Package leaflet: Information for the user

Sulfadiazin-Heyl® 500 mg tablets
Active substance: Sulfadiazine

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.

- 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. See section 4.

What is in this leaflet

1. What Sulfadiazin-Heyl is and what it is used for

Sulfadiazin-Heyl contains sulfadiazine and is a bacteriostatic chemotherapeutic agent from the group of intermediately acting sulfonamides.

Sulfadiazin-Heyl is used for treatment of toxoplasmosis (acute and recurrent forms) in combination with pyrimethamine.

2. What you need to know before you take Sulfadiazin-Heyl

Do not take Sulfadiazin-Heyl

- if you are allergic to sulfadiazine, sulfonamides or any of the other ingredients of this medicine (listed in section 6).
- in cases of severe allergic reactions (Erythema exsudativum multiforme or DRESS-syndrome), even in the anamnesis.
- in cases of inflammatory skin reddening (Stevens-Johnson syndrome or toxic epidermal necrosis), even in the anemnesis.
- in cases of pathological changes in blood count with leucopenia and thrombopenia.
- in cases of congenital glucose-6-phosphate dehydrogenase deficiency of erythrocytes.
- in cases of dysfunction in the formation of hemoglobin (hemoglobin anomalies such as Hb Cologne and Hb Zurich, acute porphyria).
- in cases of severe renal dysfunction (creatinine clearance less than 25 ml/min/1,73 m²).
- in cases of severe liver damage or hepatic dysfunction (e.g. acute hepatitis).
- during lactation if you have a premature baby.

Warnings and precautions
Talk to your doctor or pharmacist before taking Sulfadiazin-Heyl.

Potentially life-threatening skin rashes (Stevens-Johnson syndrome, toxic epidermal necrolysis) have been reported with the use of sulfadiazine, appearing initially as reddish target-like spots or circular patches often with central blisters on the trunk. The rash may progress to widespread blistering or peeling of the skin.Additional signs to look for include ulcers in the mouth, throat, nose, genitals and red and swollen eyes (conjunctivitis) . These potentially life-threatening skin rashes are often accompanied by flu-like symptoms (headache, fever, limb pain).

The highest risk for occurrence of serious skin reactions is within the first few weeks of treatment. If you or your child have developed Stevens-Johnson syndrome or toxic epidermal necrolysis with the use of sulfadiazine, you or your child must not re-use on sulfadiazine at any time.

If you or your child develop a rash or other of these skin symptoms, **stop taking** Sulfadiazin-Heyl, **seek urgent advice from a doctor** and tell him that you or your child are taking sulfadiazine.

Immediate blood count checks must be carried out with the occurrence of sore throats, fever or flu-like symptoms during the therapy.

In the following cases Sulfadiazin-Heyl should only be taken under certain conditions and with caution (i.e. at longer intervals or at a reduced dose and under medical supervision). Please consult your doctor for this. This also applies if you have experienced any of these symptoms in the anamnesis. Special caution for taking Sulfadiazin-Heyl is required:

- in case of mild renal or hepatic dysfunction,
- in case of thyroid dysfunction,
- in case of hypersensitivity to sulfonylurea antidiabetics and sulfonamide-based diuretics.

Photosensitization may develop while taking sulfonamide-containing drugs. This should be taken into consideration if there is strong exposure to sun and UV light.

To avoid serious impairment of blood formation concurrent intake of folinic acid (in the form of calciumfolinat) is recommended during combination therapy of sulfadiazine and the folinic acid antagonist pyrimethamine.

Checks of urine and blood count should be carried out during therapy.

Children and adolescents
Sulfadiazin-Heyl is suitable for children older than two months.

Other medicines and Sulfadiazin-Heyl
Tell your doctor or pharmacist if you are taking / using, have recently taken / used or might take / use any other medicine.

The effectiveness of the following drugs or product groups can be influenced by concomitant treatment with Sulfadiazin-Heyl:
Probenecid, indomethacine, phenylbutazone, salicylates or sulfinpyrazone may increase the effects of sulfonamides.
Furthermore, a direct reaction with other substances can take place. Concomitant administration of **antacids** reduces the absorption of the sulfonamide.With concomitant administration of **paraldehyde** the sulfonamide is metabolized faster. Together with **hexamethylene tetramine (methenamine)** there is a risk of urinary calculus (crystalluria). The combination with **mandelic acid** increases the risk of crystallization due to acidification of the urine.
Finally, the effectiveness of the sulfonamide may be modified by competition in the site of action. Antagonistically acting substances with a similar structure (**benzocaine, procaine, tetracaine**) may reduce the effectiveness of the sulfonamides.

