

Trade name: Methotrexate tablets medac

Status: 18.02.2009

Version: 2.1.0 / GB

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1.) Identification of the substance/preparation and of the company/undertaking

Identification of the substance or preparation

Trade name

Methotrexate tablets medac

Use of the substance/preparation

pharmaceutical products

Company/undertaking identification

Address

medac Gesellschaft für klinische Spezialpräparate mbH

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Advice on Safety Data Sheet

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2.) Hazards identification

Classification

Repr.Cat.2; R61 May cause harm to the unborn child.
 Repr.Cat.2; R60 May impair fertility.
 Muta.Cat.2; R46 May cause hereditary genetic damage.

Hazard symbols

T Toxic

R phrases

46 May cause hereditary genetic damage.
 60 May impair fertility.
 61 May cause harm to the unborn child.

3.) Composition / information on ingredients

Hazardous ingredients

methotrexate

EC no.	200-413-8	Index no.	-	CAS no.	59-05-2
Concentration	< 3			%-b.w.	
Classification	Repr.Cat.2; R61	Repr.Cat.2; R60	Muta.Cat.2; R46	T; R25	Xi; R36/37/38
Hazard symbols	T	R phrases			46-60-61-25-36/37/38

4.) First aid measures

General information

In case of persisting adverse effects, consult a physician.

After inhalation

In the event of symptoms take medical treatment. Ensure supply of fresh air.

After skin contact

When in contact with the skin, clean with soap and water.

After eye contact

In case of contact with eyes rinse thoroughly with copious amounts of water and seek medical advice.

After ingestion

Rinse out mouth and give plenty of water to drink. Induce vomiting if patient is conscious, seek medical advice.

5.) Fire-fighting measures

Suitable extinguishing media

Foam; extinguishing powder; ABC powder

Special exposure hazards arising from the substance or preparation itself, combustion products, resulting gases

Fire gas of organic material has to be classed invariably as respiratory poison.

Special protective equipment for fire-fighters

Use self-contained breathing apparatus.

6.) Accidental release measures

Personal precautions

Cordon and mark contaminated area. Personal protection equipment for removal of unintentional contamination or in the event of rupture :

- Overshoes
- liquid-proof protective long-sleeved coat with close-fitting sleeve-band
- protective goggles with side protection shield
- protective gloves
- Protective face mask min. P2 according to the provisions of the professional organisation "Rules for use of breathing apparatuses"
- cut cellulose in sufficient quantity
- receptacle and waste container, shovel

Environmental precautions

Do not allow to enter drains or waterways.

Methods for cleaning up/taking 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 with several layers of cellulose contaminated area carefully over its whole surface, so that the cellulose can be wetted cautiously from above. A dispersal 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.

Decontamination procedure for handling exposed persons:

- Remove contaminated clothes immediately.
- As for prevention, shower thoroughly.
- After direct contact with skin, seek medical advice.
- In case of eye contact, rinse with isotonic saline solution and seek medical advice.
- Prepare a full accident report / make a record in the accident book.

Additional informations (chapter 6)

Refrain from a chemical inactivation as no standard method exists for inactivation. In many cases strong acids or lyes are necessary; optionally oxidants such as hypochlorite solution can also be used. Inactivating agents must be added in abundance and left for a longer period of time to take effect. One would be constrained to render innocuous a CMR substance using "hazardous substances" which are substances of concern. The use of heat to inactivate in case of spills is all but impossible because of the high temperatures. Likewise it is possible that the described methods release other, toxic artefacts.

Chemical inactivating method and combustion temperature of Methotrexate:

- Deactivation: not recommended
- Thermal destruction with at least 1000°C

References:

Barth, J.(2007): Zytostatikaherstellung in der Apotheke, deutscher Apotheker Verlag

Allwood, M., Wright, P. (1997): The cytotoxics handbook, 3rd edition. Radcliffe Medical Press Ltd. 18 Marcham Road Abingdon Oxon OX14 1AA, UK

7.) Handling and storage

Handling

Advice on safe handling

Avoid the formation and deposition of dust. Open and handle container with care. Only qualified and trained persons are authorised to handle

Classification of fires

A

Storage

Further information on storage conditions

Keep container tightly closed. Protect from heat and direct sunlight. Keep in a cool place. Store in a dry place.

8.) Exposure controls / personal protection

Exposure limit values

N O N E

Exposure controls

Occupational exposure controls

Handling of cytostatics / virusstatics calls always for separated, clearly marked working spaces in compliance with TRGS 525 (technical provisions for hazardous substances).

