**MELATONIN FOR BETTER SLEEP IN PARKINSON’S DISEASE**

**PARTICIPANT INFORMATION SHEET**

**Part 1 What does my participation involve?**

**1. Introduction**

We would like to give you the opportunity to take part in this research project, which is being run by The University of Queensland and Wesley Medical Research, because you have Parkinson’s Disease and are having trouble sleeping. This research project is testing whether melatonin can help sleep problems in adults who have a diagnosis of Parkinson’s Disease. This study has been approved by the UnitingCare Health Human Research Ethics Committee and the University of Queensland Human Research Ethics Committee**.**

This Participant Information Sheet/Consent Form tells you about the research project. It explains the tests and treatments involved. Knowing what is involved will help you decide if you want to continue to take part in the research.

Please read this information carefully. Ask questions about anything that you don’t understand or want to know more about. Before deciding whether or not to take part, you might want to talk about it with a relative, friend or your local doctor.

Participation in this research is voluntary. If you don’t wish to continue to take part, you don’t have to. You will receive the best possible care whether or not you take part.

If you decide you want to continue to take part in the research project, you will be asked to sign the consent section. By signing it you are telling us that you:

• Understand what you have read

• Consent to continue to take part in the research project

• Consent to have any ongoing tests and treatments that are described

• Consent to the use of your personal and health information as described.

You will be given a copy of this Participant Information and Consent Form to keep.

**2. What is the purpose of this research?**

This study aims to test the effectiveness of melatonin for sleep problems in adults who have a diagnosis of Parkinson’s Disease. Many patients with Parkinson’s Disease report sleep difficulties, particularly in getting off to sleep. Some doctors are prescribing melatonin to help with this sleep problem. This study aims to see whether using melatonin assists with sleep problems in patients with Parkinson’s Disease.

**WHAT IS MELATONIN?**

Melatonin is a natural hormone secreted by the pineal gland in the brain. It helps regulate other hormones and maintains the body's circadian rhythm. The circadian rhythm is an internal 24-hour “clock” that plays a critical role in when we fall asleep and when we wake up. When it is dark, your body produces more melatonin; when it is light, the production of melatonin drops.

**WHAT ARE INDIVIDUAL MEDICATION EFFECTIVENESS TESTS (IMET)?**

IMET stands for Individual Medication Effectiveness Tests. An IMET is a new way of working out whether a medication is working for you and will be used in this study. Most studies that test the effectiveness of medicines give information about the effects of that medication on groups of people. This makes it difficult to apply the findings to an individual person like you. IMETs give information about the effectiveness of the medicine for the person doing the test. Another name for IMET is N-of-1 trial or N-of-1 test, which means we are testing the medication in just one person.

The IMET will take 14 weeks (2 weeks to find the right dose for you and 12 weeks to test it). It will use active and placebo (inactive) medication. Placebo and active medication look exactly the same, but the placebo is not active and has no effect. The IMET team will arrange things so that neither you nor your study doctor, will know what medication you will be taking at any one time. But everyone will know that you will be taking either medication for periods of two weeks at a time, and in a **random order.**

**WHY THE IMET IS NEEDED?**

Often, doctors and patients try to decide what treatment is best by starting a drug, and seeing if the patient feels better. But, sometimes the doctor and the patient may think the drug works, even if it does not. This may be because the patient may have become better anyway, without any medication. Also, people may sometimes feel better when they are taking medication, even when it doesn't have any effect on their illness. The IMET offers you a more scientific way of determining whether melatonin works as a treatment for your sleep symptoms.

**PARTICIPANTS**

We aim to recruit 44 adults to this study. You may be eligible to take part if you:

* Have a diagnosis of Parkinson’s Disease without dementia
* And have a problem getting off to sleep.

If you are already taking melatonin, this does not stop you taking part in the study but this melatonin would need to be ceased on the Thursday before the study starts on Saturday, and during the study.