How Sulfadiazin-Heyl influences the effect of other drugs:
There are different types of interactions with other medicines. One possibility is the change of concentration of active substances due to competing reactions to the plasma protein binding. This can result in an increase of the effect of other drugs (**anticoagulants, oral antidiabetics from the group of the sulfonylureas, diphenylhydantoin, methotrexate, thiopental**).

Pregnancy and breast-feeding
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

Pregnancy
There is no adequate experience in humans with the use of Sulfadiazin-Heyl during pregnancy. Sulfadiazin-Heyl should not be used in the first three months of pregnancy. For this period your doctor should prescribe drugs with another active substance.

During pregnancy, the administration of sulfonamides, the class of active ingredients to which Sulfadiazin-Heyl belongs, can increase the risk of hyperbilirubinemia (increased concentration of the bile pigment bilirubin in the blood), particularly in premature babies. From the second trimester of pregnancy Sulfadiazin-Heyl may therefore be applied as part of a combination therapy only on the advice of the attending doctor, and only after he has made a very strict risk / benefit assessment.

Breast-feeding
Sulfonamides are excreted in breast milk. For healthy babies the ingested amount of Sulfadiazin-Heyl by the milk is most likely no particular risk. Babies with hyperbilirubinemia or certain metabolic diseases, however, should not be breastfed. So, talk with your doctor before breast-feeding.
Mothers of premature babies should not take Sulfadiazin-Heyl during the lactation period.

Driving and using machines
During treatment with sulfadiazine a temporary shortsightedness can occur very rarely. This could influence the ability of the active participation in traffic or for operating heavy machinery.

3. How to take Sulfadiazin-Heyl

Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

Posology
The recommended dose for treatment of toxoplasmosis in combination with pyrimethamine is:

Adults
Adults should take an initial and temporary dose of 50 mg per kilogram body weight per day of sulfadiazine up to a maximum of 4.0 g (corresponding to 4 - 8 tablets) per day. For a patient of 60 kg this would result in 6 tablets daily.

Children over 2 months of age
Children over 2 months of age receive 50 to 100 mg of sulfadiazine/kg body weight (maximum 1.5 g per day). The initial dose in children over 2 months is half of the daily dose.

Route and method of administration
For oral use.
The total dosage is divided into 4 single doses.

Please take the tablets with sufficient liquid (primarily a glass of drinking water).

Care must be taken to ensure adequate fluid intake during treatment (in adults at least 1,200 ml urine output daily). If an adequate fluid intake cannot be achieved, then sodium hydrogen carbonate should be administered in order to reduce the risk of crystalluria.

Duration of treatment
The duration of treatment will be decided by your doctor.

If you take more Sulfadiazin-Heyl than you should
The symptoms of overdosage are the excretion of crystals in the urine (crystalluria), decreased or absent diuresis (oliguria, anuria), nausea, vomiting, diarrhoea, headaches and dizziness. In these cases consult your doctor as soon as possible so that he can start necessary treatment depending on the severity of the symptoms of overdosage.

If you forget to take Sulfadiazin-Heyl
Do not take a double dose to make up for a forgotten dose.

If you stop taking Sulfadiazin-Heyl
If you discontinue or reduce the duration of the medical treatment, there is the danger of relapse. It is essential that you discuss this matter with your doctor beforehand.

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

4. Possible side effects

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

Some side effects can be serious. If you notice any of the following signs contact a doctor immediately. Possibly, he will decide to perform liver, kidney or blood checks and give the order to discontinue the intake of this medicine.

Very rare: may affect up to 1 in 10 000 people

- severe, potentially life-threatening skin rashes (Stevens-Johnson syndrome, toxic epidermal necrolysis). For further information see section 2 " Warnings and precautions".
- severe reduction or absence of granulocytes in the blood (agranulocytosis).
  This potentially life-threatening reaction manifests in severe general ill feeling, associated with fever, chills, palpitations, sore throat and swallowing problems as well as painful inflammations of the oral, nasal and pharyngeal mucosa and in the anal and genital area. In these cases stop therapy with Sulfadiazin-Heyl **immediately** and contact a doctor. Do not treat symptoms on your own with pain relievers or medication to reduce fever. When the symptoms have ceased do not re-use Sulfadiazin-Heyl.