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Personal protective equipment

Respiratory protection

If ventilation insufficient, use a respiratory protection apparatus.

Respiratory filter (part): min. P2

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 DIN EN 374
- finger area designed with double wall thickness
- advantageous: dyed gloves recommendation
- Wearing of two pairs of gloves (i.e. Biogel@Indicator™); According to TRGS 525 cytostatics protective gloves must be changed every 30 minutes.

Material thickness > 0,2 mm

Eye protection

Safety glasses with side protection shield (EN 166)

Skin protection

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

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). At work do not eat, drink, smoke or take drugs. Keep separated from food-stuffs and feed-stocks.

9.) Physical and chemical properties

General information

Form	Tablets
Colour	whitish
Odour	odourless

10.) Stability and reactivity

Hazardous decomposition products

No hazardous decomposition products known.

Thermal decomposition

Remarks No decomposition if used as prescribed.

11.) Toxicological information

Acute toxicity

Acute oral toxicity

LD50		135	mg/kg
Species	rat		
Reference substance	Methotrexate		
LD50		146	mg/kg
Species	mouse		
Reference substance	Methotrexate		

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Acute toxicity / further data

LD50		14	mg/kg
Species	rat		
Route of exposure	i.v.		
Reference substance	Methotrexate		
LD50		65	mg/kg
Species	mouse		
Route of exposure	i.v.		
Reference substance	Methotrexate		
LD50		6	mg/kg
Species	rat		
Route of exposure	intraperitoneal		
Reference substance	Methotrexate		
LD50		50	mg/kg
Species	mouse		
Route of exposure	intraperitoneal		
Reference substance	Methotrexate		
LD50		58	mg/kg
Species	rat		
Route of exposure	s.c.		
Reference substance	Methotrexate		
LD50		250	mg/kg
Species	mouse		
Route of exposure	s.c.		
Reference substance	Methotrexate		

Effects after repeated or prolonged exposition (subacute, subchronic, chronic)

Mutagenicity

Reference substance	Methotrexate	
Value		Can cause malformations.
Remarks		Product contains over 0.1% of a substance classified as mut. cat. 2 that is also classified as mut. cat. 2 according to the directive 1999/45/CE.

Reproduction toxicity

Reference substance	Methotrexate	
Remarks		Product contains over 0.5% of a substance classified as rep. cat. 2 that is also classified as rep. cat. 2 according to the directive 1999/45/CE.

Other information (chapter 11.)

The product is a substance of Repr. Cat. 2
The toxicological information is based on the main components.

12.) Ecological information

Ecotoxicity

Behaviour in sewers [waste treatment plants]

Remarks	When low concentrations are discharged correctly into adapted biological sewage treatment plants, disturbance of the degradation activity of activated sludge is not likely.
Remarks	Treat by state-of-the-art technology before discharging into drains.

Persistence and degradability

Physico-chemical eliminability

Value		1200	mgO2/g
Type	COD decrease		
Reference substance	Methotrexate		

Other adverse effects

Do not discharge product unmonitored into the environment.

13.) Disposal considerations

Product

Cytostatic remainders as well as with cytostatics contaminated materials can form both with preparation and with application.

During formulation various quantities of following materials are produced:

- residues of concentrated solutions of cytostatic agent (injections)
- residues of diluted solutions (infusions, instillations)
- empty material (original receptacles, syringes)
- auxiliary means for formulation/preparation (cannula, swabs, pads, gloves etc.)

Following waste materials are produced when used:

- empty material (syringes, infusion receptacles)
- cytostatic residues from injections, that have not been completely consumed

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- injection residues in hoses, infusion sets, unemptied bags/bottles of infusion

Note:

Collect waste material separately in suitable waste containers where produced (on cytostatic workbench in pharmacy, during preparation of administration, in the treatment room) and prepare for in-house transport. The legal provisions relating to waste of the respective state must be adhered to.

German Federal States follow the so-called "Guidelines ruling the correct disposal of waste from health service facilities" issued by the Working Group of the Federal States on Waste (LAGA).

Following cytostatic waste materials must be disposed of as hazardous waste ("special waste"):

- original receptacles that are not completely emptied such as cytostatics resulting from discontinued therapy or unintended use
- decayed CMR drugs in original packing
- residues of dry substances and broken tablets
- syringe barrel and infusion bottles / bags with visible filling level/residual contents (> 20 ml)
- Infusions systems and other cytostatics contaminated material (> 20 ml)
- material that has been evidently contaminated through spillage of large quantities of liquids or solids during preparation or use of the aforementioned drugs (i.e. pads, strongly contaminated individual protective equipment).

