

Patient leaflet:
Information for the user

Magnevist® 0.5 mmol/ml Solution for Injection, in pre-filled syringe

Gadopentetate dimeglumine

**Read all of this leaflet carefully
before you are given this
medicine.**

- Keep this leaflet. You may need to read it again.
- If you have any further questions, please ask the doctor giving you Magnevist (the radiologist) or the hospital/MRI-centre staff.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor, radiologist or the hospital/MRI-centre staff.

In this leaflet:

- 1. What Magnevist is and what it is used for**
- 2. Before you are given Magnevist**
- 3. How you will be given Magnevist**
- 4. Possible side effects**
- 5. How to store Magnevist**
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1. What Magnevist is and what it is used for

Magnevist is used together with a technique called Magnetic Resonance Imaging (MRI) to create artificial contrast or enhancement to help make an MRI scan of the area of your body that your doctor wants to investigate clearer.

MRI is a modern scanning technique which produces very high quality pictures of various parts of your body without using X rays. The use of MRI can provide a quick, early and accurate diagnosis.

The scanner uses a strong magnetic field and radiowaves to measure the magnetic properties of body tissues. Using a computer, this information is converted into a black and white picture which can help your doctor to see and investigate the difference between normal and abnormal tissue.

Sometimes MRI is used in areas where it cannot produce a clear black and white picture. This is when Magnevist is used. Magnevist produces a clearer image and allows the doctor to see the area of interest better. Sometimes several scans will be taken before Magnevist is injected, then further scans taken after the injection.

This medicine is for diagnostic use only.

This medicine is provided as a solution for intravenous injection only.

**2. Before you are given
Magnevist**

Do not use Magnevist if:

- you are **allergic** (hypersensitive) to gadopentetate dimeglumine or any of the other ingredients of Magnevist (see section 6: 'Further information').
- you suffer from severe kidney problems, and/or have recently experienced sudden loss of kidney function, or if you are a patient who is about to have or has recently had a liver transplant, as use of Magnevist in patients with these conditions has been associated with a disease called nephrogenic systemic fibrosis (NSF). NSF is a disease involving thickening of the skin and connective tissues. NSF may result in severe joint immobility, muscle weakness or may affect the normal working of internal organs which may potentially be life threatening.
- the patient is a newborn baby up to the age of 4 weeks
- you have a **heart pacemaker** or if there are any implants or clips containing iron inside your body. (This is not because of an interaction with Magnevist but because if you have any of

these, you should not be placed in a strong magnetic field).

Take special care with Magnevist

Your doctor will need to take special care when giving you Magnevist if:

- you have a **history of allergy** (e.g. hay fever, hives), **asthma**, or have had a reaction to another type of contrast media. This is because you may be more likely to have an allergic reaction
 - you suffer from **heart or blood circulation problems**. This is because in the rare event that you have an allergic reaction, it is more likely to be serious or fatal
 - you have **epilepsy** or have ever had fits, seizures or other diseases of the brain. Fits or seizures have occurred rarely in patients with similar conditions. Tell the radiographer or MRI-centre staff so that they will be prepared to deal with any problems that occur
 - you have any **kidney problems**. Tell your doctor if your kidneys do not work properly. Magnevist should only be given after careful consideration if you have kidney problems. Before you receive Magnevist, you will need to have a blood test to check how well your kidneys are working. Magnevist should not be given if you have severe kidney problems and/or have recently had sudden loss of kidney function.
 - if you have recently had, or soon expect to have, a **liver transplant**
 - the patient is a **newborn or infant**. Magnevist should not be used in newborn babies up to the age of 4 weeks. As kidney function is immature in infants up to 1 year of age, Magnevist will only be used in infants after careful consideration by the doctor. In infants the required dose should be administered manually.
 - you are **over 65 years** of age as you are more likely to have reduced kidney function.
- Before you receive Magnevist, you must tell your doctor, the

radiologist or MRI-centre staff if any of these apply to you. Your doctor will decide whether the intended examination is possible or not.

Allergy-like reaction may occur after the use of Magnevist. Severe reactions are possible. Most of these reactions occur within 30 minutes after administration. Therefore, you will be observed for at least 30 minutes after the injection.