**3. What does participation in this research involve?**

Please read this information sheet which describes what would be involved. We will also give you an information sheet for your doctor so that you may discuss the study with him/ her if you wish. Before deciding whether or not to take part you may like to discuss the matter with a relative or friend as well. You are very welcome to do this. If you have any questions please do not hesitate to get in touch with the study coordinator (Dr Jane Nikles) on the phone number given on page 11 of this information sheet.

If you agree to participate in this study, you will be asked to sign the Participant Consent Form. The following outlines the requirements of the study:

**Screening Phase**

Prior to commencing any of the study procedures you will be evaluated (during the screening period) to determine if you are eligible to participate.

The following is a detailed description of what happens during the Screening Phase:

The study doctor and/or study staff will discuss by phone/email/ in person with you whether this study is suitable for you. You will also be asked some questions to check if you may be eligible for the study. If the study is suitable for you and you may be eligible, you will be invited to take part in the study.

Your involvement in the study will be for approximately 4 months, with follow-up questionnaires 6 and 12 months later.

You will be asked to sign a consent form and a medical information release permission form.

If you agree to take part in this study, study staff will talk to you by phone/email/ in person and ask some more questions about your sleep and to determine if you meet the requirements to participate in this study. At this point there will be three questionnaires about your sleep quality, whether you have sleep apnea, and cognitive function that we estimate will take altogether about 15-20 minutes to complete.

The research team will collect your medical information from your GP and/or neurologist.

If you are eligible after we have all this information, you can participate in the study from home by phone or skype (or similar).

We will review your medical history including questions about your sleep, medications currently taken, any disease condition that might affect sleep and your intake of melatonin.

The study doctor and / or study staff will discuss with you any health conditions that may be detected during screening or during the trial itself which affect your ability to participate. If necessary, you will be referred for follow-up tests with your General Practitioner or medical specialist.

Otherwise, the study staff will explain all the trial procedures and give you some information about the study, as well as a special watch to monitor your sleep patterns.

You will be asked to fill in a questionnaire about your sleep related issues and personal information. This will take 5-10 minutes. This self-administered questionnaire will be given to you by the research staff.

**4. What do I have to do?**

If you agree to take part in this study, then you must be willing to complete all tests and treatments that are outlined in this participant information/consent sheet and agree to follow the study schedules to the best of your ability. If you do not follow the instructions from your research doctor, you may not be able to continue in the study.

You may choose to stop receiving the melatonin at any time.

You are not permitted to take part in any other interventional studies without approval from the research doctor(s) in each study, as there may be additional unanticipated side effects. Being in more than one study at one time may increase your risks and could affect the results of each study.

Please tell the study doctor or study staff right away if you have any side effects.

Before commencing any new medications during this study, you should discuss it with the research doctor.

**Run in study period (2 weeks)**

You will be asked to pick up the study medication from your preferred pharmacy. The study team will organize to send your study medication to this pharmacy. You will be asked to take melatonin 3 mg every day 30 minutes before bed time.

You will need to keep a sleep diary of the time you go to bed, the time you go to sleep, the time you wake up in the morning and significant wake periods during the night. You will be asked to fill in the sleep diary either online or on paper and send it to us. We estimate the daily diary will take approximately 1 minute on days 1-6, and up to 5 minutes on day 7 of each week.

You will also need to wear a special watch, called an Actiwatch or Motionwatch, throughout the study period. This will help us determine how useful the melatonin has been in helping you sleep better. It is commonly used to measure when we are asleep, by measuring movement. It is important that this is done in conjunction with a sleep diary. The watch looks like a small watch and is generally fairly tough. It does not tolerate significant water exposure and you need to remove it at these times such as swimming or showering. This is not a problem. The research nurse will call you weekly to ask how you are going.

We do the run in period to find out which dose of melatonin to test you on in the trial study period. At the end of the two weeks, the research staff will look at your results and let you know what to do next.