Such waste needs to be collected in pedal bins or waste containers with an opening mechanism in order to avoid any direct contact of hands/gloves with the waste.

According to the legal provisions relating to hazardous goods and waste, such waste needs to be placed in appropriate, airtight and sound containers for disposal at a special facility displaying the following information: "AS 18 0108* – Cytotoxic and cytostatic waste" and the proper UN No. (pls. see below) according to the Transport of Dangerous Goods Regulations.

The ADR label No 6.1 (Symbol „skull and crossbones“) shall be always affixed to the disposal containers. According to the regulation on hazardous substances Gefahrstoffverordnung (GefStoffV) disposal containers containing cytostatics labelled with the ADR label No 6.1 need no additional labelling (hazard symbol T, skull and crossbones on an orange background).

Cytostatic waste disposed of under the waste name "AS 18 0108* – Cytotoxic and cytostatic waste" shall be provided with one of the following UN No.:

- UN 2810 "TOXIC LIQUID, ORGANIC, N.O.S.": Suitable for liquid cytostatics residues. In case of low liquid quantities, the packaging must only comply with the requirements of the Packaging group III.
- UN 2811 "TOXIC SOLID ORGANIC, N.O.S.": Suitable for solid cytostatic residues (i.e. broken tablets) and strongly contaminated materials.
- UN 3243 "SOLIDS CONTAINING TOXIC LIQUID, N.O.S.": Can be used as an alternative to UN 2810 and UN 2811.

Usually following low-contaminated waste does not fall under the scope of the aforementioned group of hazardous waste:

- gauntlets
- gloves
- face masks
- single-use lab coats
- swabs
- wipes
- empty cytostatics containers after intended use (ampoules, syringes, infusion accessories, infusion receptacles)
- air filters from safety workbenches

Low contaminated cytostatic waste shall be collected in airtight, plastic bags before final disposal immediately at the point of origin. They are disposed of using the official code and name "AS 18 01 04 – Wastes whose collection and disposal is not subject to special requirements in order to prevent infection (for example dressings, plaster casts, linen, disposable clothing, diapers)". They may be disposed of together with hospital waste (former B waste). Sharp or pointed objects such as cannula, transfer cannula, spikes and cullets shall be collected at the point of waste origin, in puncture resistant and safely closed containers (i.e. sharps bin). When disposing of waste that is containing cytostatics, the provisions of the respective local waste regulation must be adhered to (i.e. does exist a duty to offer to an official buyer).

14.) Transport information

Other information (chapter 14.)

Containerise cytostatics only in unbreakable, liquid-proof and tightly closed containers.

Marking of transport containers:

Name and address of patient or surgery or hospital ward

if necessary label: „Caution cytostatics“

if necessary label: „refrigerated ware“

if necessary label: „Caution breakable glass“, and instructions for the event of breakage

Heat-sealing of primary containers recommended.

15.) Regulatory information

Labelling in accordance with EC directives

The product is not subject to the chemicals act. However it has been classified according to the rules of the chemicals act, so that the precautionary measures comply with the procedures generally foreseen for chemicals handling and to make them comparable.

Hazard symbols

T

Toxic

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Hazardous component(s) to be indicated on label, contains:

methotrexate

R phrases

46 May cause hereditary genetic damage.
60 May impair fertility.
61 May cause harm to the unborn child.

S phrases

53 Avoid exposure - obtain special instructions before use.
22 Do not breathe dust.
45 In case of accident or if you feel unwell, seek medical advice immediately (show the label where possible).

Council Directive 96/82/EC on the control of major-accident hazards involving dangerous substances

Remarks Annex I: not listed.

16.) Other information

Further 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:

EC Directive 67/548/EC resp. 99/45/EC as amended in each case.
Regulation (EC) No 1907/2006 (REACH) as amended in each case.
EC Directives 2000/39/EC, 2006/15/EC as amended in each case.
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 chapter.

Relevant R-phrases (chapter 3):

25 Toxic if swallowed.
36/37/38 Irritating to eyes, respiratory system and skin.
46 May cause hereditary genetic damage.
60 May impair fertility.
61 May cause harm to the unborn child.

Department issuing safety data sheet

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Ready-made medical preparations are not ruled by the chemical's 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.