Package leaflet: Information for the patient

Pradaxa 110 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.

What is in this leaflet

1. What Pradaxa is and what it is used for

Pradaxa contains the active substance dabigatran etexilate and belongs to a group of medicines called anticoagulants. It works by blocking a substance in the body which is involved in blood clot formation.

Pradaxa is used in adults to:

- prevent the formation of blood clots in the veins after knee or hip replacement surgery.

- prevent blood clots in the brain (stroke) and other blood vessels in the body if you have a form of irregular heart rhythm called nonvalvular atrial fibrillation and at least one additional risk factor.

- 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 (e.g., stomach ulcer, injury or bleeding in the brain, recent surgery of the brain or eyes).
- if you have an increased tendency to bleed. This may be inborn, of unknown cause or due to other medicines.
- 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 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 oral cyclosporine, a medicine to prevent organ rejection after transplantation.
- if you are taking dronedarone, a medicine used to treat abnormal heart beat.
- if you have received an artificial heart valve which requires permanent blood thinning.

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 an increased bleeding risk, such as:
  - 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. See 'Other medicines and Pradaxa' below.
  - 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 have a liver disease that is associated with changes in the blood tests. The use of Pradaxa is not recommended in this case.

Take special care with Pradaxa

- if you need to have an operation:
  In this case Pradaxa will need to be stopped temporarily due to an increased bleeding risk during and shortly after an operation. It is very important to take Pradaxa before and after the operation exactly at the times you have been told by your doctor.

- if an operation involves a catheter or injection into your spinal column (e.g. for epidural or spinal anaesthesia or pain reduction):
  - it is very important to take Pradaxa before and after the operation exactly at the times you have been told by your doctor.
  - tell your doctor immediately if you get numbness or weakness of your legs or problems with your bowel or bladder after the end of anaesthesia, because urgent care is necessary.

- 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 is not recommended 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. **In particular you should tell your doctor before taking Pradaxa**, **if you are taking one of the medicines listed below:**

- Medicines to reduce blood clotting (e.g. warfarin, phenprocoumon**,** acenocoumarol, heparin, clopidogrel, prasugrel, ticagrelor, rivaroxaban, acetylsalicylic acid)
- Medicines to treat fungal infections (e.g. ketoconazole, itraconazole), unless they are only applied to the skin
- Medicines to treat abnormal heart beats (e.g. amiodarone, dronedarone, quinidine, verapamil). If you are taking amiodarone, quinidine or verapamil containing medicines, your doctor may tell you to use a reduced dose of Pradaxa depending on the condition for which Pradaxa is prescribed to you. See section 3.
- Medicines to prevent organ rejection after transplantation (e.g. tacrolimus, cyclosporine)
- Anti-inflammatory and pain reliever medicines (e.g. acetylsalicylic acid, ibuprofen, diclofenac)
- 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)
- Anti-viral medicines for AIDS (e.g. ritonavir)
- Certain 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.

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.

Take Pradaxa as recommended for the following conditions:

<u>Prevention of blood clot formation after knee or hip replacement surgery</u>

The recommended dose is **220 mg once a day** (taken as 2 capsules of 110 mg).

If your **kidney function is decreased** by more than half or if you are **75 years of age or older**, the recommended dose is **150 mg once a day** (taken as 2 capsules of 75 mg).

If you are taking **amiodarone, quinidine or verapamil** containing medicines the recommended dose is **150 mg once a day** (taken as 2 capsules of 75 mg).

If you are taking **verapamil containing medicines and your kidney function is decreased** by more than half, you should be treated with a reduced dose of **75 mg** Pradaxa because your bleeding risk may be increased.

For both surgery types, treatment should not be started if there is bleeding from the site of operation. If the treatment cannot be started until the day after surgery, dosing should be started with 2 capsules once daily.

After knee replacement surgery

You should start treatment with Pradaxa within 1-4 hours after surgery finishes, taking a single capsule. Thereafter two capsules once a day should be taken for a total of 10 days.

After hip replacement surgery
You should start treatment with Pradaxa within 1-4 hours after surgery finishes, taking a single capsule. Thereafter two capsules once a day should be taken for a total of 28-35 days.

Prevention of brain or body vessel obstruction by blood clot formation developing after abnormal heart beats and Treatment of blood clots in the veins of your legs and lungs including prevention of blood clots from re-occuring in the vein of your legs and lungs

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 a day**.

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.

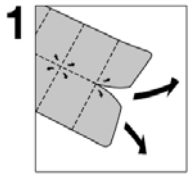
If you have a **potentially higher risk for bleeding**, your doctor may decide to prescribe a dose of Pradaxa 220 mg taken as **one 110 mg capsule twice a day**.