**Trial study period (12 weeks)**

This part of the study is what is called an “Individual Medication Effectiveness Test” (IMET). This uses real medication and placebo (inactive) medication. Placebo and active medication look exactly the same, but the placebo is not active and so has no effect. But we do know that you will be taking each medication in **random order**, something like the following example. Random order means that the order was decided by a computer, something like tossing a coin. So during each treatment, neither you nor your doctor will know which treatment you are taking. This phase will last 12 weeks.

**Example arrangement of treatment order**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Week 1-2 | Week 3-4 | Week 5-6 | Week 7-8 | Week 9-10 | Week 11-12 |
| Treatment1 | Treatment2 | Treatment3 | Treatment4 | Treatment5 | Treatment6 |
|  |  |  |  |  |  |
| activemelatonin | placebo | activemelatonin | placebo | placebo | activemelatonin |

There are six treatment periods, and one treatment is taken every 2 weeks.

Again, you will be asked to pick up the study medication from your preferred pharmacy. The study team will organize to send your study medication to this pharmacy. The medication will come out to you in a pack telling you which medication to take each day.

You will need to keep a sleep diary again, either online or on paper, and wear the watch for this phase of the study as well. This will help us determine how useful the melatonin has been in helping you sleep.

**After the study**

The study team will prepare your individual report and send it to your GP or neurologist. You will be asked to make appointment with your GP or neurologist to discuss whether melatonin was helpful for your insomnia.

**6 and 12 month follow up questionnaires**

You will be asked to fill out a one week sleep diary and some questions about your sleep and medications for the past 6 months. The questionnaire will be mailed to your address or sent by email.

**5. Do I have to take part in this research project?**

Participation in any research project is voluntary. If you do not wish to take part, you do not have to. If you decide to take part and later change your mind, you are free to withdraw from the study at any stage.

If you do decide to take part, you will be given this Participant Information and Consent Form to sign and you will be given a copy to keep.

Your decision whether to take part or not to take part, or to take part and then withdraw, will not affect your routine treatment.

**6. What are the alternatives to participation?**

Instead of being in this study, you would receive the usual treatment for your condition provided by your physician.

**7. What are the possible benefits of taking part?**

This trial will give you and your doctor clear information as to whether melatonin has a significant effect on your sleep patterns. At the end of the trial this information may help you and your doctor decide whether melatonin is helpful for you. If so then your doctor will be able to prescribe melatonin for you. At this stage this is through a private script as Melatonin is not currently on the Pharmaceutical Benefits Scheme.

Other benefits will not necessarily directly affect you, but will help us determine the overall effectiveness of melatonin in people who have a diagnosis of Parkinson’s Disease and a sleeping problem.

**8. What are the possible risks and disadvantages of taking part?**

Medical treatments often cause side effects. You may have none, some or all of the effects listed below, and they may be mild, moderate or severe. If you have any of these side effects, or are worried about them, talk with your study doctor. Your study doctor will also be looking out for side effects.

There may be side effects that the researchers do not expect or do not know about and that may be serious. Tell your study doctor immediately about any new or unusual symptoms that you get.

Many side effects go away shortly after treatment ends. However, sometimes side effects can be serious, long lasting or permanent. If a severe side effect or reaction occurs, your study doctor may need to stop your treatment and he/she will discuss the best way of managing any side effects with you.

**Below are potential risks and side effects of undergoing melatonin treatment. If you do not understand what any of these side effects mean, please ask the research doctor or study staff to explain these terms to you.**

**Risks and Side Effects of participating in this study:**

In this study the active medication is melatonin. Melatonin is a medication that is currently licensed for insomnia in adults. It is available in Australia by private prescription and many adults and children are being prescribed melatonin. A number of studies have demonstrated its usefulness with a variety of problems and associated sleep problems but it has not been evaluated properly in people with Parkinson’s Disease.

Melatonin uses the same pathway in the liver as a number of other medications to be metabolised and excreted. Sometimes this can cause interactions or alter the concentrations of other medications you may be prescribed. You should let your GP know you are taking part in this trial, and if extra medications are being prescribed please let the research team know prior to starting. There is also an information sheet for your GP that you will be given at the start of the study.

