Sandoz Limited.
Park View, Riverside Way,
Watchmoor Park,
Camberley, Surrey, GU15 3YL

Telephone: 01276698020

Date: 27th April 2020

DIRECT HEALTHCARE PROFESSIONAL COMMUNICATION

Propofol 10 mg/ml (1%) Emulsion for Injection/Infusion
Interim Supply of Sweden Stock to Mitigate Supply Disruption

Dear Healthcare Professional,

Summary: Propofol 10 mg/ml (1%) Emulsion for Injection/Infusion in the UK.

To ensure continuity in supply during the current Covid-19 situation, Sandoz Ltd has obtained approval from the MHRA to supply Swedish product (batches numbers: JF5630; JG1079; JH9230; JK2551).

Please note the following:

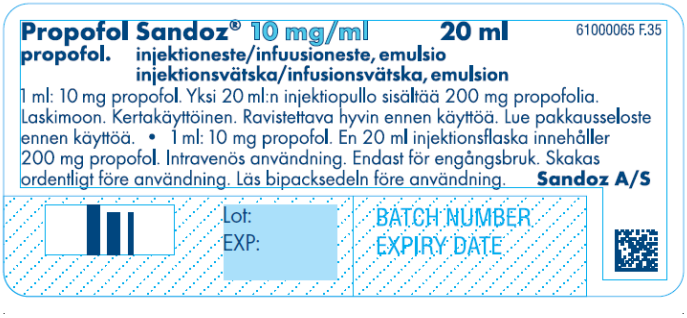
- This product is considered licensed in the UK.
- The product from Sweden has the same formulation as the UK product.
- The product from Sweden is manufactured according to the same manufacturing process and quality controls as the UK product.
- Please refer to the UK approved SPC available on the eMC website https://www.medicines.org.uk/emc and the leaflet attached to this letter. Discard the Swedish leaflet in the pack.
- For additional copies of the leaflet, please contact the company contact point (see below).
- The MHRA has approved this product under a batch specific variation to the marketing authorisation.

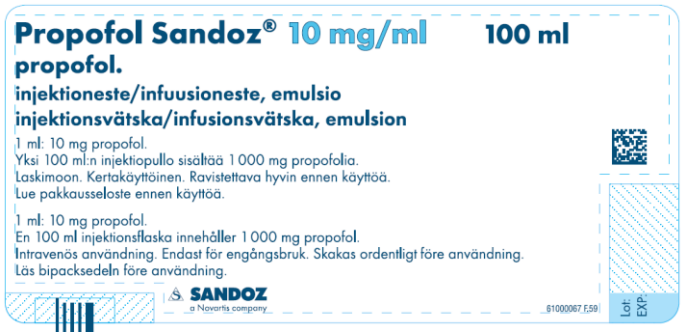
Please ensure all relevant staff are made aware of the content of this letter and that the information is communicated to the patients.
To assist in identification of the product, the Swedish ampoule labels are provided at the end of this letter, together with an example of the Swedish carton.

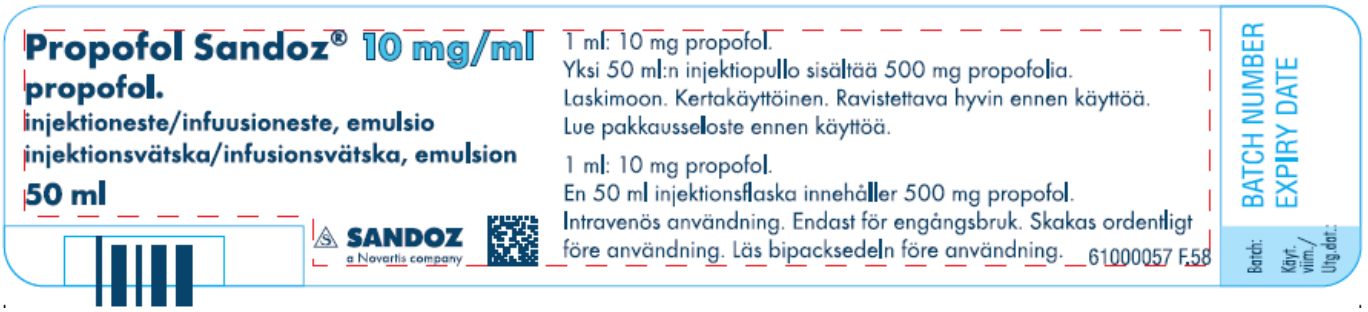
Call for reporting
Healthcare professionals are asked to report any suspected adverse reactions to the Yellow Card Scheme electronically. Report via the website https://www.gov.uk/yellowcard, the free Yellow Card app available from the Apple App Store or Google Play Store, and some clinical IT systems (EMIS, SystmOne, Vision, MiDatabank) for healthcare professionals. Suspected side effects can also be reported by calling 0800 731 6789 for free.
When reporting please provide as much information as possible, including information about medical history, any concomitant medication, onset, treatment dates, and product brand name.

