Package leaflet: **Information for the patient**

Ditripentat-Heyl® (DTPA)
1 000 mg solution for injection

For use in adults

Active substance: Calcium trisodium pentetate (Ca-DTPA)

Read all of this leaflet carefully before this medicine will be administered to you because it contains important information for you.
Always let this medicine exactly be administered as described in this leaflet or as your doctor or pharmacist has told you.
- Keep this leaflet. You may need to read it again.
- Ask your pharmacist if you need further information or advice.
- 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.
- You must talk to a doctor if you do not feel better or if you feel worse after a week.

What is in this leaflet

1. What Ditripentat-Heyl (DTPA) is and what it is used for

Ditripentat-Heyl (DTPA) contains calcium trisodium pentetate (Ca-DTPA) and is an antidote at radionuclide poisoning.

Ditripentat-Heyl (DTPA) is used for long-term treatment of poisoning with radioactive metals (americium, plutonium, curium, californium, berkelium).

2. What you need to know before you use Ditripentat-Heyl (DTPA)

Do not use Ditripentat-Heyl (DTPA),
- if you are allergic to DTPA, its salts or any of the other ingredients of this medicine (listed in section 6.)
- during pregnancy
- with children and adolescents
- at hypercalcemia
- at patients with damages of the kidneys (nephrotic syndrome) or of the bone marrow (bone marrow depression, leucocytopenia, thrombocytopenia) or
- at an oral uptake of radionuclides as long as the nuclide is still in the gastro-intestinal tract, since the complexed radionuclide may be better absorbed than the uncomplexed one.

Ditripentat-Heyl (DTPA) should not be used at poisoning with uranium, neptunium or cadmium.

Warnings and precautions
Talk to your doctor or pharmacist before Ditripentat-Heyl (DTPA) is administered.

The daily dose may not be given in several divided doses.

Regular monitoring of the urine and blood count should be carried out before and during treatment. The blood pressure should be regularly monitored during administration of Ditripentat-Heyl (DTPA).

If diarrhea occurs, therapy should be discontinued.

Long-term treatment should be carried out under regular monitoring of the radioactive nuclides and of the essential trace elements.

Delayed initiation of treatment should be avoided because the chelating effect of Ditripentat-Heyl (DTPA) is greatest when the radioactive metals are still circulating in the blood and are outside the cells. The therapeutic efficacy of this drug decreases with time after contamination because the radioactive metals may be deposited in hard-to-reach compartments such as bone.

The treatment of intoxications with Ditripentat-Heyl (DTPA) does not preclude other forms of therapies of intoxications, for instance gastrolavage, dialysis, plasma exchange, surgical resection of depots etc.

Children and adolescents
Ditripentat-Heyl (DTPA) is not approved for the treatment of children.
In this case it can be switched to Zn-DTPA.

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

At simultaneous administration of Ditripentat-Heyl (DTPA) with essential heavy metals, such as zinc or iron, the drugs can mutually cancel each other out in their effectiveness. It is therefore recommended to carry out a perhaps necessary substitution of the trace elements temporally staggered.

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 using this medicine.

Pregnancy
Ditripentat-Heyl (DTPA) may not be used during pregnancy. In this case it can be switched to Zn-DTPA.

Breast-feeding
Breast-feeding should not be carried out in the presence of radionuclide uptake generally.

Driving and using machines
No effects are known to this day.

Ditripentat-Heyl contains sodium.
This medicine contains 138.8 mg sodium (main component of cooking/table salt) in each ampoule. This is equivalent to 6.9 % of the recommended maximum daily dietary intake of sodium for an adult.

3. How to use Ditripentat-Heyl (DTPA)

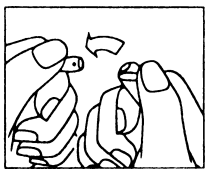
You receive Ditripentat-Heyl as an intravenous injection or infusion.

Posology
Treatment of poisoning requires individual dosage, depending on the symptoms of intoxication.

The recommended dose is for
Adults: 1 ampoule per day

The following dosage regimen is recommended for the therapy of adults:
- First week: 1 000 mg of Ca-DTPA on 5 days each
- Following 6 weeks: 1 000 mg of Ca-DTPA from 2 to 3 times per week
- Following 6 weeks: therapy pause
- Further alternating 3 weeks therapy (1 000 mg of Ca-DTPA 2-3 times weekly) and 3 weeks therapy pause or 1 000 mg of Ca-DTPA i.v. every 2 weeks.
- The therapy pause can also be 4 to 6 months depending on the individual case.

Route and method of administration
Initially administer 1 000 mg of Ca-DTPA (about 15 mg/kg/d) in 20 ml of physiological saline solution or 5% glucose solution as a very slow i.v. injection (duration of the injection: about 15 min) or preferably as an infusion in 250 ml of the dilution solution over ½ to 2 h. The solution for injection or infusion is to be used immediately after preparation.



