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

1.1 Product identifier

Trade name

Methotrexate medac 50 mg/ml solution for injection (methotrexate)

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

Relevant identified uses of the substance or mixture
Ready-made medicinal product/solution for injection
Function of the substance/mixture:
Cytostatic from the pharmacotherapeutic group: Antineoplastic agents/ Antimetabolites/Folic acid analogues, ATC code: L01BA01.

Uses advised against
No data available.

1.3 Details of the supplier of the safety data sheet

Address
medac Gesellschaft für klinische Spezialpräparate mbH
Theaterstrasse 6
22880 Wedel
Germany

Telephone no. +49-4103-8006-0
Fax no. +49-4103-8006-100

Information provided by / telephone
Product Safety
Health, Safety & Environment (HSE)
productsafety@medac.de

Advice on Safety Data Sheet
sdb_info@umco.de

1.4 Emergency telephone number

For medical advice (in German and English):
+49-551-192-40 (Giftinformationszentrum Nord)

SECTION 2: Hazards identification

2.1 Classification of the substance or mixture

Classification in accordance with Regulation (EC) No 1272/2008 (CLP)
Muta. 1B; H340
Repr. 1B; H360FD

Classification information
This product is assessed and classified using the methods and criteria below referred to in Article 9 of Regulation (EC) n° 1272/2008:
Physical hazards: determined through assessment data based on the methods or standards referred to in part 2 of Annex I to CLP
Health hazards and environmental hazards: determined through toxicological and ecotoxicological assessment data based on the methods or standards referred to in Part 3, 4 and 5 of Annex I to CLP.

2.2 Label elements

Labelling according to Regulation (EC) No 1272/2008 (CLP Regulation)

Hazard pictograms

GHS08

Signal word
Danger

Hazardous component(s) to be indicated on label:
methotrexate

Hazard statement(s)

H340	May cause genetic defects.
H360FD	May damage fertility. May damage the unborn child.

Precautionary statement(s)

P201	Obtain special instructions before use.
P202	Do not handle until all safety precautions have been read and understood.

P280	Wear protective gloves/protective clothing/eye protection.
P308+P313	IF exposed or concerned: Get medical advice/attention.
P405	Store locked up.

Supplemental label elements
"Restricted to professional users"

Labelling information
Ready-made medicinal preparations are not ruled by the 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 basing on the Safety Data Sheet structure.

2.3 Other hazards

PBT assessment
The components of this product are not considered to be a PBT.

vPvB assessment
The components of this product are not considered to be a vPvB.

SECTION 3: Composition/information on ingredients

3.1 Substances

Not applicable. The product is not a substance.

3.2 Mixtures

Hazardous ingredients

No	Substance name		Additional information	
	CAS / EC / Index / REACH no	Classification (EC) 1272/2008 (CLP)	Concentration	%
1	**methotrexate**			
	59-05-2 200-413-8 - -	Acute Tox. 3; H301 Eye Irrit. 2; H319 Muta. 1B; H340 Repr. 1B; H360FD Skin Irrit. 2; H315 STOT SE 3; H335	5.00	wt%

Full Text for all H-phrases and EUH-phrases: pls. see section 16

Acute toxicity estimate (ATE) values			
No	oral	dermal	inhalative
1	135 mg/kg bodyweight		

SECTION 4: First aid measures

4.1 Description of first aid measures

General information
First aid assistant: Pay attention to self protection!

After inhalation
Ensure supply of fresh air. Call a doctor immediately.

After skin contact
Remove contaminated clothing immediately and dispose of safely. Launder clothes before reuse. In case of contact with skin wash off immediately with copious amounts of water. Call a doctor immediately.

After eye contact
In case of contact with eyes rinse thoroughly with water. Remove contact lenses if present and easy to do. Continue rinsing. Call a doctor immediately.

After ingestion
Rinse out mouth and give plenty of water to drink. Call a doctor immediately.

4.2 Most important symptoms and effects, both acute and delayed

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

4.3 Indication of any immediate medical attention and special treatment needed

Show Safety Data Sheet, expert information or product insert.

SECTION 5: Firefighting measures

5.1 Extinguishing media

Suitable extinguishing media
Product itself is non-combustible; adapt fire extinguishing measures to surrounding areas.

Unsuitable extinguishing media
For this product no limitations of extinguishing agents are given.

5.2 Special hazards arising from the substance or mixture
None known.

5.3 Advice for firefighters
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. Run-off water from fire fighting must not be discharged into drains or enter surface water.