Company contact point
If you have any questions about this letter or wish more information about Propofol 10 mg/ml (1%) Emulsion for Injection/Infusion, please contact Sandoz Ltd Medical Information at Park View, Riverside Way, Watchmoor Park, Camberley, Surrey, GU15 3YL or telephone : 01276 698 101 or Sandozgb@EU.propharmagroup.com.

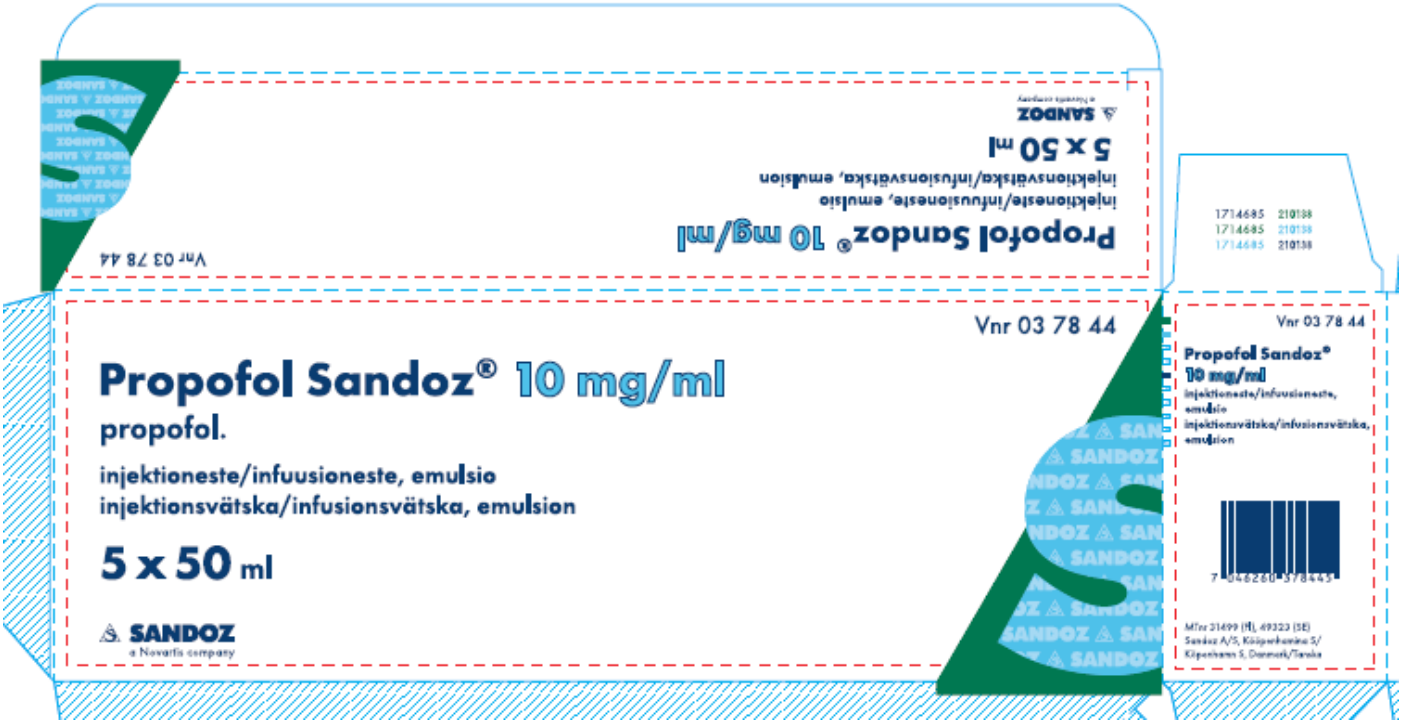
- **Swedish ampoule labels (20 mL ; 50 mL ; 100 mL)**







