Package leaflet and summary of product characteristics

TOXAVIT

Dental paste (for dental pulp devitalisation)

Package leaflet and summary of product characteristics: Information for the user

TOXAVIT Paste

Active substances paraformaldehyde, lidocaine hydrochloride 1 H_2O and metacresol (Ph.Eur.)

Read all of this leaflet carefully before you start using 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 dentist or pharmacist.
- If you get any side effects, talk to your dentist or pharmacist. This includes any possible side effects not listed in this leaflet. (see section 4).

What is in this leaflet

1. What TOXAVIT is and what it is used for

TOXAVIT is used to devitalise dental pulp in particular cases where endodontic surgical measures (e.g. vital extirpation) are not possible. Prior to use, it should be checked whether successful treatment might be able to be achieved using other, aldehyde-free procedures (e.g. anaesthesia or bleeding control).

2. What you need to know before you use TOXAVIT

Do not use TOXAVIT

if you are allergic to paraformaldehyde, lidocaine, metacresol or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions

Talk to your dentist before using TOXAVIT.

While the paste is in place, the cavity must be sealed tightly at all events. The paste should not remain in place for longer than a maximum of 14 days prior to mortal extirpation. TOXAVIT may not be used in the presence of perforation. Any contact between the paraformaldehyde-containing TOXAVIT paste and the surrounding soft tissue during insertion into or sealing of the tooth resulting from oozing out of the paste is to be avoided due to its extremely caustic and necrotising effect.

Should the use of TOXAVIT cause necrosis of the gum, the periapical tissue or bone, the inlay is to be removed and the patient admitted to hospital.

In the event that the paste accidentally comes into contact with the skin or mucous membranes, the affected areas should be rinsed with ample amounts of water.

Prior to using the preparation, the patient should be informed about the eventual risks associated with treatment as well as about alternative forms of treatment.

Children

Particular care should be taken with children (see section 4).

Other medicines and TOXAVIT

If used as intended, none known.

Tell your dentist if you are taking/using, have recently taken/used or might take/use any other medicines.

Pregnancy, breast-feeding and fertility

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

Because of the anticipated low systemic exposure of paraformaldehyde following topical application of TOXAVIT no effect on the pregnancy or the breastfed newborns/infant of treated women are anticipated. TOXAVIT can be used during pregnancy and lactating with caution.

For TOXAVIT there are no clinical studies on exposed pregnant women available. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/fetal development, parturition or postnatal development (see section 7.3).

Driving and using machines

TOXAVIT has no or negligible influence on the ability to drive and use machines.

3. How to use TOXAVIT

In general, 20 - max. 25 mg (pinhead-sized pellet) TOXAVIT, equivalent to

9.2 - max. 11.5 mg paraformaldehyde

7.4 - max. 9.3 mg lidocaine hydrochloride 1 H_2O

is applied.

After making a wide opening in the roof of the pulp, insert a pinhead-sized pellet (20 - max. 25 mg) of TOXAVIT paste into the tooth using a spatula and carefully spread with a pellet plugger using as little pressure as possible, until the TOXAVIT insert is in direct contact with the pulp. If necessary, the paste can also be inserted into the exposed pulp using a lentulo spiral. Cover

the insert with a cotton wool pellet to absorb any eventual pressure from the seal. The seal must also be applied without using any pressure and must be completely leak-proof. Where cavity seals are not leak-proof, and
approximal leakage occurs, and where the paste oozes out, papillary burning may lead to extremely severe soft tissue and bone necrosis.
The paste may not remain in place for longer than a maximum of 14 days prior to mortal extirpation; where the pulp shows residual vitality, application of the paste may be repeated after removal of dead pulp tissue. In this case, the paste should also remain in place for no longer than a maximum of 14 days.

If you use more TOXAVIT than you should
When using TOXAVIT for devitalisation of the dental pulp no cases of overdose were reported.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.
In the assessment of adverse events following frequencies are used:
Very common: may affect more than 1 in 10 people
Common: may affect up to 1 in 10 people
Uncommon: may affect up to 1 in 100 people
Rare: may affect up to 1 in 1,000 people
Very rare: may affect up to 1 in 10 000 treated
Not known: frequency cannot be estimated based on available data

Uncommon:
Upon extirpation of the pulp, occasional bleeding occurs at the apical site of detachment despite devitalisation.

Very rare:
When used on milk-teeth, damage to the dental germ of the subsequent adult tooth may occur during the early stages of development (before mineralisation is complete) in extremely rare cases.

Not known:
Following application to the exposed pulp cavity, more or less severe pulpitis-like complaints occur. These are relieved through the addition of the local anaesthetic lidocaine hydrochloride to the paste.
In the event of insufficient diffusion or inadequate release of formaldehyde, vital tissue fragments can remain in the canal and cause considerable pain.
If formaldehyde extravasates from the apex or the furcation area or side canals or leaking filling edges, inflammation or necrosis of periapical tissue, surrounding bone or the gums may result.
Systemic effects cannot be ruled out.

There are no findings on this method of application and local carcinogenicity.
Local and systemic allergic reactions are possible.

Reporting of side effects
Reporting of suspected adverse reactions after marketing authorisation is of great importance. It allows continuous monitoring of the risk-benefit ratio of medicinal product. Health professionals are encouraged to report any suspect case of an adverse reaction to the Federal Institute for Drugs and Medical Devices, Department of Pharmacovigilance, Kurt-Georg-Kiesinger-Allee 3, D-53175 Bonn, website: *www.bfarm.de*
Please inform your doctor or pharmacist if any of the side effects affecting you significantly, or if you notice any side effects not listed in this package leaflet or technical information.
You can also report side effects directly to the Federal Institute for Drugs and Medical Devices, Department of Pharmacovigilance, Kurt-Georg-Kiesinger-Allee 3, D-53175 Bonn, website: *www.bfarm.de*
By reporting side effects, you can help provide more information about the safety of this medicine.

