Package leaflet: Information for the user

Pradaxa 150 mg hard capsules
dabigatran etexilate

Read all of this leaflet carefully before you start taking 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 pharmacist.
- 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 or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

In this leaflet:

1. What Pradaxa is and what it is used for

Pradaxa is a medicine which contains the active substance dabigatran etexilate. It works by blocking a substance in the body which is involved in blood clot formation.

Pradaxa is a medicine which is used to reduce the risk of brain or body vessel obstruction by blood clot formation in adult patients with an abnormal heart beat (atrial fibrillation) and additional risk factors. Pradaxa is a blood thinner medicine that lowers the risk of blood clot formation.

Pradaxa is a medicine which is used to treat blood clots in the veins of your legs and lungs and to prevent blood clots from re-occuring in the vein of your legs and lungs

2. What you need to know before you take Pradaxa

Do not take Pradaxa

- if you are allergic to dabigatran etexilate or any of the other ingredients of this medicine (listed in section 6).
- if you have severely reduced kidney function.
- if you are currently bleeding.
- if you have a disease in an organ of the body that increases the risk of serious bleeding.
- if you have an increased tendency to bleed. This may be inborn, of unknown cause or due to other medicines.
- if you have a severely reduced liver function or liver disease which could possibly cause death.
- if you are taking oral ketoconazole or itraconazole, medicines to treat fungal infections.
- if you are taking cyclosporine, a medicine to prevent organ rejection after transplantation.
- if you are taking dronedarone, a medicine used to prevent repetition of your problem of irregular heart beat.
- if you are taking medicines to prevent blood clotting (e.g.warfarin, rivaroxaban, apixaban or heparin), except when changing anticoagulant treatment or while having a venous or arterial line and you get heparin through this line to keep it open.

- if you have received an artificial heart valve

Warnings and precautions

Talk to your doctor before taking Pradaxa. You may also need to talk to your doctor during treatment with Pradaxa if you experience symptoms or if you have to undergo surgery.Tell your doctor if you have or have had any medical conditions or illnesses, in particular any of those included in the following list:

- if you have a liver disease that is associated with changes in the blood tests, the use of Pradaxa is not recommended.

- if you have an increased bleeding risk, as could be the case in the following situations:
  - if you have been recently bleeding.
  - if you have had a surgical tissue removal (biopsy) in the past month.
  - if you have had a serious injury (e.g. a bone fracture, head injury or any injury requiring surgical treatment).
  - if you are suffering from an inflammation of the gullet or stomach.
  - if you have problems with reflux of gastric juice into the gullet.
  - if you are receiving medicines which could increase the risk of bleeding such as aspirin (acetylsalicylic acid), clopidogrel, ticagrelor.
  - if you are taking anti-inflammatory medicines such as diclofenac, ibuprofen, piroxicam.
  - if you are suffering from an infection of the heart (bacterial endocarditis).
  - if you know you have impaired kidney function, or you are suffering from dehydration (symptoms include feeling thirsty and passing reduced amounts of dark-coloured (concentrated) urine).
  - if you are older than 75 years.
  - if you weigh 50 kg or less.

- if you have had a heart attack or if you have been diagnosed with conditions that increase the risk to develop a heart attack.

- if you undergo a planned surgery. Pradaxa will need to be stopped temporarily due to an increased bleeding risk during and shortly after an operation. If possible, Pradaxa should be stopped at least 24 hours before an operation. In patients with a higher risk for bleeding your doctor may decide to stop treatment earlier.

- if you need to undergo an unplanned surgery. If possible, a surgery should be delayed until at least 12 hours after the last dose. If surgery cannot be delayed, there may be an increased risk of bleeding. Your doctor will consider this risk of bleeding together with the urgency of the surgery.

- if you have a tube (catheters) inserted into the back:
  A tube can be inserted into your back e.g. for anaesthesia or pain relief during or after surgery. If you are administered Pradaxa after removal of a catheter, your doctor will examine you regularly.

- if you fall or injure yourself during treatment, especially if you hit your head, please seek urgent medical attention. You may need to be checked by a doctor, as you may be at increased risk of bleeding.

Children and adolescents

Pradaxa should not be used in children and adolescents below 18 years old.

Other medicines and Pradaxa

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. For instance:

- Medicines to reduce blood clotting (e.g. warfarin, phenprocoumon**,** heparin, clopidogrel, prasugrel, ticagrelor, rivaroxaban)
- Anti-inflammatory and pain reliever medicines (e.g. aspirine)
- St. John´s wort, a herbal medicine for depression
- Antidepressant medicines called selective serotonin re-uptake inhibitors or serotonin-norepinephrine re-uptake inhibitors
- Rifampicin or clarithromycin, two antibiotics
- Medicines to treat abnormal heart beats (e.g. Amiodarone, dronedarone, quinidine, verapamil)

  If you are taking verapamil-containing medicines, you should be treated with a reduced Pradaxa dose of 220 mg taken as one 110 mg capsule twice a day, because your bleeding risk may be increased. Pradaxa and verapamil-containing medicines should be taken at the same time.

