Package leaflet: Information for the user

Dotagraf 279.32 mg/ml
Solution for injection

Gadoteric acid

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 doctor or radiologist.
- If you get any side effects, talk to your doctor, radiologist or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Dotagraf is and what it is used for

Dotagraf is a contrast agent that contains gadoteric acid. It is for diagnostic use only.

Dotagraf is used to enhance the contrast of the images obtained in examinations with Magnetic Resonance Imaging (MRI). This contrast enhancement improves the visualisation and delineation in:

Adult and paediatric population (0-18 years)
- MRI of the Central Nervous System including defects (lesions) in brain, spinal cord and adjacent tissue;
- Whole body MRI including defects (lesions) in liver, kidneys, pancreas, pelvis, lungs, heart, breast and musculoskeletal system.

Adult population
- MR angiography including defects (lesions) and narrowing (stenosis) in arteries, except in coronary arteries.

2. What you need to know before Dotagraf is used

You should <u>NOT</u> be given Dotagraf
- if you are allergic to the active substance or any of the other ingredients of this medicine (listed in section 6).
- if you are allergic to medicines containing gadolinium (like other contrast agents used for magnetic resonance imaging).

Warnings and precautions
Inform your doctor or radiologist if the following applies to you:
- you have previously reacted to a contrast agent during an examination
- you have asthma
- you have a history of allergy (such as seafood allergy, urticaria, hay fever)
- you are being treated with a beta-blocker (medicine for heart and blood pressure disorders, such as metoprolol)
- your kidneys do not work properly
- you have recently had, or soon expect to have, a liver transplant
- you have a disease affecting your heart or your blood vessels
- you have had convulsions or you are being treated for epilepsy.

In all these cases, your doctor or radiologist will assess the benefit-to-risk ratio and decide whether you should be given Dotagraf. If you are given Dotagraf, your doctor or radiologist will take the precautions necessary and the administration of Dotagraf will be carefully monitored.

Your doctor or radiologist may decide to take a blood test to check how well your kidneys are working before making the decision to use Dotagraf, especially if you are 65 years of age or older.

Neonates and infants
As kidney function is immature in babies up to 4 weeks of age and infants up to 1 year of age, Dotagraf will only be used in these patients after careful consideration by the doctor.

Remove all metallic objects you may wear before the examination. Inform your doctor or radiologist if you have:
- a pacemaker
- a vascular clip
- an infusion pump
- a nerve stimulator
- a cochlear implant (implant in the inner ear)
- any suspected metallic foreign bodies, particularly in the eye.

This is important as these can result in serious problems, as magnetic resonance imaging devices use very strong magnetic fields.

Other medicines and Dotagraf
Tell your doctor or radiologist if you are taking, have recently taken or might take any other medicines. In particular, please inform your doctor, radiologist or pharmacist if you are taking or have recently taken medicines for heart and blood pressure disorders such as beta-blocking agents, vasoactive substances, angiotensin-converting enzyme inhibitors, angiontensin II receptor antagonists.

Dotagraf with food and drink
There are no known interactions between Dotagraf and food and drinks. However, please check with your doctor, radiologist or pharmacist if it is required not to eat or drink before the examination.

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 radiologist for advice before taking this medicine.

Pregnancy

Dotagraf should not be used during pregnancy unless strictly necessary.

Breast-feeding
Your doctor or radiologist will discuss whether you should continue breast-feeding or interrupt breast-feeding for a period of 24 hours after you receive Dotagraf.

Driving and using machines
No data are available on the effects of Dotagraf on the ability to drive. If you feel unwell after the examination, you should not drive or use machines.

3. How Dotagraf is used

Dotagraf will be administered to you by intravenous injection.

During the examination, you will be under the supervision of a doctor or radiologist. A needle will be left in your vein; this will allow the doctor or radiologist to inject you with appropriate emergency drugs if necessary. If you experience an allergic reaction, the administration of Dotagraf will be stopped.

Dotagraf can be administered by hand or by the mean of an automatic injector. In neonates and infants, the product will only be administered by hand.

The procedure will be carried out in a hospital, clinic or private practice. The attending staff know what precautions have to be taken for the examination. They are also aware of the possible complications that can occur.

Dosage
Your doctor or radiologist will determine the dose you will receive and supervise the injection.

