

# Media Releases

## Pradaxa (dabigatran etexilate): Questions and Answers

### 1. What is Pradaxa?

Pradaxa is a medicine that contains the active substance dabigatran etexilate. It is available in strengths of 75mg, 110mg and 150mg per capsule.

Pradaxa is only available on prescription.

### 2. What is Pradaxa used for?

Pradaxa is a 'blood thinner'. It helps to prevent the formation of blood clots in the veins after surgery. It is also used to prevent strokes and the formation of blood clots in patients who have an abnormal heart beat (atrial fibrillation).

It is very important that patients should not stop taking any blood thinning medicine, unless on the advice of their doctor, due to the risk of experiencing a blood clot or stroke. If any patients have concerns about their medicines they should discuss these with their doctor.

### 3. How does Pradaxa work?

Pradaxa stops a substance called thrombin from forming blood clots. Blood clots can cause deep vein thrombosis, pulmonary embolism and strokes.

### 4. How do I take Pradaxa

Pradaxa capsules should be swallowed whole with water. Do not break, chew, or empty the pellets from the capsule. The following dosing is recommended:

*If you are taking Pradaxa after surgery to prevent blood clots*

For patients who have had surgery treatment starts with one 110mg capsule one to four hours after the operation. Treatment continues with two 110mg capsules taken once a day for 28 to 35 days after hip replacement and for 10 days after knee replacement. Treatment is delayed in patients who are still bleeding from the site of surgery. A lower dose is used in patients with moderate kidney problems.

*If you are taking Pradaxa to prevent strokes due to an abnormal heart beat*

One 150mg capsule is taken twice a day long term. A lower dose (one 110mg twice a day) is used in patients over 80 years of age or with moderate kidney problems, or who are at high risk of bleeding.

It is important to take Pradaxa regularly to prevent strokes and blood clots. There is no requirement for regular blood tests but patients should still look out for any signs of bleeding such as: exceptional weakness, tiredness, paleness, dizziness, headache, unexplained bruising or unexplained swelling.

### 5. When will my doctor prescribe a lower dose of Pradaxa

If you are taking Pradaxa after surgery to prevent blood clots, your doctor may reduce the dose you take if you:

- Have kidney problems.
- Are taking other medicines containing amiodarone, quinidine or verapamil.

If you are taking Pradaxa to prevent strokes due to an abnormal heart beat, your doctor may reduce the dose you take if you are:

- Aged 80 years or more.
- At risk of bleeding.

Patients who may be at higher risk of bleeding include those:

- With kidney problems.
- Taking medicines containing amiodarone, quinidine or verapamil.
- Taking other medicines that thin the blood such as aspirin or clopidogrel.
- Have a blood clotting problem.
- Have a stomach ulcer or stomach irritation.
- Have had a recent bleed or surgery.
- Are aged 75 years or more.
- Weighing 50kg or less.

Your doctor will weigh your risk of bleeding against your risk of having a blood clot before deciding if the reduced dose is right for you.

## **6. Are there any risks associated with Pradaxa?**

All medicines have risks as well as benefits. The most serious risk associated with Pradaxa is bleeding. Bleeding is a risk for all medicines that thin the blood (including warfarin and aspirin).

Patients should contact their doctor immediately if they experience any of the following: long or excessive bleeding, exceptional weakness, tiredness, paleness, dizziness, headache, unexplained bruising or unexplained swelling.

Other common effects are upset stomach and feeling sick (nausea).

## **7. Why aren't there prescribing restrictions for Pradaxa?**

Medsafe generally does not place prescribing restrictions on medicines; historically this has only occurred in very rare cases where the potential for very serious harm had been identified.

The patient's physician is best placed to decide on the choice of appropriate medicine and dose based on:

- The patient's medical history and the physician's current assessment of their symptoms.
- The risks and benefits of the medicine in the individual patient.

- The overall risks and benefits of the medicine are outlined in the data sheet and in other material that has been published about Pradaxa (see links in Question 8 below).

Since this medicine is used as a fixed dose for all patients Medsafe saw no reason to impose prescribing restrictions. In addition other anticoagulants have similar risks and are not restricted.

## **8. What measures are being taken to ensure the safe use of Pradaxa?**

Information on how to use Pradaxa has been given to prescribers by the company, PHARMAC and Medsafe. This information is available in the following links:

<http://www.pharmac.govt.nz/2011/06/15/BPAC%20Dabig%20insert.pdf>  
<http://www.pharmac.govt.nz/2011/06/13/Dabigatran%20testing%20and%20perioperative%20management.pdf>  
<http://www.pharmac.govt.nz/2011/06/13/Dabigatran%20bleeding%20management.pdf>  
<http://www.medsafe.govt.nz/profs/Datasheet/p/Pradaxacap.pdf>

Packages of Pradaxa contain a copy of the Consumer Medicine Information (CMI) also published on the Medsafe website at:

<http://www.medsafe.govt.nz/Consumers/cmi/p/pradaxa.pdf>

The company who makes Pradaxa is continuing to investigate the safety of this medicine in clinical studies. Should these show any new safety issues, Medsafe will take appropriate action (see how Medsafe regulates medicines at: <http://www.medsafe.govt.nz/Consumers/Safety-of-Medicines/Safety-and-Quality-of-Medicines.asp>)

## **9. How is the safety of Pradaxa being monitored in New Zealand?**

The Ministry of Health contracts the Centre for Adverse Reactions Monitoring (CARM) to collect reports of suspected adverse reactions to all medicines including Pradaxa. Healthcare professionals and consumers can report to CARM.