Delayed reactions may occur (hours or even days later). (see section 'Possible Side Effects')

If you have any **blood tests** tell your doctor you have been given Magnevist. This is because some tests for iron levels in the blood may be affected for up to 24 hours after Magnevist has been given.

There is limited experience of using Magnevist in patients younger than two years, other than in examinations of the brain and spine.

Taking or using other medicines

Please tell your doctor, the radiologist or MRI-centre staff if you are taking or have recently taken any other medicines, including medicines obtained without a prescription. This is particularly important if you are taking:

- **beta-blockers** (drugs used to treat heart problems or high blood pressure). This is because in the rare event that you have an allergic reaction, you may need to be given different medicines than normal to treat the reaction.

Pregnancy

- You must tell your doctor, the radiologist or the MRI-centre staff if you think you are or might become pregnant as Magnevist should only be used during pregnancy if it is strictly necessary.

Breast feeding

- Tell your doctor if you are breast-feeding or about to start breast-feeding. Breast-feeding should be discontinued for at least 24 hours after you receive Magnevist.

Ask your doctor for advice before taking any medicine

3. How you will be given Magnevist

You will be asked to lie down on the MRI scanning bed and then Magnevist is injected by a doctor via a needle or catheter into a vein. The MRI staff will observe you after the injection just in case you have any side effects.

The dose of Magnevist that is right for you varies depending on your weight, the body region being examined and how much the image of the area needs to be made clearer. In adults, a single injection of 0.2 ml Magnevist per kilogram body weight is used. In special cases, this may be increased in adults to 0.4 ml or even 0.6 ml per kilogram body weight and in children (over 2 years) to 0.4ml per kilogram body weight at maximum as a single dose. The radiologist will decide how much Magnevist is needed for your investigation.

With the exception of the brain and spine examinations there is limited experience for using Magnevist in patients younger than two years.

Scanning may start immediately after Magnevist injection.

You should not be given Magnevist if you suffer from severe kidney problems and/or have recently experienced sudden loss of kidney function, or if you are a patient who is about to have or has recently had a liver transplant. Magnevist should also not be used in newborn babies up to the age of 4 weeks.

If you have moderate kidney problems, you should only receive one dose of Magnevist during a scan and you should not receive a second injection for at least 7 days.

As kidney function is immature in infants up to 1 year of age, infants should only receive one dose of Magnevist during a scan and should not receive a second injection for at least 7 days.

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

Further information regarding the administration and handling of Magnevist is given at the end of this leaflet (see section 'Further Information').

If you receive more Magnevist than you should

No symptoms of overdosing have so far been reported. If overdosing does happen, the doctor will treat any resulting symptoms and will check whether your kidneys are working normally. If your kidneys do not work properly, your doctor may need to

use a kidney dialysis machine to remove Magnevist. There is no evidence to suggest that this will prevent the development of NSF (see section 4 Possible side effects) and should not be used as treatment for the condition.

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

4. Possible side effects

Like all medicines, Magnevist can cause side effects, although not everybody gets them. Most of the side effects are mild to moderate.

The most frequently observed side effects in patients receiving Magnevist (may affect 4 or more in 1000 users) are various injection site reactions, headache and nausea (feeling sick).

The most serious side effects in patients receiving Magnevist are Nephrogenic Systemic Fibrosis (NSF) and anaphylactoid reactions (allergy-like reactions) including severe reactions such as shock. NSF is a severe reaction, mainly involving a thickening of the skin and connective tissues, and may result in severe joint immobility, muscle weakness or may affect the normal working of internal organs which may potentially be life-threatening.

In rare cases **allergy-like reactions** may occur including severe reactions such as shock that may need immediate medical intervention. .

If you notice:

- itching of the skin, rash, wheals on the skin (urticaria)
- difficulty breathing, gagging, feeling of suffocation
- swelling of the face, lips, tongue, throat, neck or body
- itchy or watery eyes, tickling in the throat or nose, hoarseness, runny nose, hives, coughing or sneezing
- headache, dizziness, feeling faint
- feeling particularly hot or cold, sweating
- paleness or reddening of the skin
- chest pain, cramp, tremor
- feeling sick

Tell your doctor, the radiologist or MRI staff immediately as these may be the first signs that a severe reaction is happening. Your

investigation may need to be stopped, and you may need further treatment.