Dosage in special patient groups
The use of Dotagraf is not recommended in patients with severe kidney problems and patients who have recently had, or soon expect to have, a liver transplant. However if use is required you should only receive one dose of Dotagraf during a scan and you should not receive a second injection for at least 7 days.

Neonates, infants, children and adolescents
As kidney function is immature in babies up to 4 weeks of age and infants up to 1 year of age, Dotagraf will only be used in these patients after careful consideration by the doctor. Neonates and infants should only receive one dose of Dotagraf during a scan and should not receive a second injection for at least 7 days.
Use for angiography is not recommended in children less than 18 years of age.

Elderly
It is not necessary to adjust your dose if you are 65 years of age or older but you may have a blood test to check how well your kidneys are working.

If too much Dotagraf has been administered to you
It is highly unlikely that you will be given an overdose. You will be given Dotagraf in a medical setting by a trained person. In the real case of overdose, Dotagraf can be removed from the body by haemodialysis (blood cleaning).

Additional information regarding the use and handling by the medical or healthcare professional is given at the end of this leaflet.

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

4. Possible side effects

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

After the administration, you will be kept under observation for at least half an hour. Most side effects occur immediately or sometimes delayed. Some effects can occur up to seven days after Dotagraf injection.

There is a small risk that you may have an allergic reaction to Dotagraf. Such reactions can be severe and result in shock (case of allergic reaction that could put your life in danger). The following symptoms may be the first signs of a shock. Inform immediately your doctor, radiologist or health professional if you feel any of them:

- swelling of the face, mouth or throat which may cause you difficulties in swallowing or breathing
- swelling of hands or feet
- lightheadedness (low blood pressure)
- breathing difficulties
- whistling respiration
- coughing
- itching
- runny nose
- sneezing
- eye irritation
- hives
- skin rash

Uncommon side effects (may affect up to 1 in 100 people)

- hypersensitivity (allergic reaction)
- headaches
- unusual taste in the mouth
- dizziness
- somnolence (sleepiness)
- sensation of tinglings, warmth/burning, cold and/or pain
- low or high blood pressure
- nausea (feeling sick)
- stomach pain
- rash
- feeling hot, feeling cold
- asthenia (loss of energy; weakness)
- injection site discomfort, injection site reaction, injections site coldness, injection site swelling, diffusion of the product outside of blood vessels that can lead to inflammation (redness and local pain)

Rare side effects (may affect up to 1 in 1,000 people)
- anxiety, faintness (dizziness and feeling of imminent loss of consciousness)
- eyelid swelling
- palpitations
- sneezing
- vomiting (being sick)
- diarrhea
- increased saliva secretion
- hives, itching, sweating
- chest pain, chills

Very rare side effects (may affect up to 1 in 10,000 people)
- anaphylactic or anaphylactic-like reactions (a serious, potentially life-threatening allergic reaction)
- agitation
- coma, seizures, syncope (brief loss of consciousness), disorder of smell (perception of often unpleasant odours), tremor
- conjunctivitis, red eye, blurred vision, increased tear secretion
- cardiac arrest, accelerated or slow heart beat, irregular heart beat, vascular dilatation, pallor
- respiratory arrest, pulmonary oedema, breathing difficulties, wheezing, stuffy nose, cough, dry throat, throat constriction with feeling of suffocation, respiratory spasms, throat swelling
- eczema, redness of the skin, swelling of the lips and localized in the mouth
- muscle cramps, muscle weakness, back pain
- malaise, chest discomfort, fever, swelling of the face, diffusion of the product outside of blood vessels that can lead to tissue dying off at the injection site, inflammation of a vein
- decrease in oxygen level in blood

There have been reports of nephrogenic systemic fibrosis (which causes hardening of the skin and may affect also soft tissue and internal organs), most of which were in patients who received Dotagraf together with other gadolinium-containing contrast agents. If, during the weeks following the MRI examination, you notice changes in the colour and/or thickness of your skin in any part of your body, inform the radiologist who performed the examination.

Reporting of side effects
If you get any side effects, talk to your radiologist, pharmacist, doctor or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via HPRA Pharmacovigilance Website: www.hpra.ie. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Dotagraf

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

This medicinal product does not require any special precaution for storage.