How to take Pradaxa

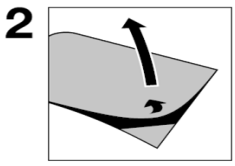
Pradaxa can be taken with or without food. The capsule should be swallowed whole with a glass of water, to ensure delivery to the stomach. Do not break, chew, or empty the pellets from the capsule since this may increase the risk of bleeding.

Instructions for opening the blisters

The following pictogram illustrates how to take Pradaxa capsules out of the blister



Tear off one individual blister from the blister card along the perforated line



Peel off the backing foil and remove the capsule.

- Do not push the capsules through the blister foil.
- Do not peel off the blister foil until a capsule is required.

Instructions for the bottle

- Push and turn for opening.
- After removing the capsule, place the cap back on the bottle and tightly close the bottle right away after you take your dose.

Change of anticoagulant treatment

Without specific guidance from your doctor do not change your anticoagulant treatment.

If you take more Pradaxa than you should

Taking too much Pradaxa increases the risk of bleeding. Contact your doctor immediately if you have taken too many Pradaxa capsules. Specific treatment options are available.

If you forget to take Pradaxa

Prevention of blood clot formation after knee or hip replacement surgery
Continue with your remaining daily doses of Pradaxa at the same time of the next day.
Do not take a double dose to make up for a forgotten dose.

Prevention of brain or body vessel obstruction by blood clot formation developing after abnormal heart beats and treatment of blood clots in the veins of your legs and lungs including prevention of blood clots from re-occuring in the vein of your legs and lungs
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 a forgotten dose.

If you stop taking Pradaxa

Take Pradaxa exactly as prescribed. Do not stop taking Pradaxa without talking to your doctor first, because the risk of developing a blood clot could be higher if you stop treatment too early. Contact your doctor if you experience indigestion after taking Pradaxa.

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.

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

Prevention of blood clot formation after knee or hip replacement surgery

Common (may affect up to 1 in 10 people):
- A fall in the amount of haemoglobin in the blood (the substance in the red blood cells)
- Unusual laboratory test results on liver function

Uncommon (may affect up to 1 in 100 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), from piles, from the rectum, under the skin, into a joint, from or after an injury or after an operation
- Haematoma formation or bruising occuring after an operation
- Blood detected in the stools by a laboratory test
- A fall in the number of red cells in the blood
- A decrease in the proportion of red cells in the blood
- Allergic reaction
- Vomiting
- Frequent loose or liquid bowel movements
- Feeling sick
- Wound secretion (liquid exuding from the surgical wound)
- Liver enzymes increased
- Yellowing of the skin or whites of the eyes, caused by liver or blood problems

Rare (may affect up to 1 in 1,000 people):
- Bleeding
- Bleeding may happen in the brain, from a surgical incision, from the site of entry of an injection or from the site of entry of a catheter into a vein
- Blood-stained discharge from the site of entry of a catheter into a vein
- Coughing of blood or blood stained sputum
- A fall in the number of platelets in the blood
- A fall in the number of red cells in the blood after an operation
- 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
- Sudden change of the skin which affects its colour and 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
- Belly ache or stomach ache
- Indigestion
- Difficulty in swallowing
- Fluid exiting a wound
- Fluid exiting a wound after an operation

Not known (frequency cannot be estimated from the available data):
- Difficulty in breathing or wheezing

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

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, from 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 and 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, or 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

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

<u>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</u>

Common (may affect up to 1 in 10 people):
- Bleeding may happen from the nose, into the stomach or bowel, from 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
- 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

In the trial program the rate of heart attacks with Pradaxa was higher than with warfarin. The overall occurence was low. No imbalance in the rate of heart attacks was observed in patients treated with dabigatran versus patients treated with placebo.

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 (see details below). By reporting side effects you can help provide more information on the safety of this medicine.

United Kingdom
Yellow Card Scheme
Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store

Ireland
HPRA Pharmacovigilance
Earlsfort Terrace
IRL – Dublin 2
Tel: +353 1 6764971
Fax: +353 1 6762517
Website: www.hpra.ie
e-mail: medsafety@hpra.ie

Malta
ADR Reporting
Website: www.medicinesauthority.gov.mt/adrportal

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. 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. Each hard capsule contains 110 mg dabigatran etexilate (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, and hypromellose.

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

What Pradaxa looks like and contents of the pack

Pradaxa 110 mg are hard capsules with an opaque, light blue-coloured cap and an opaque, light blue -coloured body. The Boehringer Ingelheim logo is printed on the cap and "R110" on the body of the capsule.

Pradaxa is available in packs containing 10 x 1, 30 x 1 or 60 x 1 capsules, 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 is available in packs containing 60 x 1 capsules in aluminium perforated unit dose white blisters.

Pradaxa 110 mg hard capsules are also available in polypropylene (plastic) bottles with 60 hard capsules.

Not all pack sizes may be marketed.

Marketing Authorisation Holder

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This leaflet was last approved in 06/2018.

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