- **Example of the Swedish carton**



PACKAGE LEAFLET:
INFORMATION FOR THE PATIENT

Propofol 10 mg/ml (1%) Emulsion for Injection/ Infusion

Propofol SANDOZ

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, pharmacist or nurse.
- 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, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1 WHAT PROPOFOL IS AND WHAT IT IS USED FOR

Propofol belongs to a group of medicines called 'general anaesthetics'. General anaesthetics are used to cause unconsciousness (sleep) so that surgical operations or other procedures can be performed. They can also be used to sedate you (so that you are sleepy but not completely asleep).

Propofol will be given to you as an injection by a doctor.

Propofol is used to:
- Induce and maintain general anaesthesia in adults and children > 1 month
- Sedate patients > 16 years of age receiving artificial respiration in intensive care
- Sedate adults and children > 1 month during diagnostic and surgical procedures, alone or in combination with local or regional anaesthesia

2 WHAT YOU NEED TO KNOW BEFORE YOU RECEIVE PROPOFOL

Do not use Propofol
- if you are allergic to propofol or any of the other ingredients of this medicine (listed in section 6).
- in patients allergic to peanut or soya. This is because Propofol contains soya-bean oil.
- in patients of 16 years of age or younger for sedation in intensive care.

Warnings and precautions
The use of Propofol is not recommended in newborn infants. Propofol must not be used in patients of 16 years of age or younger for sedation for intensive care.

Talk to your doctor, anaesthesist or nurse before taking Propofol
- if you have any other health problems, such as problems with your heart, breathing, kidneys or liver.
- if your body has lost lots of water (you are hypovolaemic).
- if you have ever had a fit or convulsion
- if you have ever been told that you have very high levels of fat in your blood. In these cases your doctor might have to determine your blood fat levels.
- if you have ever been told that your body has problems using fat. In these cases your doctor might have to determine your blood fat levels.
- if you have a condition called hereditary predisposition to acute porphyria.
- if you have mitochondrial disease.

If you are able to go home shortly after receiving propofol you should not go home unaccompanied.

If you are not sure if any of the above apply to you, talk to your doctor or nurse before receiving Propofol.

Other medicines and Propofol
Tell your doctor if you are taking, have recently taken or might take any other medicines.

Take special care when taking/ receiving the following medicines:
- Certain premedications (your anaesthesist knows which medicines can be influenced)
- Other anaesthetics (including general, local or volatile anaesthetics)
- Painkillers (analgetics)
- Strong painkillers (fentanyl or opioids)
- Parasympatholytic agents (medicines used to treat e.g. painful cramps of organs, asthma or Parkinson's disease)
- Benzodiazepines (medicines used to treat anxiety)
- Suxamethonium (muscle relaxant)
- Neostigmin (medicine used to treat a disease called myasthenia gravis)
- Ciclosporin (medicine used to prevent transplant rejection).
- Rifampicin (an antibiotic)
- Valproic acid (medicine used to treat epilepsy)

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 nurse for advice before taking this medicine.
Propofol should not be used unless absolutely necessary if you are pregnant.

You should not breast-feed while receiving Propofol and breast milk must be discarded for 24 hours after receiving Propofol.

Driving and using machines
After having Propofol you may still feel sleepy for some time.
Do not drive or use any tools or machines until you are sure the effects have worn off.