OPC ampoule
To open, turn so that the point faces upward and break off the neck with a downward movement.

Duration of treatment
Treatment with Ditripentat-Heyl (DTPA) should be started as soon as possible, since a loss of effect caused by a delay in starting treatment later cannot be compensated. If Ditripentat-Heyl (DTPA) is not immediately available, taking it later can also be useful and effective.

The duration of the treatment depends on the clinical and laboratory results (radionuclide excretion in the urine). As long as the excretion rate of the metals is increased by the administration of DTPA, the therapy should be continued.
The necessary treatment can be very protracted (in individual cases about several years) and requires a multitude of injections.

At a long-term therapy zinc should be substituted regularly. The long-term therapy can alternatively be switched to Zn-DTPA.

You should drink well while using Ditripentat-Heyl (DTPA).

If you assume that more Ditripentat-Heyl (DTPA) was applied than it should
High doses of Ca-DTPA can lead to severe damages of the kidneys, of the intestinal mucosa and of the liver. As a cause a depletion of zinc and manganese is suspected. At appearance of corresponding symptoms the trace elements have to be checked and to be substituted. In addition, a symptomatic therapy can be required.

Ditripentat-Heyl (DTPA) should be used according to the instructions of the doctor or to the dosage regimen described in this leaflet. If you have the impression to feel no sufficient alleviation of your complaints ask your doctor.

If you assume that application of Ditripentat-Heyl (DTPA) has been forgotten
If you assume that the previous application has been forgotten address to professional health care staff. It should not be used twice the dose if the previous application was forgotten. Continue with the dosage indicated. However, please take into account that Ditripentat-Heyl (DTPA) only can work safely and sufficiently if it is used regularly.

If you stop using Ditripentat-Heyl (DTPA)
As there is a risk that the poisoning continues to exist please contact your doctor in any case before you interrupt or shorten the medical treatment.

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.

Depending on kind and severity of the illness, as well as on the appropriately necessary dosage and duration of the medical treatment the following side effects can appear in individually different frequency:

- Local irritation symptoms (thrombophlebitic reactions) have been described at a rapid intravenous injection.
- At repeated administrations of Ca-DTPA with too short regeneration intervals between the single ones, the following symptoms may occur: Delayed fever reaction, nausea, vomiting, diarrhoea, shiver, headaches, itching (pruritus), muscular cramps.
- Rare: may effect up to 1 in 1 000 people
  - reduction in blood pressure
  - tingling (paresthesias)
  - rhinitis vasomotorica
  - allergic reactions in the form of skin reactions.
- DTPA increases the excretion of some trace elements particularly of zinc. In individual cases with long-term treatment clinically manifest zinc deficiency was described (alopecia, skin reactions, mucosa changes [exanthemas, enanthemas]). The symptoms were reversible after the supplementation of zinc. A reversible loss of smell was described at one patient.
- The increased zinc excretion is presumably also the main cause for other side effects. So kidney lesions, intestine disturbances and bone marrow damages (thrombocytopenia) are described at Ca-DTPA therapy.
  At lack of minerals the appropriate trace elements must be substituted.
- DTPA can lead to kidney damages (nephrotic syndrome and renal insufficiency). A deterioration of the kidney function has been proved at pre-lesion of the kidney. A special caution is therefore advised at poisonings with metals which have themselves kidney damaging effects. The changes at the kidneys are reversible after removing DTPA.
  The therapy with Ditripentat-Heyl (DTPA) should be stopped at occurrence of changes of the kidneys (e.g. proteinuria, hematuria, urinary cast) or of the blood count. This also applies to occurrence of diarrhoea. In addition, a symptomatic therapy can be required.

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 Ditripentat-Heyl (DTPA)

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

Do not store above 25 °C.

Store in the original package.

The solution for injection or infusion is to be used immediately after the preparation.

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

Do not throw away any medicines via wastewater (e.g., via toilet or washbasin). Ask your pharmacist how to throw away medicines you no longer use. These measures will help to protect the environment. You can find further information at www.bfarm.de/arzneimittelentsorgung.

6. Contents of the pack and further information

What Ditripentat-Heyl (DTPA) contains

- The active substance is: calcium trisodium pentetate.
  1 ampoule with 5 ml solution for injection contains 1 000 mg calcium trisodium pentetate (Ca-DTPA)

- The other ingredients are: Calcium carbonate, hydrochloric acid for pH adjustment, sodium hydroxide, pentetic acid, water for injections.

What Ditripentat-Heyl (DTPA) looks like and contents of the pack
Ditripentat-Heyl (DTPA) is a clear, colourless to slightly yellowish solution for injection.

Ditripentat-Heyl (DTPA) is available in packages with 5 ampoules with 5 ml of clear solution for injection each.

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