Delayed reactions hours to several days after the administration of Magnevist, have been observed in rare cases. If this should happen to you tell your doctor or radiologist.

Below the reported/experienced side effects are listed by frequency:

Uncommon (may affect 1 to 10 users in 1,000)

- headache, dizziness, dysgeusia (disturbed sense of taste)
- nausea (feeling sick), vomiting (being sick)
- pain, feeling hot, feeling cold
- sensations or reactions at the injection site such as:
coldness, paresthesia ("pins and needles"), swelling, warmth, pain, edema, irritation, hemorrhage (bleeding), erythema (reddish painful skin), discomfort, necrosis (death of tissue), thrombophlebitis (inflammation of a vein caused by or associated with a blood clot), phlebitis (inflammation of a vein), inflammation, extravasation (bleeding into the tissue at the injection site), pain, bruising, change in skin color

Rare: (may affect 1 to 10 users in 10,000)

- hypersensitivity (allergy)/ anaphylactoid (allergy-like) reactions, e.g. anaphylactoid shock (severe allergy-like reaction); shock (circulatory collapse); hypotension (low blood pressure); conjunctivitis; loss of consciousness; throat tightness; sneezing; urticaria (hives, nettle-type rash); pruritus (severe itching); rash; erythema (redness of the skin); dyspnea (difficulty in breathing); respiratory arrest (stopped breathing); bronchospasm (difficulty in breathing); wheezing; laryngospasm (voice box spasm); laryngeal edema (voice box edema); pharyngeal edema (swelling of the throat); cyanosis (blue lips); rhinitis (runny nose); angioedema (e.g. swelling of the face, throat, mouth, lips and/or tongue); face edema (swelling of the face); reflex tachycardia (abnormally fast or slow heartbeat)
- disorientation

- convulsion (fits or seizures); paresthesia (numbness and tingling); burning sensation; tremor
- tachycardia (abnormally fast heart beat); arrhythmia (irregular heart beat)
- thrombophlebitis (inflammation of a vein caused by or associated with a blood clot); flushing; vasodilatation (widening of blood vessels)
- throat irritation
pharyngolaryngeal pain/ pharynx discomfort (pain or discomfort in the throat); coughing
- stomach (abdominal) pain or discomfort; diarrhoea; toothache; dry mouth; oral soft tissue pain and paresthesia (pains or numbness and tingling in the mouth)
- pains in the arms, hands, legs and feet (extremities)
- chest pain; fever; swelling of the arms, hands, legs and feet (edema peripheral); generally feeling unwell (malaise); tiredness (fatigue); thirst; weakness (asthenia).

Not known (frequency cannot be estimated from the available data):

- increased serum iron (changes of levels may be detected in blood tests)
- agitation; confusion
- coma; somnolence (sleepiness); problems with speech; parosmia (disturbed sense of smell)
- problems with eyesight; watery eyes (lacrimation); pain in the eyes
- problems with hearing; ear pain
- cardiac arrest (sudden stopping of the heart); bradycardia (decreased heart rate)
- syncope (fainting); vasovagal reaction (temporary rapid decrease of blood pressure, pallor, may result in unconsciousness), high blood pressure
- difficulty breathing, increase or decrease in breathing rate, pulmonary edema (fluid in the lungs)
- watery mouth (salivation)
- bilirubin (bile pigment) increased, liver enzyme increased (changes of levels may be detected in blood tests)
- nephrogenic systemic fibrosis (NSF is a severe reaction, mainly involving a thickening of the skin and connective tissues,

and may result in severe joint immobility, muscle weakness or may affect the normal working of internal organs which may potentially be life-threatening)

- back pain, arthralgia (joint pain)
- kidney failure in patients who already have kidney problems, increased serum creatinine (blood marker for kidney function; changes of levels may be detected in blood tests), loss of control of bladder (incontinence); urgent need to pass urine
- chills, sweating, changes in body temperature

In patients with dialysis-dependent kidney failure who received Magnevist, delayed and passing inflammatory-like reactions such as fever, chills and C-reactive protein increase (a blood test marker for inflammatory reactions) have been commonly observed. These patients had the MRI examination with Magnevist on the day before hemodialysis.