- Medicines to treat fungal infections (e.g. ketoconazole, itraconazole, posaconazole), unless they are only applied to the skin
- Medicines to prevent organ rejection after transplantation (e.g. tacrolimus, cyclosporine)
- Anti-viral medicines for AIDS (e.g. ritonavir)
- Medicines for treatment of epilepsy (e.g. carbamazepine, phenytoin)

Pregnancy and breast-feeding

The effects of Pradaxa on pregnancy and the unborn child are not known. You should not take Pradaxa if you are pregnant unless your doctor advises you that it is safe to do so. If you are a woman of child-bearing age, you should avoid becoming pregnant while you are taking Pradaxa.

You should not breast-feed while you are taking Pradaxa.

Driving and using machines

Pradaxa has no known effects on the ability to drive or use machines.

Pradaxa contains sunset yellow (E110)

This medicine contains a colorant called sunset yellow (E110), which may cause allergic reactions.

3. How to take Pradaxa

Always take this medicine exactly as your doctor has told you. Check with your doctor if you are not sure.

The recommended dose is 300 mg taken as one 150 mg capsule twice a day.

If you are 80 years or older, the recommended dose of Pradaxa is 220 mg taken as one 110 mg capsule twice daily.

If you are taking verapamil-containing medicines, you should be treated with a reduced Pradaxa dose of 220 mg taken as one 110 mg capsule twice a day, because your bleeding risk may be increased.

If you have a potentially higher risk for bleeding, your doctor may decide to prescribe a dose of Pradaxa 220 mg taken as one 110 mg capsule twice a day.

Pradaxa can be taken with or without food. The capsule should be swallowed whole with a glass of water, to ensure delivery to the stomach. Do not break, chew, or empty the pellets from the capsule since this may increase the risk of bleeding.

When taking Pradaxa capsules out of the blister pack, please observe the following instructions

- take the capsules by peeling off the backing foil of the blister card.
- do not push the capsules through the blister foil.
- do not peel off the blister foil until a capsule is required.

When taking Pradaxa capsules out of the bottle, please observe the following instructions

- push and turn for opening

Change of anticoagulant treatment

- *Changing from treatment with Pradaxa to anticoagulant treatment given by injection:*
  Do not start treatment with injectable anticoagulant medicines (for example, heparin) until 12 hours after the final dose of Pradaxa.

- *Changing from anticoagulant treatment given by injection to treatment with Pradaxa:*
  Start taking Pradaxa 0-2 hours before the time you would have had the next injection.

- *Changing from Pradaxa to blood thinners containing vitamin-K antagonists (e.g. phenprocoumon):*
  Your doctor needs to do blood-measurements and instruct you when to start vitamin-K antagonist treatment.

- *Changing from blood thinners containing vitamin-K antagonists (e.g. phenprocoumon) to Pradaxa:*
  Stop taking the medicine containing a vitamin-K antagonist. Your doctor needs to do blood-measurements and instruct you when to start Pradaxa treatment.

If you take more Pradaxa than you should
If you take more Pradaxa than recommended, you may have an increased risk of bleeding. Your doctor can perform a blood test to assess the risk of bleeding.
Inform your doctor immediately, if you take more than the prescribed dose of Pradaxa. If bleeding occurs, surgical treatment or treatment with blood transfusions may be required.

If you forget to take Pradaxa
A forgotten dose can still be taken up to 6 hours prior to the next due dose.
A missed dose should be omitted if the remaining time is below 6 hours prior to the next due dose.
Do not take a double dose to make up for missed doses.

If you stop taking Pradaxa
Take Pradaxa exactly as prescribed. Do not stop taking Pradaxa without first consulting your doctor. Stopping Pradaxa may increase the risk of a brain or body vessel obstruction in patients with abnormal heart beats.

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.

Pradaxa affects blood clotting, so most side effects are related to signs such as bruising or bleeding. Major or severe bleeding may occur, these constitute the most serious side effects and, regardless of location, may become disabling, life-threatening or even lead to death. In some cases these bleedings may not be obvious.

If you experience any bleeding event that does not stop by itself or if you experience signs of excessive bleeding (exceptional weakness, tiredness, paleness, dizziness, headache or unexplained swelling) consult your doctor immediately. Your doctor may decide to keep you under closer observation or change your medicine.

Tell your doctor immediately, if you experience a serious allergic reaction which causes difficulty in breathing or dizziness.

The side effects are listed below, grouped by how likely they are to happen.