If you are able to go home shortly after receiving Propofol, do not drive a car.
Ask your doctor when you can start doing these activities again and when you can go back to work.

Propofol contains soya-bean oil
If you are allergic to peanut or soya, do not use this medicine (see above "Do not use Propofol").

This medicinal product contains less than 1 mmol sodium (23 mg) per 100 ml, i.e. essentially 'sodium- free'.

3 HOW TO USE PROPOFOL

You will be given Propofol by, or under the direct supervision of your anaesthesist or intensive care doctor. It will be given to you as an injection or infusion (drip) into a vein. This is usually in the back of your hand or in your forearm.

- Your doctor will give you the injection using a needle or through a fine plastic tube called a 'cannula'
- For maintenance of anaesthesia or sedation your medicine may be given as an intravenous infusion (drip) using an electric pump which automatically control the rate at which the infusion is given. This may be done if you are having a long operation or if you are in an Intensive Care Unit.

The dose you are given will vary depending on your age, body weight and physical condition. The doctor will give the correct dose to start and to sustain anaesthesia or to achieve the required level of sedation, by carefully watching your responses and vital signs (pulse, blood pressure, breathing etc.).

You may need several different medicines to keep you asleep or sleepy, free from pain, breathing in a healthy way and to keep your blood pressure steady. The doctor will decide which medicines you need and when you need them.

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General anaesthesia

Adults
- For induction of anaesthesia most adult patients aged less than 55 years are likely to require 1.5 to 2.5 mg/kg body weight.
- For maintenance of anaesthesia generally doses of 4 to 12 mg/kg/h or repeat bolus injections (using Propofol) dose increments of 25 mg to 50 mg are given.

Dose requirements may be lower for older people.

Sedation

Adults and adolescents older than 16 years of age
- For sedation of adults and adolescents older than 16 years of age during intensive care the dose should be adjusted according to the level of sedation required. Using continous infusion doses of 0.3 to 4.0 mg/kg/h are typically given. Rates of infusion greater than 4.0 mg propofol/kg body weight/hr are not recommended.

Adults
- For sedation for diagnostic and surgical procedures in adults generally doses of 0.5 to 1 mg/kg body weight over 1 to 5 minutes are required for onset of sedation. Maintenance of sedation will require 1.5 to 4.5 mg/kg/h. Additionally, single administration of 10 to 20 mg can be given if a rapid increase of the level of sedation (sleepiness) is required.

General anaesthesia

Children over 1 month of age
- For induction of anaesthesia most paediatric patients over 8 years are likely to require approximately 2.5 mg/kg body weight Propofol.
  In children younger than 8 years the dose might be higher (2.5-4 mg/kg body weight).
- For maintenance of anaesthesia using continuous infusion doses of 9 to 15 mg/kg/h usually achieve satisfactory anaesthesia.
  In younger children, especially between the age of 1 month and 3 years, may have higher dosage requirements.

Sedation

Children over 1 month of age
- For **sedation** of paediatric patients **during diagnostic and surgical procedures** the dose should be adjusted according to the depth of sedation required.
  Most paediatric patients require doses of 1 – 2 mg/kg body weight Propofol for onset of sedation. Maintenance of sedation will require 1.5-9 mg/kg/h Propofol. Additionally, single administration of up to 1 mg/kg body weight can be given if a rapid increase of level of sedation is required.

- Propofol must not be used in paediatric patients of 16 years of age or younger in the indication for **sedation in intensive care**.

Duration of treatment
When used for sedation, Propofol must not be administered for more than 7 days.

If you received more Propofol than you should
Your doctor will ensure that you receive the right amount of Propofol for you and for the procedure you are undergoing. However, different people need different doses and if you do receive too much for you, your anaesthesist may need to take measures to make sure your heart and breathing are adequately supported. This is why anaesthetic drugs are only administered by doctors trained in anaesthesia or in the care of patients in intensive care.

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

4 POSSIBLE SIDE EFFECTS

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

Side effects that can happen during anaesthesia
The following side effects can happen during anaesthesia (while the injection is being given to you or when you are sleepy or asleep). Your doctor will be looking out for these. If they happen, your doctor will give you appropriate treatment.