If you think you have experienced an adverse effect after taking Pradaxa, please report this to CARM (You can report online <https://nzphvc-01.otago.ac.nz/carm-adr/reporting.php> or by phoning 03 4797247). CARM inform Medsafe if they detect a safety issue with a medicine and Medsafe takes appropriate action (for more information see:

<http://www.medsafe.govt.nz/Consumers/Safety-of-Medicines/Medicines-Safety-and-Pharmacovigilance.asp>).

## **10. What adverse reactions to Pradaxa have so far been reported to CARM?**

As of 15 September 2011, CARM report that they have 122 reports for Pradaxa in their database. None of the reports received by CARM to date have identified any cases of fatal bleeding or death caused by dabigatran.

In a number of reports of bleeding, the patient was taking other blood-thinning medicines. In other reports, the patient was taking other medicines or had an ongoing medical problem that may also have caused the reported events.

The number of reports received so far by CARM is not unexpected for a new medicine. This is a recognised phenomenon and is described in the literature as the Weber effect.

### **11. I am worried that I am experiencing a side effect to my medicine, what should I do?**

If you are concerned you are experiencing side effects to dabigatran, you should discuss these with your doctor. Your doctor is in the best position to review your medication and decide if changes need to be made.

### **12. I read in the newspaper that people had died after taking Pradaxa, is this true?**

CARM have received a number of reports of suspected adverse reactions to Pradaxa. As of 15 September 2011, this included four reports where the patients had died. After carefully investigating these reports, the expert medical assessors at CARM have concluded that the patients' deaths were not caused by taking dabigatran.

It is very important that patients should not stop taking any blood thinning medicine, unless on the advice of their doctor, due to the risk of experiencing a blood clot or stroke. If any patients have concerns about their medicines they should discuss these with their doctor.

### **13. I read in the newspaper that Pradaxa wasn't studied for long enough before being approved in New Zealand?**

Before Pradaxa was approved in New Zealand Medsafe reviewed data from clinical trials involving more than 26,000 patients worldwide, including:

- For the prevention of blood clots after surgery clinical trials that included more than 8,500 patients.
- For the prevention of stroke in patients with atrial fibrillation, a clinical trial studied over 18,000 patients for an average of two years, about 6000 of these patients took warfarin, about 6000 took 110 mg Pradaxa twice a day and about 6000 took 150 mg Pradaxa twice a day. This study is considered to be one of the largest studies carried out in patients with atrial fibrillation and the average age of patients was 71 years.

The clinical trial data generated before Pradaxa was approved for use in New Zealand has also been reviewed by a number of other countries and Pradaxa is approved in the Australia, the United States, Canada, and Europe.

### **14: I read in the newspaper that Medsafe refuses to monitor Pradaxa on the Intensive Medicines Monitoring Programme (IMMP)?**

Medsafe decided that an IMMP study was not necessary when Pradaxa was approved in New Zealand. Since then the Medicines Adverse Reaction Committee (MARC) has also reviewed the known safety information for Pradaxa and did not recommend that this medicine be added to the IMMP.

IMMP studies can be useful in generating information on the real-world usage of medicines and can potentially detect previously unknown safety signals. However, these studies also have weaknesses. IMMP studies lack a comparator group, meaning it is difficult to tell if adverse

events being experienced by patients taking the monitored medicine are occurring more or less frequently than an alternative medicine (such as dabigatran compared to warfarin). IMMP studies are also subject to bias and under-reporting.

The manufacturer of Pradaxa is sponsoring a number of ongoing studies to monitor the safety of Pradaxa. One of these studies is an internationally conducted study specifically designed to review the real-world use of dabigatran. Medsafe will be monitoring the outcome of these studies.

The medicines safety group who was recently quoted in the newspaper asked Medsafe to place Pradaxa on the IMMP in July this year. A copy of Medsafe's response to this group including the reasons for not commissioning an IMMP study are provided in the link below:

[Medsafe response to Safe and Quality Use of Medicines Group](#)

PHARMAC and a PHARMAC advisory group also asked Medsafe to consider whether Pradaxa should be added to the IMMP. A copy of Medsafe's response and the reasons for not commissioning an IMMP study are provided in the link below:

[Medsafe response to PHARMAC](#)

[Medsafe response to PHARMAC advisory group](#)

Medsafe is monitoring the safety of dabigatran in New Zealand through adverse reaction reports that are sent to the New Zealand Pharmacovigilance Centre (NZPhvC). The Centre is contracted to collect reports, analyse them, and alert Medsafe of any emerging potential safety issues. Medsafe can then take appropriate action if necessary.