Because alcohol can decrease the effectiveness of melatonin, we request that you do not consume alcohol during the course of the study, or limit to 1 standard alcoholic drink per day before 5 pm.

**WHAT SHOULD I DO IF I HAVE ANY CONCERNS ABOUT MEDICATION SIDE EFFECTS?**

If you have any concerns about the medication please contact the project staff on the phone number on page 11 of this information sheet.

If you have any problems with the medication you will be advised to stop the trial medication.

**Can I talk to a doctor after hours if I feel I need to?**

One of the study doctors (Prof Geoff Mitchell) at The University of Queensland carries a mobile phone that that you can call 24hrs if you have any urgent concerns. The phone number is 0412 775 117.

If you are unable to get in touch with anyone then do not take the medication until you have been able to speak to one of the study researchers.

**PREGNANCY**

The effects of melatonin on the unborn child and on the newborn baby are not known. Because of this, it is important that research project participants are not pregnant or breast-feeding and do not become pregnant during the course of the research project. You must not participate in the research if you are pregnant or trying to become pregnant, or breast-feeding. If you are female and child-bearing is a possibility, you will be required to undergo a pregnancy test prior to commencing the research project.  If you are male, you should not father a child or donate sperm for at least 1 month after the last dose of study medication.

Both male and female participants must avoid pregnancy during the course of the research and for a period of 1 month after completion of the research project.  They should discuss effective methods of avoiding pregnancy with the study doctor.

*[For female participants]* If you become pregnant whilst participating in the research project, you should advise your study doctor immediately. Your study doctor will withdraw you from the research project and advise on further medical attention should this be necessary. You must not continue in the research if you become pregnant.

*[For male participants]* You should advise your study doctor if you father a child while participating in the research project. Your study doctor will advise on medical attention for your partner should this be necessary.

**9. What if new information arises during this research project?**

Sometimes during the course of a research project, new information becomes available about the treatment that is being studied. If this happens, your study doctor will tell you about it and discuss with you whether you want to continue in the research project. If you decide to withdraw, your study doctor will make arrangements for your regular health care to continue. If you decide to continue in the research project you will be asked to sign an updated consent form.

Also, on receiving new information, your study doctor might consider it to be in your best interests to withdraw you from the research project. If this happens, he/ she will explain the reasons and arrange for your regular health care to continue.

**10. Can I have other treatments during this research project?**

You may be able to have other treatments - please check with your study doctor before commencing other treatments.

**11. What if I withdraw from this research project?**

If you decide to withdraw from the project, please notify a member of the research team before you withdraw. This notice will allow that person or the research supervisor to discuss any health risks or special requirements linked to withdrawing.

If you do withdraw your consent during the research project, the study doctor and relevant study staff will not collect additional personal information from you, although personal information already collected will be retained to ensure that the results of the research project can be measured properly and to comply with law. You should be aware that data collected by The University of Queensland and Wesley Medical Research up to the time you withdraw will form part of the research project results. If you do not want them to do this, you must tell them at the point of withdrawal fromthe research project.

**12. Could this research project be stopped unexpectedly?**

This research project may be stopped unexpectedly for a variety of reasons. These may include reasons such as:

• Unacceptable side effects

• The treatment being shown not to be effective

If the research study stops you will continue to receive standard care and treatment for your condition.

**13. What happens when the research project ends?**

At the end of the study, you and your doctor will be told when you were taking the active medication and when you were taking the placebo. The symptom diaries and information from the Actiwatch (Motionwatch) will be analysed and the results sent to your doctor. After looking at these results, you, and your doctor will be able to decide if the melatonin is effective for your insomnia.

Note: If you and your doctor decide to continue melatonin as a sleep medication, the preparation you find in the local pharmacies in Australia might be different. We are importing the melatonin medication from overseas for the purpose of this research. It is different to the Circadin melatonin that is available in Australia because it is faster acting and better absorbed, so may be more effective. You will still be able to get this same kind of melatonin from some compounding pharmacies in Australia after the study finishes.