The following side effects have been life-threatening or fatal in some cases: nephrogenic systemic fibrosis (NSF; a severe reaction, mainly involving a thickening of the skin and connective tissues), anaphylactoid shock (severe allergy-like reaction), anaphylactoid (allergy-like) reaction, hypersensitivity reactions (allergy), shock (circulatory collapse), hypotension (low blood pressure), loss of consciousness, throat tightness, dyspnea (difficulty in breathing), respiratory arrest (stopped breathing), bronchospasm (difficulty in breathing), laryngospasm (voice box spasm), laryngeal edema (voice box edema), pharyngeal edema (swelling of the throat), cyanosis (blue lips), angioedema (e.g. swelling of the face, throat, mouth, lips and/or tongue), face edema (swelling of the face), convulsion (fits or seizures), tachycardia (abnormally fast heart beat), increased serum iron, coma, somnolence (sleepiness), cardiac arrest (sudden stopping of the heart), bradycardia (decreased heart rate), syncope (fainting) and pulmonary edema (fluid in the lungs).

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie.

By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Magnevist

Keep out of the sight and reach of children.

Do not use Magnevist after the expiry date which is stated on the syringe and the pack. The expiry date refers to the last day of that month.

Do not store above 30°C.

Magnevist is sensitive to light. Keep the syringe in the outer carton, in order to protect from light. No light protection during handling required.

After the prefilled syringe has been prepared for use, Magnevist remains stable for 24 hours at max. 30 °C and must then be discarded.

6. Further information

What Magnevist contains

The active substance is gadopentetate dimeglumine.. Each ml of the solution for injection contains 0.5 mmol of gadopentetate dimeglumine (equivalent to 469 mg gadopentetate dimeglumine).

The other ingredients are meglumine, pentetic acid and water for injections.

Instructions for use/ handling

Visual inspection

This medicinal product should be visually inspected before use. Magnevist is supplied as a clear, colorless to pale yellow solution.

Do not use Magnevist if you notice severe discoloration, the occurrence of particulate matter or a defective container.

Prefilled Syringes

The prefilled syringe must be taken from the pack and prepared for the injection immediately before the administration.

Remove the tip cap from the prefilled syringe immediately before use.

Discard any contrast medium solution not used in one examination

Incompatibilities

In the absence of compatibility studies, do not mix this medicinal product with other medicinal products.

What Magnevist looks like and contents of the pack

Magnevist is a solution for injection available in packs of five of 5ml, 10ml, 15ml, or 20ml pre-filled syringes.

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder:
Bayer Limited
The Atrium
Blackthorn Road
Dublin 18

Manufacturer:
Bayer Pharma AG
D-13342 Berlin
Germany

For any information about this medicine, please contact the local representative of the Marketing Authorization Holder.

This leaflet was last approved in:

[To be inserted upon approval]

7. Additional information for healthcare professionals only

The following additional information is intended for medical or healthcare professionals only. Please also refer to information provided in section 1 to 6.

Method of administration

This medicinal product is for intravenous administration, only (see section 'How you will be given Magnevist').

Dosage regimen

Adults

- Cranial and spinal MRI (see section 'What Magnevist is and what it is used for')

0.2 ml Magnevist per kg body weight (equivalent to 0.1 mmol gadopentetate dimeglumine per kg body weight).

Maximum single dose: 0.6 ml Magnevist per kg body weight.

- Whole body MRI (see section 'What Magnevist is and what it is used for')

0.2 ml Magnevist per kg body weight.

Maximum single dose: 0.6 ml Magnevist per kg body weight.

Additional information on special populations

Renal impairment

Magnevist is contraindicated in patients with severe renal impairment (GFR < 30 ml/min/1.73m²) and/or acute kidney injury, and in patients in the perioperative liver transplantation period. Magnevist should only be used after careful risk/benefit evaluation in patients with moderate renal impairment (GFR 30-59 ml/min/1.73m²) at a dose not exceeding 0.2ml/kg body weight. More than one dose should not be used during a scan. Because of the lack of information on repeated administration, Magnevist injections should not be repeated unless the interval between injections is at least 7 days.

Patients with hepatic impairment

Since gadopentetate is exclusively eliminated in an unchanged form via the kidneys, no dosage adjustment is considered necessary in patients with moderate hepatic impairment. Data on patients with severe hepatic impairment are not available.