Chemical and physical in-use stability has been demonstrated 72 hours at room temperature. From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer that 24 hours at 2 to 8 °C, unless opening has taken place in controlled and validated aseptic

conditions.

Do not use this medicine after the expiry date which is stated on the vial and on the carton, after the abbreviation “Exp”. The expiry date refers to the last day of that month.

6. Contents of the pack and other information

What Dotagraf contains

- The active substance is gadoteric acid. One millilitre of solution for injection contains 279.32 mg of gadoteric acid (as meglumine salt), equivalent to 0.5 mmol of gadoteric acid (as meglumine salt).
- The other ingredients are meglumine, 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid (DOTA) and water for injection.

What Dotagraf looks like and contents of the pack
Dotagraf is a clear, colourless to yellow solution for intravenous injection.
The Dotagraf pack contains one or ten vials with 10, 15 and 20 ml of solution for injection.
Not all pack sizes may be marketed.

Marketing Authorisation Holder
Bayer Limited, 1st Floor, The Grange Offices, The Grange, Brewery Road, Stillorgan, Co. Dublin, A94 H2K7, Ireland

Manufacturer
Sanochemia Pharmazeutika GmbH
Landegger Straße 7
2491 Neufeld/Leitha, Austria

This medicinal product is authorised in the Member States of the EEA under the following names:

Austria	Dotagraf 0,5 mmol/ml Injektionslösung im Einzeldosisbehältnis
Belgium	Dotagraph 0,5 mmol/ml oplossing voor injectie / solution injectable / Injektionslösung
Bulgaria, Malta, United Kingdom	Dotagraf 0.5 mmol/ml solution for injection
Croatia	Dotagraf 0,5 mmol/ml otopina za injekciju
Cyprus, Denmark, Estonia, Greece, Iceland, Italy, Norway, Poland, Portugal, Sweden	Dotagraf
Czech Republic	Dotagraf 0,5 mmol/ml
Finland	Dotagraf 0,5 mmol/ml injektioneste, liuos
France	ACIDE GADOTÉRIQUE BAYER HEALTHCARE 0,5 mmol/ml, solution injectable
Germany	Dotagraf 0.5 mmol/ml Injektionslösung
Hungary	Dotagraf 0,5 mmol/ml oldatos injekció, egyadagos
Ireland	Dotagraf 279.32 mg/ml solution for injection

Latvia	Dotagraf 0,5 mmol/ml šķīdums injekcijām
Lithuania	Dotagraf 0,5 mmol/ml injekcinis tirpalas
Luxembourg	Dotagraph 0,5 mmol/ml solution injectable
Netherlands	Dotagraf 0,5 mmol/ml, oplossing voor injectie
Romania	Dotagraf 0,5 mmol/ml soluţie injectabilă în flacon unidoză
Slovakia	Dotagraf 0,5 mmol/ml injekčný roztok
Slovenia	Dotagraf 0,5 mmol/ml raztopina za injiciranje
Spain	Dotagraf 0,5 mmol/ml solución inyectable unidosis EFG

This leaflet was last revised in September 2022

The following information is intended for medical or healthcare professionals only:

Posology
The lowest dose that provides sufficient enhancement for diagnostic purposes should be used. The dose should be calculated based on the patient's body weight, and should not exceed the recommended dose per kilogram of body weight detailed in this section.