SECTION 6: Accidental release measures

6.1 Personal precautions, protective equipment and emergency procedures
For non-emergency personnel
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
- protective face mask with combination filter A2-P3 according to the provisions of the professional organisation "Rules for use of breathing apparatuses"
- cut cellulose in sufficient quantity
- receptacle and waste container, shovel.

For emergency responders
Personal protective equipment (PPE) - see section 8. Keep unprotected persons away.

6.2 Environmental precautions
Do not allow to enter drains.

6.3 Methods and material for containment and cleaning up
Remove immediately and appropriately soiling. 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.

6.4 Reference to other sections
Information regarding safe handling, see section 7. Information regarding personal protective measures, see section 8. Information regarding waste disposal, see section 13.

SECTION 7: Handling and storage

7.1 Precautions for safe handling
Advice on safe handling
Avoid formation of aerosols. Open and handle container with care. Only qualified and trained persons are authorised to handle.

General protective and hygiene measures
An antechamber equipped with separated storage facilities must exist for changing (protective clothes and normal clothes) before the working space (lock).

Advice on protection against fire and explosion
Void.

7.2 Conditions for safe storage, including any incompatibilities
Technical measures and storage conditions
Store in the dark. Store container dry, tightly closed in the original box. Do not store beyond 25 °C! Store in a locked cabinet with access restricted to technical experts or their assistants.

Recommended storage temperature

Value	15	-	25	°C

Storage stability

Comments see expiry date

7.3 Specific end use(s)

Recommendations
Apart from the uses mentioned in Section 1.2 no other specific uses are stipulated.

SECTION 8: Exposure controls/personal protection

8.1 Control parameters

No parameters available for monitoring.

8.2 Exposure controls

Appropriate engineering controls
Handling of cytostatics / virusstatics calls always for separated, clearly marked working spaces in an adequate safety cabinet in compliance with the respective national Guidelines/Recommendations for Safe Handling of Cytotoxic Drugs.

Personal protective equipment

Respiratory protection
If ventilation insufficient, use a respiratory protection apparatus. Short term: filter apparatus, combination filter A2-P3

Eye / face protection
Safety glasses with side protection shield (EN 166)

Hand protection
Disposable gloves with long gauntlet and, if possible, revolving sleeve made of natural Latex, PVC or synthetics with tight closing band around the gauntlet (i.e. Biogel®Standard; Biogel®Skinsense™ or Biogel®Indicator)
- unpowdered, poor protein content, close-fitting, firm surface
- quality requirements according to EN 374
- finger area designed with double wall thickness
- advantageous: dyed gloves
- material thickness > 0.2 mm
- recommendation: wearing of two pairs of gloves (i.e. Biogel®Indicator™)
- for safe handling of Cytotoxic Drugs protective gloves must be changed every 30 minutes.

Other
Liquid-proof protective long-sleeved coat with close-fitting sleeve-bands obligatory.

Environmental exposure controls
Do not empty into drains.

SECTION 9: Physical and chemical properties

9.1 Information on basic physical and chemical properties

State of aggregation
liquid

Form
Solution

Colour
Clear, yellow and orange-yellow, respectively

Odour
odourless

pH value				
Value	7.0	-	9.0	
Reference temperature			20	°C

Boiling point / boiling range
No data available

Melting point/freezing point
No data available

Decomposition temperature
No data available

Flash point
Not applicable

Ignition temperature
No data available

Flammability
No data available

Lower explosion limit

No data available

Upper explosion limit
No data available

Vapour pressure
No data available

Relative vapour density
No data available

Relative density
No data available

Density			
Value	appr.	1.05	mg/ml
Reference temperature		20	°C

Solubility in water	
Comments	completely soluble

Solubility	
Comments	Soluble in: 5% glucose or 0.9% sodium chloride solution.

Partition coefficient n-octanol/water (log value)
No data available

Kinematic viscosity
No data available

Particle characteristics
No data available

9.2 Other information

Other information
No data available.

SECTION 10: Stability and reactivity

10.1 Reactivity
No data available.

10.2 Chemical stability
Stable under recommended storage and handling conditions (See section 7).

10.3 Possibility of hazardous reactions
Dangerous reactions are not to be expected when handling product according to its intended use.