Paediatric population

all indications (see section 'What Magnevist is and what it is used for')

Children: 0.2 ml Magnevist per kg body weight

Maximum single dose: 0.4 ml Magnevist per kg body weight.

Children below two years of age: limited experience in whole body MRI.

In children below two years of age the required dose should be administered manually and must not be administered in combination with an autoinjector to avoid injury.

Neonates up to 4 weeks of age and infants up to 1 year of age

Magnevist is contraindicated in neonates up to 4 weeks of age.

Due to immature renal function in infants up to 1 year of age, Magnevist should only be used in these patients after careful consideration at a dose

not exceeding 0.2ml/kg body weight. More than one dose should not be used during a scan. Because of the lack of information on repeated administration, Magnevist injections should not be repeated unless the interval between injections is at least 7 days.

Elderly (aged 65 years and above)

No dosage adjustment is considered necessary. Caution should be exercised in elderly patients (see section 4.4).

Special warnings and precautions for use

- Hypersensitivity

In patients with an allergic disposition the decision to use Magnevist must be made after particularly careful evaluation of the risk-benefit ratio.

Post-procedure observation of the patient is recommended.

Medication for the treatment of hypersensitivity reactions as well as preparedness for institution of emergency measures are necessary (see also section 'Take special care with Magnevist').

- Impaired renal function

Prior to administration of Magnevist all patients should be screened for renal dysfunction by obtaining laboratory tests.

There have been reports of nephrogenic systemic fibrosis (NSF) associated with use of Magnevist and some other gadolinium-containing contrast agents in patients with acute or chronic severe renal impairment ($\text{GFR} < 30 \text{ ml/min/1.73m}^2$) and/or acute kidney injury. Patients undergoing liver transplantation are at particular risk since the incidence of acute renal failure is high in this group. Therefore Magnevist must not be used in patients with severe renal impairment, in patients in the perioperative liver transplantation period and in neonates.

The risk for development of NSF in patients with moderate renal impairment ($\text{GFR } 30\text{--}59 \text{ ml/min/1.73 m}^2$) is unknown, therefore, Magnevist should be only used after careful risk-benefit evaluation in patients with moderate renal impairment.

Haemodialysis shortly after Magnevist administration may be useful at removing Magnevist from the body. Approximately 70% of the administered dose is removed with each dialysis session, such that after 3 dialysis sessions of 3 hours each, about 97% of the total administered dose is eliminated 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.

- Seizure disorders

Patients with seizure disorders or intracranial lesions may be at increased risk of seizure activity as has been reported rarely in association with Magnevist administration.

- Neonates and infants

Magnevist is contraindicated in neonates up to 4 weeks of age. Due to immature renal function in infants up to 1 year of age, Magnevist should only be used in these patients after careful consideration.

- Elderly

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

Interaction with other medicinal products and other forms of interaction

- Interference with diagnostic tests

Serum iron determination using methods measuring complexes (e.g. bathophenanthroline) may result in falsely low values for up to 24 hours after the administration of Magnevist due to the free DTPA contained in Magnevist.

Pregnancy

Adequate and well controlled studies with gadopentetate were not conducted in pregnant women. Animal studies have shown reproductive toxicity at repeated high doses (see section 5.3). The potential risk for humans is unknown. Magnevist should only be used in pregnant women after a clear benefit-to-risk analysis.

Lactation

It is unknown whether gadopentetic acid is excreted in human milk. There is insufficient information on the excretion of gadopentetic acid in animal milk. A risk to the suckling child cannot be excluded. Breast-feeding should be discontinued for at least 24 hours after the administration of Magnevist.

Undesirable effects

The overall safety profile of Magnevist is based on data from post-marketing surveillance and from more than 11,000 patients in clinical trials (see also section 'Possible side effects').