Very common (may affect more than 1 in 10 people)
- A feeling of pain at the site of the injection (while the injection is being given, before you fall asleep).

Common (may affect up to 1 in 10 people)
- *Slow heart beat*
- *Low blood pressure*
- *Temporrary changes in your breathing pattern (apnoea) (while the injection is being given, before you fall asleep)*
- *Hyperventilation and coughing (while the injection is being given, before you fall asleep)*
- *Hiccups*
- *Hot flushes*

Uncommon (may affect up to 1 in 100 people)
- Cough (during maintenance)

Rare (may affect up to 1 in 1,000 people)
- Twitching and shaking of your body, or fits (may also happen when you wake up).

Very rare (may affect up to 1 in 10,000 people)
- Serious allergic reaction which causes difficulty in breathing or dizziness
- Build up of fluid in the lungs which can make you very breathless (may also happen when you wake up)
- Unusual colour of urine (may also happen when you wake up).

Not known (frequency cannot be estimated from the available data)
- Involuntary movements
- Respiratory depression (dose dependant)

Side effects that can happen after anaesthesia
The following side effects can happen after anaesthesia (when you are waking up or after you have woken up).

Common (may affect up to 1 in 10 people)
- Excitations, headache
- Feeling sick (nausea), being sick (vomiting).

Uncommon (may affect up to 1 in 100 people)
- Swelling and redness or blood clots at the vein along the injection site.

Rare (may affect up to 1 in 1,000 people)
- Dizziness, chills and sensations of cold
- Cough (when you are waking up)

Very rare (may affect up to 1 in 10,000 people)
- Being unconscious after the operation (when this has happened, the patients have recovered without problems)
- Inflamed pancreas (pancreatitis) which causes severe stomach pain (a causal relationship could not be shown)
- Feeling sexually aroused
- Fever following surgery
- Changes in ECG (Brugada type ECG)
- Severe tissue damage and tissue necrosis after accidental extravascular administration

Not known (frequency cannot be estimated from the available data)
- Feeling euphoric
- Irregular heart beat
- Increase in liver size
- Kidney failure
- Breakdown of muscle cells (rhabdomyolysis), increase in acidity of your blood, high potassium and fat levels in your blood, heart failure
- Local pain, swelling after accidental extravascular administration
- Drug abuse and drug dependance, mostly by healthcare professionals

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 the Yellow Card Scheme (www.mhra.gov.uk/yellowcard).
By reporting side effects you can help provide more information on the safety of this medicine.

5 HOW TO STORE PROPOFOL

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 after EXP. The expiry date refers to the last day of that month.

Store below 30°C.
Do not freeze.
Keep the vial/ampoule in the outer carton in order to protect from light.

Shelf life after first opening/dilution
The mixture should be prepared aseptically immediately prior to administration and must be administered within 6 hours after preparation.
In accordance with established guidelines for other lipid emulsions, a single infusion of Propofol must not exceed 12 hours. At the end of the procedure or at 12 hours, whichever is the sooner, both the container of Propofol and the infusion line must be discarded and replaced as appropriate.

Chemical and physical in-use stability of the reconstituted product has been demonstrated for 24 hours at 25°C.

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.
Do not use this medicine if you notice particulate matter.

Do not throw away any medicines via wastewater or household waste. 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 Propofol contains

- The active substance(s) is propofol. Each 1 milliliter emulsion for injection/infusion contains 10 mg propofol.
- The other ingredients are refined soya-bean oil, egg phospholipids, glycerol, sodium hydroxide (for pH-adjustment), water for injections.

What Propofol looks like and contents of the pack
Propofol 10 mg/ml (1%) Emulsion for Injection/Infusion is a white aqueous isotonic oil-in-water emulsion. It is available in 20 ml Type I glass ampoules, or 20, 50 and 100 ml Type I glass vials with bromobutyl rubber stoppers.