Other possible side effects

Uncommon: may affect up to 1 in 100 people

- gastrointestinal disorders such as nausea, vomiting and diarrhoea.
- hypersensitivity reactions such as skin rashes of various types (nettle rash, erythema-like, blotchy or measles-like)
- reddish skin haemorrhages (purpura)
- skin reactions due to light sensitivity (photodermatosis)
- nodular erythema (erythema nodosum)
- acute loss of the upper layers of skin (Lyell syndrome, epidermolysis acuta toxica);
- skin inflammation with loss of skin (exfoliative dermatitis)
- excretion of crystals in the urine (crystalluria). This can result in a renal failure.
- drug fever
- headaches and joint pains

Rare: may affect up to 1 in 1 000 people

- folic acid deficiency with symptoms of anaemia and diarrhoea
- liver damage with disorders of bile flow (cholestatic hepatosis)

Very rare: may affect up to 1 in 10 000 people

- changes in the blood count with reduction of blood platelets and white blood cells (thrombopenia, leukopenia)
- increase of the eosin-staining granulocytes in the blood (eosinophilia)
- bone marrow damage resulting in impaired formation of red blood cells (aplastic anaemia)
- increased destruction of red blood cells (acute haemolytic anaemia)
- severe drug allergy with eosinophilia and systemic symptoms (DRESS syndrome)

- lowered blood sugar level (hypoglycaemia)
- temporary visual disorders (transitory myopia)
- focal to diffuse liver necrosis
- punctate skin haemorrhages (petechia)
- cyanosis due to insufficient oxygen saturation in the presence of congenital glucose-6-phosphate dehydrogenase deficiency of the red blood cells or anomalies of the red pigment, such as Hb Cologne and Hb Zurich
- interstitial inflammation of the kidneys

Please inform your doctor about the appearance of diarrhoeas since this can result in an impairment of the absorption and so in the effectiveness of Sulfadiazin-Heyl.

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly to Bundesinstitut für Arzneimittel und Medizinprodukte, Abt. Pharmakovigilanz, Kurt-Georg-Kiesinger Allee 3, D-53175 Bonn, Website: www.bfarm.de. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Sulfadiazin-Heyl

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the blister and carton after ”Verwendbar bis”. The expiry date refers to the last day of that month.

Do not store above 25 ºC.

Store in the original package in order to protect from light and moisture.

Do not throw away any medicines via wastewater. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Sulfadiazin-Heyl contains
The active substance is: sulfadiazine.
1 tablet contains 500 mg of sulfadiazine.

The other ingredients are: Calcium behenate, copovidone, crospovidone, maize starch, colloidal anhydrous silica, talc.

What Sulfadiazin-Heyl looks like and contents of the pack
Sulfadiazin-Heyl consists of white, circular tablets.

Sulfadiazin-Heyl is available in packs with 30 or 100 tablets in blister packs.

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Properties
Toxoplasmosis is an infectious disease caused by the pathogen Toxoplasma gondii. The usual host of this organism is the cat. They excrete resistant early stages of the organism. These can be ingested by humans directly (e.g. from unwashed fruit) or indirectly via infected beef or pork eaten raw or insufficiently cooked. Generally the infection proceeds without symptoms, possibly there may be flu-like symptoms with swelling of the lymph nodes in the neck region. With an intact immune system it results in a life-long protection against infection and is not necessarily in need of treatment.

It must be treated, however, in

1. pregnant women, even if the infection disease is asymptomatic, as the child may be born with severe handicaps through transmission of the organism to the developing baby;
2. any symptomatic disease (e.g. affecting the heart, lungs and brain), which occurs especially in patients with compromised immune systems;
3. ocular toxoplasmosis.

The treatment of toxoplasmosis is generally done with sulfadiazine in combination with pyrimethamine and folinic acid. The aim of this combination treatment with chemotherapeutic agents kills even the precursors of the pathogen by interfering with their important biochemical processes of life such as the folic acid synthesis.