10.4 Conditions to avoid
Storage above 25 °C; light

10.5 Incompatible materials
No data available.

10.6 Hazardous decomposition products
Nitrogen oxides, carbon monoxide, carbon dioxide.

SECTION 11: Toxicological information

11.1 Information on hazard classes as defined in Regulation (EC) No 1272/2008

Acute oral toxicity (result of the ATE calculation for the mixture)	
No	**Product Name**
1	**Methotrexate medac 50 mg/ml solution for injection (methotrexate)**
Comments	The result of the applied calculation method according to the European Regulation (EC) 1272/2008 (CLP), Paragraph 3.1.3.6, Part 3 of Annex I is outside the values that imply a classification / labelling of this mixture according to table 3.1.1 defining the respective categories (ATE oral > 2000 mg/kg).

Acute oral toxicity			
No	**Substance name**	**CAS no.**	**EC no.**
1	**methotrexate**	**59-05-2**	**200-413-8**
LD50		135	mg/kg bodyweight
Species	rat		
Source	medac		

Acute dermal toxicity
No data available

Acute inhalational toxicity
No data available

Skin corrosion/irritation			
No	**Substance name**	**CAS no.**	**EC no.**
1	**methotrexate**	**59-05-2**	**200-413-8**
Source	medac		
Evaluation	irritant		

Serious eye damage/irritation			
No	**Substance name**	**CAS no.**	**EC no.**
1	**methotrexate**	**59-05-2**	**200-413-8**
Source	medac		
Evaluation	Irritating to eyes		

Respiratory or skin sensitisation			
No	**Substance name**	**CAS no.**	**EC no.**
1	**methotrexate**	**59-05-2**	**200-413-8**
Route of exposure	respiratory tract		
Source	medac		
Evaluation	non-sensitizing		
Route of exposure	Skin		
Source	medac		
Evaluation	non-sensitizing		

Germ cell mutagenicity			
No	**Substance name**	**CAS no.**	**EC no.**
1	**methotrexate**	**59-05-2**	**200-413-8**
Source	medac expert information		
Evaluation/classification	Methotrexate induces gene and chromosome mutations in vitro and in vivo. A mutagenic effect is suspected in humans.		

Reproduction toxicity			
No	**Substance name**	**CAS no.**	**EC no.**
1	**methotrexate**	**59-05-2**	**200-413-8**
Source	medac expert information		
Evaluation/classification	Teratogenic effects have been observed in 4 species (rat, mouse, rabbit, cat). There is evidence of a teratogenic risk in pregnant women.		

Carcinogenicity			
No	**Substance name**	**CAS no.**	**EC no.**
1	**methotrexate**	**59-05-2**	**200-413-8**
Source	medac expert information		
Evaluation/classification	Long-term studies in rats, mice and hamsters did not provide any evidence of a carcinogenic potential of methotrexate.		

STOT - single exposure
No data available

STOT - repeated exposure
No data available

Aspiration hazard
No data available

11.2 Information on other hazards

Endocrine disrupting properties
No data available.

Other information
No data available.

SECTION 12: Ecological information

12.1 Toxicity

Toxicity to fish (acute)
No data available

Toxicity to fish (chronic)
No data available

Toxicity to Daphnia (acute)
No data available

Toxicity to Daphnia (chronic)
No data available

Toxicity to algae (acute)
No data available

Toxicity to algae (chronic)
No data available

Bacteria toxicity
No data available

12.2 Persistence and degradability
No data available.

12.3 Bioaccumulative potential
No data available.

12.4 Mobility in soil
No data available.

12.5 Results of PBT and vPvB assessment

Results of PBT and vPvB assessment	
PBT assessment	The components of this product are not considered to be a PBT.
vPvB assessment	The components of this product are not considered to be a vPvB.

12.6 Endocrine disrupting properties
No data available.

12.7 Other adverse effects

Other adverse effects
Product is water hazardous (see Section 15.1).

12.8 Other information

Other information
Do not discharge product unmonitored into the environment.

SECTION 13: Disposal considerations

13.1 Waste treatment methods

Product

Product residues have to be disposed of according to national and regional regulations in each the latest versions.

- Collection and disposal of cytostatics or contaminated materials have to be performed in compliance with the European Waste Catalogue (EWC code). In addition the respective local waste rules in their latest version have to be followed.

- Cytostatic residues belong to the type of waste requiring special supervision Cytostatic residues include original receptacles that are not completely emptied, expired CMR drugs in original packing as well as residual solutions in infusion systems. Infusion systems (Infusion set and infusion container) must not be disconnected but have to be disposed of completely as unit.