Pack sizes:
5 x 20 ml ampoules
5 x 20 ml vials
1 x 50 ml vial
5 x 50 ml vials
1 x 100 ml vial

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer
Marketing Authorisation Holder:

Sandoz Ltd,
Frimley Business Park, Frimley,
Camberley, Surrey, GU16 7SR, UK.

Manufacturer:
Corden Pharma S.p.A.,
Viale dell'Industria 3 E, Reparto via Galilei 17,
Caponago, 20040.

Or

Salutas Pharma GmbH
Otto-Guericke Allee 1
39179 Barleben
Germany

Or

Lek Pharmaceuticals d.d.
Verovskova 57, 1526 Ljubljana
Slovenia

This leaflet was last revised in 03/2017.

Continued on the next page >>

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

Method of administration

For intravenous use.

Administering Propofol through a TCI-system for sedation in intensive care is not recommended.

For single use only.

Parenteral products should be inspected visually for particulate matter prior to administration.
If particulate matter is evident emulsion should not be used.

Containers should be shaken before use. If two layers can be seen after shaking, the emulsion should not be used.

Propofol can be used for infusion undiluted or diluted with glucose 50 mg/ml (5%) intravenous infusion solution or sodium chloride 9 mg/ml (0.9%) intravenous infusion solution or a combination solution of glucose 40 mg/ml (4%) and sodium chloride 1.8 mg/ml (0.18%).

Prior to use, the ampoule neck and rubber stopper should be disinfected using a medicinal alcohol (spray or dipped swab). After use, any remaining contents must be discarded.

Propofol does not contain antimicrobial preservatives and is capable of supporting the growth of microorganisms. The emulsion must be drawn aseptically into a sterile syringe or infusion system immediately after opening the ampoule or spiking the vial.

Administration must commence without delay. During infusion sterility of Propofol as well as the infusion system must be maintained.

Medicinal products or liquids that are added to a running Propofol infusion should be added close to the cannula.

Propofol must not be administered via infusion systems that are provided with a microbiological filter.

The contents of one vial of Propofol and any infusion equipment are intended for **single** use in **one** patient.

Any remainder must be discarded immediately after use.

Infusion of undiluted Propofol
When Propofol is administered as a continuous infusion, it is recommended that equipment such as burettes, drop counter, syringe pumps or volumetric infusion pumps should always be used to control infusion rates.
As applies to parenteral administration of all kinds of fat emulsions, the duration of use for **one** infusion system for a continuous infusion of Propofol must not exceed 12 hours. The infusion system and the container must be discarded and replaced after a maximum of 12 hours.

The simultaneous administration of Propofol together with an infusion solution of glucose 50 mg/ml (5%), sodium chloride 9 mg/ml (0.9%) intravenous infusion solution or a combination solution of glucose 40 mg/ml (4%) and sodium chloride 1.8 mg/ml (0.18%) close to the Y-connector near the place of injection, is possible.
Any Propofol remaining at the end of the infusion period or after changing the system needs to be discarded and destroyed.

Infusion of diluted Propofol
When Propofol is administered diluted as a continuous infusion it is recommended that equipment such as burettes, drop counter, syringe pumps or volumetric infusion pumps should always be used to control infusion rates and to prevent the accidental administration of large volumes of diluted Propofol.

The maximum dilution must not exceed 1 part of Propofol and 4 parts of glucose 50 mg/ml (5%) (at least 2 mg propofol/ml) intravenous infusion solution or sodium chloride 9 mg/ml (0.9%) intravenous infusion solution or a combination solution of glucose 40 mg/ml (4%) and sodium chloride 1.8 mg/ml (0.18%).
The mixture should be prepared aseptically immediately prior to administration and must be administered within 6 hours after preparation.

Propofol must not be mixed with other solutions for injection or infusion except those mentioned above.

To reduce pain on the injection site lidocaine may be injected immediately before the use of Propofol may be mixed, immediately prior to administration, with preservative-free lidocaine injection.

The infusion system should be rinsed before administration of muscle relaxants like atracurium and mivacurium when using the same infusion system for Propofol.

Disposal
Any remaining contents after use should be discarded.

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