<u>Prevention of brain or body vessel obstruction by blood clot formation developing after abnormal heart beats</u>

Common (may affect up to 1 in 10 people):
- Bleeding may happen from the nose, into the stomach or bowel, from penis/vagina or urinary tract (incl. blood in the urine that stains the urine pink or red), or under the skin
- A fall in the number of red cells in the blood
- Belly ache or stomach ache
- Indigestion
- Frequent loose or liquid bowel movements
- Feeling sick

Uncommon (may affect up to 1 in 100 people):
- Bleeding
- Bleeding may happen from piles, into the rectum, or in the brain.
- Haematoma formation
- Coughing of blood or blood stained sputum
- A fall in the number of platelets in the blood
- A fall in the amount of haemoglobin in the blood (the substance in the red blood cells)
- Allergic reaction
- Sudden change of the skin which affects its colour or appearance
- Itching
- Ulcer in the stomach or bowel (incl. ulcer in the gullet)
- Inflammation of the gullet and stomach
- Reflux of gastric juice into the gullet
- Vomiting
- Difficulty in swallowing
- Unusual laboratory test results on liver function

Rare (may affect up to 1 in 1,000 people):
- Bleeding may happen into a joint, from a surgical incision, from an injury, from the site of entry of an injection or from the site of entry of a catheter into a vein
- Serious allergic reaction which causes difficulty in breathing or dizziness
- Serious allergic reaction which causes swelling of the face or throat
- Skin rash notable for dark red, raised, itchy bumps caused by an allergic reaction
- A decrease in the proportion of red cells in the blood
- Liver enzymes increased
- Yellowing of the skin or whites of the eyes, caused by liver or blood problems

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

- Difficulty in breathing or wheezing

Treatment of blood clots in the veins of your legs and lungs including prevention of blood clots from re-occuring in the veins of your legs and/or lungs

Common (may affect up to 1 in 10 people):
- Bleeding may happen from the nose, into the stomach or bowel, into the rectum, from penis/vagina or urinary tract (incl. blood in the urine that stains the urine pink or red), or under the skin
- Indigestion

Uncommon (may affect up to 1 in 100 people):
- Bleeding
- Bleeding may happen into a joint or from an injury
- Bleeding may happen from piles and from haemorrhoids#
- A fall in the number of red cells in the blood
- Haematoma formation
- Coughing of blood or blood stained sputum
- Allergic reaction
- Sudden change of the skin which affects its colour and appearance
- Itching
- Ulcer in the stomach or bowel
- Inflammation of the gullet and stomach
- Reflux of gastric juice into the gullet
- Feeling sick
- Vomiting
- Belly ache or stomach ache
- Frequent loose or liquid bowel movements
- Unusual laboratory test results on liver function
- Liver enzymes increased

Rare (may affect up to 1 in 1,000 people):
- Bleeding may happen, from a surgical incision,or from the site of entry of an injection or from the site of entry of a catheter into a vein or from the brain
- A fall in the number of platelets in the blood
- Serious allergic reaction which causes difficulty in breathing or dizziness
- Serious allergic reaction which causes swelling of the face or throat
- Skin rash notable for dark red, raised, itchy bumps caused by an allergic reaction
- Difficulty in swallowing
- A decrease in the proportion of red cells in the blood

Not known (frequency cannot be estimated from the available data):
- Difficulty in breathing or wheezing
- A fall in the amount of haemoglobin in the blood (the substance in the red blood cells)
- A fall in the number of red cells in the blood
- Yellowing of the skin or whites of the eyes, caused by liver or blood problems

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 via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

In a clinical trial the rate of heart attacks with Pradaxa was numerically higher than with warfarin. The overall occurence was low.

5. How to store Pradaxa

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 carton, blister or bottle after "EXP". The expiry date refers to the last day of that month.

Blister: Store in the original package in order to protect from moisture.
Bottle: Once opened, the medicine must be used within 4 months. Keep the bottle tightly closed. Store in the original package in order to protect from moisture.

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 Pradaxa contains

- The active substance is dabigatran, which is administered in the form of 150 mg dabigatran etexilate given as mesilate.

- The other ingredients are tartaric acid, acacia, hypromellose, dimeticone 350, talc, and hydroxypropylcellulose.

- The capsule shell contains carrageenan, potassium chloride, titanium dioxide, indigo carmine, sunset yellow (E110) and hypromellose.

- The black printing ink contains shellac, iron oxide black and potassium hydroxide.

What Pradaxa looks like and contents of the pack

Pradaxa is a hard capsule.

Pradaxa 150 mg hard capsules have an opaque, light blue-coloured cap and an opaque, cream-coloured body. The Boehringer Ingelheim logo is printed on the cap and "R150" on the body of the capsule.

Pradaxa 150 mg hard capsules are available in packs containing 10 x 1, 30 x 1, 60 x 1 a multipack containing 3 packs of 60 x 1 hard capsules (180 hard capsules) or a multipack containing 2 packs of 50 x 1 hard capsules (100 hard capsules) in aluminium perforated unit dose blisters. Furthermore, Pradaxa 150 mg hard capsules are available in packs containing 60 x 1 capsules in aluminium perforated unit dose white blisters.

Pradaxa 150 mg hard capsules are also available in polypropylene (plastic) bottles with 60 hard capsules.

Not all pack sizes may be marketed.

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Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu/