expiry date.

Storage

Requirements to be met by storerooms and receptacles: Store only in the original receptacle.

Information about storage in one common storage facility: Not required.

Further information about storage conditions: Store at 15 °C to 25 °C (59 °F to 77 °F).

Specific end use(s) Apart from the uses mentioned in section 1.2 no other specific uses are stipulated.

8 Exposure controls/personal protection

Additional information about design of technical systems: No further data; see item 7.

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USA

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Control parameters

Components with limit values that require monitoring at the workplace: Not applicable.

Ingredients with biological limit values: Void.

Additional information: The official lists that were valid during the compilation were used as basis.

Exposure controls

Technical measures and appropriate working operations should be given priority over the use of personal protective equipment.

See Section 7.

Personal protective equipment

General protective and hygienic measures Avoid contact with the eyes and skin.

Breathing equipment:

No special precautions are necessary if handled correctly.

In the unlike event of accidental release and the possibility of contact with aerosols please refer to Section 6.

Protection of hands:

No special precautions necessary if handled correctly.

In the event of accidental release please refer to Section 6.

Eye protection:

No special precautions necessary if handled correctly.

In the event of accidental release please refer to Section 6.

Body protection:

No special body protection necessary if handled correctly.

In the event of accidental release please refer to Section 6.

Limitation and supervision of exposure into the environment Do not empty into drains.

9 Physical and chemical properties

Information on basic physical and chemical properties

General Information

Appearance:

Form:	Clear, liquid.
Color:	Yellowish-brown.
Odor:	Odorless.
Odour threshold:	Not determined.

pH-value at 20 °C (68 °F):	7.5 - 9.0
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Change in condition

Melting point/Melting range:	ca. 0 °C (ca. 32 °F)
Boiling point/Boiling range:	ca. 100 °C (ca. 212 °F)

Flash point:	Not applicable.
Flammability (solid, gaseous)	Not applicable.
Ignition temperature:	No information available.
Decomposition temperature:	No information available.
Auto igniting:	Not self-inflammable.
Danger of explosion:	Not explosive.
Explosion limits:	
Lower:	Not applicable.
Upper:	Not applicable.
Vapor pressure at 20 °C (68 °F):	23 hPa (17 mm Hg)
Density:	
Relative density at 20 °C (68 °F)	1.03 g/cm ³ (8.595 lbs/gal)
Vapour density	Not determined.
Evaporation rate	No information available.
Solubility in / Miscibility with	
Water:	Fully miscible Further miscibilities: 0.9% sodium chloride solution 5% glucose solution
Partition coefficient (n-octanol/water) at 20 °C (68 °F):	0.0141 log POW
Viscosity:	
dynamic:	No information available.
kinematic:	No information available.

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Solvent content:

Organic solvents: <3 %
Water: >87 %
Solids content: <10 %

Other information

No further relevant information available.

10 Stability and reactivity

Reactivity For this mixture no relevant information available.

Chemical stability The product is chemically stable under the indicated storage conditions.

Possibility of hazardous reactions No dangerous reactions known

Conditions to avoid: No further relevant information available.

Incompatible materials: Strong oxidizers.

Hazardous decomposition products:

Nitrogen oxides (NOx)
Carbon monoxide
Carbon dioxide

Additional information: No further relevant information available.

11 Toxicological information

Information on toxicological effects

Acute toxicity:

LD/LC50 values that are relevant for classification:

59-05-2 methotrexate

Oral	LD50 (dynamic)	135 mg/kg (mouse) 135 mg/kg (rat)
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Primary irritant effect:

on the skin: Irritations.

on the eye: Irritations.

after swallowing: Mucosal irritations in mouth, pharynx and oesophagus possible.

Sensitization: No sensitizing effects known.

Additional toxicological information:

Germ cell mutagenicity

Reference substance: Methotrexate

Remark: Information on genotoxicity in vitro and in vivo available.

Source: TOXNET: GENETOX / HSDB

Remark: Methotrexate has in vitro and in vivo mutagenic effects.

Source: medac expert information

Reproduction toxicity

Reference substance: Methotrexate

Remark: Impaired fertility, Miscarriage, Teratogenesis (HE5)

Source: OSHA

Remark: Experimental studies in animals showed developmental and reproductive toxicity.

Source: TOXNET: HSDB

Remark: Experimental studies in animals showed that methotrexate impairs fertility and that it is embryo- and fetotoxic as well as teratogenic

Source: medac expert information

Carcinogenicity

Remark: Classification of carcinogenicity: 1) evidence in humans: Inadequate data; 2) evidence in animals: Inadequate data. Overall summary evaluation of carcinogenic risk to humans is Group 3: The agent is not classifiable as to its carcinogenicity to humans.

Source: TOXNET: HSDB

Remark: Conventional carcinogenic studies had not been performed. Data from chronic toxicity studies in ruminants are inconsistent. Thus, methotrexate has been considered not classifiable with regard to its cancerogenicity in humans.