5. How to store TOXAVIT

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 label and carton. The expiry date refers to the last day of that month. (see also section 8.2. and 8.3)

Never dispose medicinal products via sewage (e.g. not via the toilet or the sink). Ask your pharmacy how the medicinal product is to dispose if you use it no longer. You help to protect our environment.
For more information, see *www.bfarm.de/arzneimittelentsorgung*

6. Contents of the pack and other information

What TOXAVIT contains
The active substances are: paraformaldehyde, lidocaine hydrochloride 1 H_2O and metacresol (Ph.Eur.)
1 g paste contains 460 mg paraformaldehyde, 370 mg lidocaine hydrochloride 1 H_2O and 45 mg metacresol (Ph.Eur.)
The other excipients are: Eugenol, glycerol and carbon fibres

What TOXAVIT looks like and contents of the pack
Dark grey viscous dental paste in a brown glass bottle

Package with 2 g dental paste Article-No. 0032119

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This Package leaflet and summary of product characteristics was last revised in October 2021.

The following information is intended for healthcare professionals only:

7. Pharmacological properties

7.1 Pharmacodynamic properties

TOXAVIT paste contains paraformaldehyde. Paraformaldehyde is a formaldehyde polymer with a varying number of monomers. Its depolymerisation to formaldehyde is determined by the
environment it is in and the prevailing temperature thereof. Formaldehyde binds to cell proteins and brings about denaturation of proteins and a ceasing of vital cell functions. The onset of this effect is slow.
In tissue, vasodilatation and increased capillary filling is first of all observed. Tissue dies as a
result of endothelial lesions accompanied by haemorrhaging and oedemas, as well as a loss of nuclear staining and hyaline softening of connective tissue, the development of hyaline and blood cell thrombi and finally total interruption of microcirculation. The extent of changes depends on the concentration of formaldehyde and the time it is allowed to take effect. Bacteriostatic or bactericidal effects are achieved in micro-organisms through an appropriate change in protein molecules. There are no definite differences in concentration in respect of an antibacterial and tissue-damaging effect.
There are no details pertaining to the rate of depolymerisation and the concentration of formaldehyde in the tooth. It can be concluded that, from the devitalisation of the whole pulp that occurs in most cases, sufficient amounts of formaldehyde are released.
Lidocaine relieves or prevents eventually occurring pulpitis-like pain.
Metacresol helps the paste to adhere to pulp protein. The paraformaldehyde in the paste reacts with pulp protein to form a leathery mass, which, on the whole, is easy to extirpate.
Eugenol renders the paste soft and suitable for application.

7.2 Pharmacokinetic properties

For pharmacokinetics no data are available

7.3 Preclinical safety data

Formaldehyde has cytotoxic, membrane-toxic and neurotoxic effects, and irritates mucous membranes considerably (particularly eyes, upper respiratory tract, nose). The allergenic potential of formaldehyde is relatively high. Both early type reactions (angioneurotic oedema) and delayed type reactions (contact dermatitis) have been described. As an allergen, paraformaldehyde can also lead to allergic reactions of the early type.
In vivo micronucleus tests performed on mice have usually yielded negative results for paraformaldehyde; there have, however, also been positive results. *In vivo* tests on mammalian systems have produced contradictory results.
Going on epidemiological studies and long-term animal testing, it is at present likely that the carcinogenic effect results mainly from the chronic inflammatory process, which, depending on the concentration thereof, is caused by long-term exposure to formaldehyde, and is not so much based on a direct, genotoxic mechanism.
Numerous studies have been performed on various species of animal to investigate the acute toxicity of lidocaine. Signs of toxicity have manifested themselves in the form of CNS symptoms. Other signs thereof have included lethal cramp attacks. The toxic (cardiovascular or CNS systems, cramp) plasma concentration for lidocaine in humans is specified at 5 µg/ml to > 10 µg/ml blood plasma.
Mutagenicity tests have yielded negative results for lidocaine. There are, however, indications that a metabolite of lidocaine, 2,6-xylidine, produced in rats and possibly in humans, might have mutagenic effects. This was also observed in *in vitro* tests where this metabolite was used in extremely high and almost toxic concentrations. In addition, 2,6-xylidine was seen to have a tumorigenic potential in a carcinogenicity study performed on rats, which were exposed transplacentally to 2,6-xylidine and treated for 2 years with the metabolite upon being born. In the course of this highly sensitive test system, malignant and non-malignant tumours, particularly in the nasal cavity (ethmoturbinalia) were observed after extremely high doses. As it cannot be ruled out with sufficient certainty that these findings are of relevance as far as humans are concerned, lidocaine should not be administered in high doses over long periods of time.
Upon correct use of this medicinal product, metacresol and eugenol are not expected to have any relevant mutagenic potential.
There are no clinically relevant data on the reproduction toxicity of TOXAVIT.

8 Pharmaceutical particulars

8.1 Incompatibilities

None known
In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

8.2 Storage conditions

TOXAVIT is stable for 2 years if stored unopened at 2-8°C.
TOXAVIT must be stored in the refrigerator (2-8°C) and kept always tightly closed.
After each use, the container must immediately be closed tightly and stored in the refrigerator again. (see also section 5)

8.3 Shelf life after first opening

TOXAVIT paste is to be used up within 6 months after the first opening. (see also section 5)

9. Marketing authorisation number

6031118.00.00

10. Date of renewal of the authorisation

06.09.2004

11. Deferred sales

Only for sale in pharmacies ("dental use only")