- *Encephalic and spinal MRI:* In neurological examinations, the dose can vary from 0.1 to 0.3 mmol/kg BW, corresponding to 0.2 to 0.6 ml/kg BW. After administration of 0.1 mmol/kg BW to patients with brain tumours, the additional dose of 0.2 mmol/kg BW may improve tumour characterisation and facilitate therapeutic decision- making.
- *Whole body MRI and Angiography:* The recommended dose for intravenous injection is 0.1 mmol/kg BW (i.e. 0.2 ml/kg BW) to provide diagnostically adequate contrast.
  Angiography: In exceptional circumstances (e.g. failure to gain satisfactory images of an extensive vascular territory) administration of a second consecutive injection of 0.1 mmol/kg BW, equivalent to 0.2 ml/kg BW may be justified. However, if the use of 2 consecutive doses of Dotagraf is anticipated prior to commencing angiography, use of 0.05 mmol/kg BW, equivalent to 0.1 ml/kg BW for each dose may be of benefit, depending on the imaging equipment available.
- *Paediatric population:*
  MRI of brain and spine / whole-body MRI: the recommended and maximum dose of Dotagraf is 0.1 mmol/kg BW. More than one dose should not be used during a scan.
  Due to immature renal function in neonates up to 4 weeks of age and infants up to 1 year of age, Dotagraf should only be used in these patients after careful consideration at a dose not exceeding 0.1 mmol/kg body weight. More than one dose should not be used during a scan.
  Because of the lack of information on repeated administration, Dotagraf injections should not be repeated unless the interval between injections is at least 7 days.
  Dotagraf is not recommended for angiography in children under 18 years of age due to insufficient data on efficacy and safety in this indication.
- *Patients with renal impairment:* The adult dose applies to patients with mild to moderate renal impairment (GFR $\geq$ 30 ml/min/1.73 m^2). See also below "Impaired renal function".
- *Patients with hepatic impairment:* The adult dose applies to these patients. Caution is recommended, especially in the case of perioperative liver transplantation period.

Method of administration
Dotagraf is indicated for intravenous administration only. Do not use by intrathecal route. Take care to

maintain strictly intravenous injection: extravasation may result in local intolerance reactions, requiring the usual local care.
Infusion rate: 3-5 ml/min (for angiographic procedures, higher infusion rates up to 120 ml/min, i.e. 2 ml/sec, may be used for angiographic procedures)
Optimal imaging: within 45 minutes after injection
Optimal image sequence: T1-weighted
Intravascular administration of contrast media should, if possible, be done with the patient lying down. After the administration, the patient should be kept under observation for at least half an hour, since experience shows that the majority of undesirable effects occur within this time.
Prepare a syringe with a needle. Remove the plastic disk. After cleaning the stopper with a pad soaked in alcohol, puncture the stopper with the needle. Withdraw the quantity of product required for the examination and inject it intravenously.
For single use only, any unused solution should be discarded.
The solution for injection should be inspected visually prior to use. Only clear solutions free of visible particles should be used.

Paediatric population
Depending on the amount of Dotagraf to be given to the child, it is preferable to use Dotagraf vials with a single use syringe of a volume adapted to this amount in order to have a better precision of the injected volume.
In neonates and infants the required dose should be administered by hand.

Impaired renal function

Prior to administration of Dotagraf, it is recommended that all patients are screened for renal dysfunction by obtaining laboratory tests.

There have been reports of nephrogenic systemic fibrosis (NSF) associated with use of some gadolinium- containing contrast agents in patients with acute or chronic severe renal impairment (GFR < 30 ml/min/1.73 m^2). Patients undergoing liver transplantation are at particular risk since the incidence of acute renal failure is high in this group. As there is a possibility that NSF may occur with Dotagraf, it should therefore only be used in patients with severe renal impairment and in patients in the perioperative liver transplantation period after careful risk/benefit assessment and if the diagnostic information is essential and not available with non-contrast enhanced MRI. If it is necessary to use Dotagraf, the dose should not exceed 0.1 mmol/kg body weight. More than one dose should not be used during a scan. Because of the lack of information on repeated administration, Dotagraf injections should not be repeated unless the interval between injections is at least 7 days.
Haemodialysis shortly after Dotagraf administration may be useful at removing Dotagraf from the body. There is no evidence to support the initiation of haemodialysis for prevention or treatment of NSF in patients not already undergoing haemodialysis.

Elderly
As the renal clearance of gadoteric acid may be impaired in the elderly, it is particularly important to screen patients aged 65 years and older for renal dysfunction.

Neonates and infants
See under Posology, and method of administration, paediatric population

Pregnancy and lactation
Dotagraf should not be used during pregnancy unless the clinical condition of the woman requires use of gadoteric acid.

Continuing or discontinuing breast-feeding for a period of 24 hours after administration of Dotagraf, should be at the discretion of the doctor and lactating mother.

Instructions on handling
The peel-off tracking label on the vials should be stuck onto the patient record to enable accurate recording of the gadolinium contrast agent used. The dose used should also be recorded. If electronic patient records are used, the name of the product, the batch number and the dose should be entered into the patient record.