Overdose

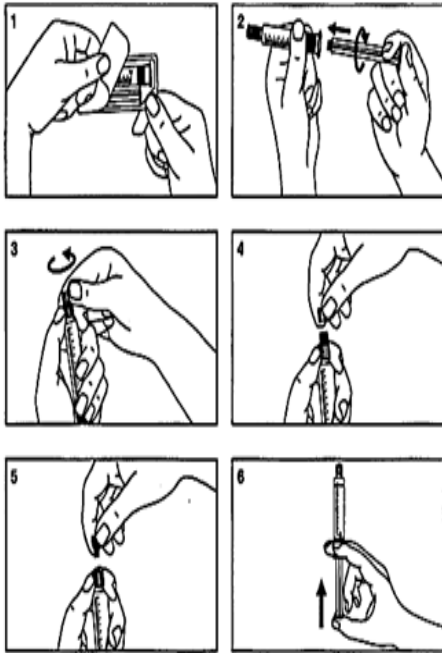
In case of inadvertent overdosage, renal function should be monitored in patients with renal impairment.

Magnevist can be removed from the body by hemodialysis (see section 'Special warnings and special precautions for use').

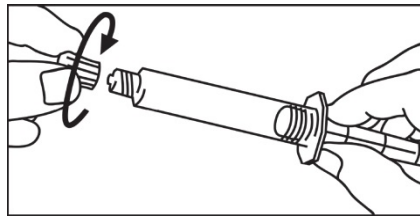
Handling

The peel-off tracking label on the syringe 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.

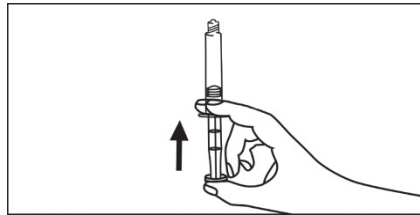
Glass syringe only:



1. Open the package
2. Screw the plunger on the syringe
3. Break the protective cover
4. Remove the protective cover
5. Remove the rubber stopper
6. Remove the air in the syringe

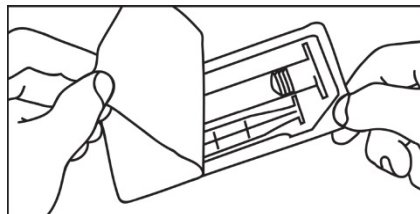


4. Open the cap with a twist

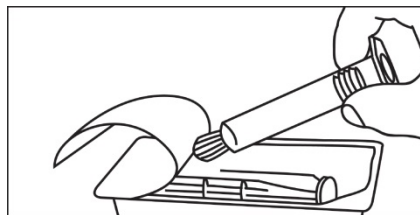


5. Remove the air in the syringe

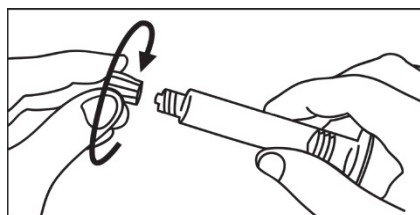
INJECTION WITH A POWER INJECTOR



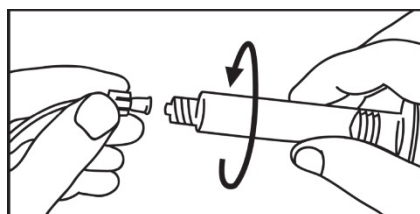
1. Open the package



2. Take syringe out of the package



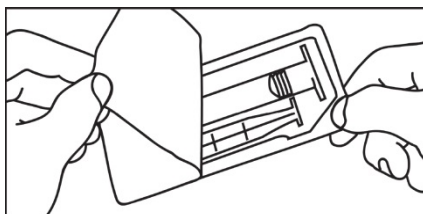
3. Open the cap with a twist



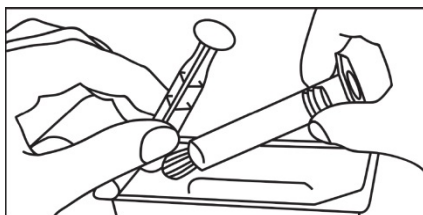
4. Connect the tip of the syringe to the tubing system clock-wise and go on according to the instructions of the device manufacturer

Plastic syringe only:

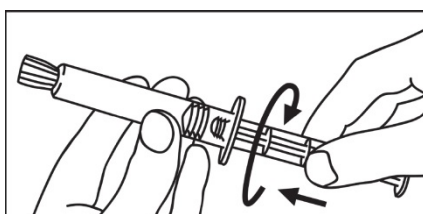
HAND INJECTION



1. Open the package



2. Take syringe and plunger rod out of the package



3. Turn clock-wise the plunger rod into the syringe