Source: medac expert information

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Carcinogenic categories

IARC (International Agency for Research on Cancer)

59-05-2 | methotrexate

3

Not Classifiable.

NTP (National Toxicology Program)

None of the ingredients is listed.

12 Ecological information

Toxicity

Aquatic toxicity: Toxic to aquatic life with long lasting effects.

Persistence and degradability No further relevant information available.

Bioaccumulative potential

Due to the distribution coefficient n-octanol/water an accumulation in organisms is not expected.

Mobility in soil No further relevant information available.

Additional ecological information:

General notes:

Do not discharge product unmonitored into the environment.
Further ecological data are not available.

Results of PBT and vPvB assessment

PBT: PBT assessment not available as chemical safety assessment not required/not conducted.

vPvB: vPvB assessment not available as chemical safety assessment not required/not conducted.

Other adverse effects No further relevant information available.

13 Disposal considerations

Waste treatment methods

Waste disposal:

Disposal should be performed in accordance with the federal, state or local regulatory requirements.

Container handling and disposal:

Handle and dispose of containers like the waste.

Uncleaned packagings:

Recommendation: Uncleaned packagings have to be disposed of in the same manner as the product residues.

14 Transport information

UN-Number

DOT, ADN, IMDG, IATA
ADR

Void

Void

No dangerous good according to EU ADR special regulation no. 601 in the latest version.

UN proper shipping name

DOT, ADN, IMDG, IATA
ADR

Void

Void.

Transport hazard class(es)

DOT, ADR, ADN, IMDG, IATA
Class

Void

Packing group

DOT, ADR, IMDG, IATA

Void

Environmental hazards:

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Marine pollutant:	U.S. DOT - Appendix B - Marine Pollutants: Not listed. U.S. DOT - Appendix B - Severe Marine Pollutant:s Not listed.
Special precautions for user	Not applicable.
Transport in bulk according to Annex II of MARPOL73/78 and the IBC Code	Not applicable.
UN "Model Regulation":	-

15 Regulatory information**Safety, health and environmental regulations/legislation specific for the substance or mixture****SARA Section 355 (extremely hazardous substances)**

None of the ingredients is listed.

SARA Section 313 (specific toxic chemical listings)

None of the ingredients is listed.

TSCA (Toxic Substances Control Act)

All ingredients are listed.

Prop 65 - Chemicals known to cause cancer

None of the ingredients is listed.

Carcinogenicity categories**EPA (Environmental Protection Agency)**

None of the ingredients is listed.

TLV (Threshold Limit Value established by ACGIH)

None of the ingredients is listed.

MAK (German Maximum Workplace Concentration)

None of the ingredients is listed.

NIOSH-Ca (National Institute for Occupational Safety and Health)

None of the ingredients is listed.

OSHA-Ca (Occupational Safety & Health Administration)

None of the ingredients is listed.

GHS label elements The product is classified and labeled according to the Globally Harmonized System (GHS).**Hazard pictograms** GHS07, GHS08**Signal word** Danger**Hazard-determining components of labeling:**

methotrexate

Hazard statements

Harmful if swallowed.

May cause genetic defects.

May damage fertility or the unborn child.

Precautionary statements

Obtain special instructions before use.

Dispose of contents/containers in accordance with the federal, state or local regulatory requirements.

National regulations

Class	Share in %
I	1.0

Chemical safety assessment: A Chemical Safety Assessment has not been carried out.**16 Other information**

Further drug-specific information can be found in the product insert accompanying this product or in the expert information.

All information and recommendations are believed to be correct as of the date of this Safety Data Sheet but shall not be taken to be all inclusive and shall be used only as a guide. All chemicals and preparations may present unknown hazards

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Trade name: RASUVO™ (methotrexate) injection

and should be used with caution. medac shall not be held liable for any damage resulting from handling or from contact with the above product. (Contd. of page 7)

Relevant phrases

H301 Toxic if swallowed

H315 Causes skin irritation

H319 Causes serious eye irritation

Department issuing MSDS: Dept. for Product Safety**Contact:** k.dreesbach@medac.de**Date of preparation / last revision** 2014/07/10**Abbreviations and acronyms:**

ADR: Accord européen sur le transport des marchandises dangereuses par Route (European Agreement concerning the International Carriage of Dangerous Goods by Road)

IMDG: International Maritime Code for Dangerous Goods

DOT: US Department of Transportation

IATA: International Air Transport Association

ACGIH: American Conference of Governmental Industrial Hygienists

EINECS: European Inventory of Existing Commercial Chemical Substances

ELINCS: European List of Notified Chemical Substances

CAS: Chemical Abstracts Service (division of the American Chemical Society)

NFPA: National Fire Protection Association (USA)

LC50: Lethal concentration, 50 percent

LD50: Lethal dose, 50 percent