- Cytostatic residues have in the EWC the code 180108* (*: cytotoxic and cytostatic waste, for incineration only). They have to be collected separately in type-approved, pierce-resistant, unbreakable, tightly closing disposable containers. They have to be clearly labelled to identify that they are suitable for and contain cytotoxic and cytostatic waste. They have to be delivered, together with a certified proof of disposal, to a special waste incineration plant. The provisions of the respective waste and transport legislation have to be followed.

- Materials which are only slightly contaminated with cytostatics (emptied containers and application systems, disposable protective clothing etc.) are considered waste of the category 180104 EWC (wastes whose collection and disposal is not subject to special requirements in order to prevent infection) and are classified as being in need for monitoring during elimination. The collection shall be performed in tearproof, moisture-resistant and tight containers, safely sealed for transport. For reasons of occupational safety the waste has to be delivered to certified plants for incineration without external pretreatment.

SECTION 14: Transport information

14.1 Transport ADR/RID/ADN
The product is not subject to ADR/RID/ADN regulations.

14.2 Transport IMDG
The product is not subject to IMDG regulations.

14.3 Transport ICAO-TI / IATA
The product is not subject to ICAO-TI / IATA regulations.

14.4 Other information

No data available.

14.5 Environmental hazards
Information on environmental hazards, if relevant, please see 14.1 - 14.3.

14.6 Special precautions for user
Transport cytostatics only in unbreakable, liquid-proof and tightly closed containers. Marking of transport containers:
name and address of patient or surgery or hospital ward
label: "Caution cytostatics“
if necessary label “Store refrigerated”
if necessary label: "Caution breakable glass“ and add instructions for the event of breakage
heat-sealing of primary containers is recommended; Heat-sealing of primary containers recommended.

14.7 Maritime transport in bulk according to IMO instruments
Not relevant

SECTION 15: Regulatory information

15.1 Safety, health and environmental regulations/legislation specific for the substance or mixture

EU regulations

Regulation (EC) No 1907/2006 (REACH) Annex XIV (List of substances subject to authorisation)
According to the data available and/or specifications supplied by upstream suppliers, this product does not contain any substances considered as substances requiring authorisation as listed on Annex XIV of the REACH regulation (EC) 1907/2006.

REACH candidate list of substances of very high concern (SVHC) for authorisation
According to available data and the information provided by preliminary suppliers, the product does not contain substances that are considered substances meeting the criteria for inclusion in annex XIV (List of Substances Subject to Authorisation) as laid down in Article 57 and article 59 of REACH (EC) 1907/2006.

Regulation (EC) No 1907/2006 (REACH) Annex XVII: RESTRICTIONS ON THE MANUFACTURE, PLACING ON THE MARKET AND USE OF CERTAIN DANGEROUS SUBSTANCES, MIXTURES AND ARTICLES				
The product is considered being subject to REACH regulation (EC) 1907/2006 annex XVII.				No 3
The product contains following substance(s) that are considered being subject to REACH regulation (EC) 1907/2006 annex XVII.				
No	**Substance name**	**CAS no.**	**EC no.**	**No**
1	**methotrexate**	**59-05-2**	**200-413-8**	**75**

Directive 2012/18/EU on the control of major-accident hazards involving dangerous substances
This product is not subject to Part 1 or 2 of Annex I.

Other regulations
Observe employment restrictions for child bearing mothers and nursing mothers in their latest version. Observe employment restrictions for young people in their latest version.

15.2 Chemical safety assessment
A chemical safety assessment has not been carried out for this mixture.

SECTION 16: Other information

Further information
Further drug-specific information can be found in the product insert accompanying this product or in the expert information.
The information is based on our current knowledge however it does not represent a guarantee of product properties nor does it create any legal obligation.

Sources of key data used to compile the data sheet:
Regulation (EC) No 1907/2006 (REACH), 1272/2008 (CLP) as amended in each case.
Directives 2000/39/EC, 2006/15/EC, 2009/161/EU, (EU) 2017/164.
National Threshold Limit Values of the corresponding countries as amended in each case.
Transport regulations according to ADR, RID, IMDG, IATA as amended in each case.
The data sources used to determine physical, toxic and ecotoxic data, are indicated directly in the corresponding section.

Full text of the H- and EUH- phrases drawn up in sections 2 and 3 (provided not already drawn up in these sections)

H301	Toxic if swallowed.
H315	Causes skin irritation.
H319	Causes serious eye irritation.
H335	May cause respiratory irritation.

Creation of the safety data sheet
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