The results of the study will be submitted for publication to journals and/or scientific or other publications and presentations. At the conclusion of the study, you will be notified of the outcomes of the study in a letter sent from the Principal Investigator (Dr Nikles).

# **You are encouraged to ask questions at any time during your participation. If you would like more information please contact the research team on 0408 599 033.**

**Part 2 How is the research project being conducted?**

**14. What will happen to information about me?**

You will be asked to enter some information about your sleeping patterns securely online, every day during the study. If you do not have the internet at home or wish to use paper diaries that is also possible. Your re-identifiable data will be stored in a database. All personal information linked to the data will however remain at The University of Queensland, so that no-one outside the study team will be able to know who the information belongs to.

All personal information and test results collected during the project will be stored securely and will only be available to doctors, researchers and scientists involved in this project. Your information can then be made available if you wish to your treating doctor. A separate file with no identifying data will be made for group analysis and to determine a group response. No patient information will have identifying information attached to it. Data derived from this project may be published in medical journals or presented at scientific conferences and if this occurs you should be aware that individual participants will **not** be identified in any of the tables or in text.

Once the data is de-identified, it must be stored for 15 years as required by hospital policy.

**15. Who is organising and funding the research?**

The University of Queensland is organising this study and Wesley Medical Research is funding the study.

**16. Who has reviewed this research project?**

### UnitingCare Health Human Research Ethics Committee and The University of Queensland Human Research Ethics Committee.

**17. Further information and who to contact**

Questions or concerns can be answered at any time during the project by contacting one of the study doctors on the telephone numbers below.

|  |  |
| --- | --- |
| Dr Jane Nikles | The University of Queenslanduqjnikle@uq.edu.auPh 0408 599 033 |
|  |
|  Prof Geoff Mitchell |  The University of Queensland g.mitchell@uq.edu.au Ph 0412 775 117 |

For general enquiries about the study and/or eligibility criteria, please contact:

Suzanne McDonald, Study coordinator at The University of Queensland (works Tuesdays)

suzanne.mcdonald@uq.edu.au

0490 936 307

Lisa Mackenzie, Research Assistant at The University of Queensland (works Tuesdays & Thursdays)

lisa.mackenzie@uq.edu.au

073346 5013

General email for research team at The University of Queensland

insompd@uq.edu.au (general email that is checked regularly)

If you are returning the consent forms by post, please return them to:

**Assoc Prof Jane Nikles**

**University of Queensland Centre for Clinical Research**

**Building 71/918 RBWH**

**Herston, Brisbane 4029**

**ETHICS APPROVAL**

### This project will be carried out according to the National Statement on Ethical Conduct in Research Involving Humans (May 2007, updated in 2013, 2015 and 2018) produced by the National Health and Medical Research Council of Australia. Additionally, this project has been approved by the UnitingCare Health Human Research Ethics Committee, and The University of Queensland Human Research Ethics Committee.

If you have any concerns or complaints about the conduct of the research, you may use the following contact:

HREC Coordinator

UnitingCare Health Human Research Ethics Committee
The Wesley Hospital
PO Box 499
Auchenflower Qld  4066

Telephone: 3232 7500

\*\*Please only contact the HREC Coordinator for concerns or complaints about the conduct of the research \*\*

**MELATONIN PATIENT INFORMATION**

NAME OF THE PRODUCT

Melatonin 3 mg immediate-release tablets

QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 3 mg melatonin.

Each tablet contains some inactive ingredients.

WHAT IS IN THIS LEAFLET

This leaflet contains answers to some common questions about MELATONIN.

It is particularly important that you read the sections "When to take it" and "How to take it"

before you take this medicine.

The leaflet does not contain all the information that is known about Melatonin.

It does not take the place of talking to your doctor or pharmacist.

All medicines have risks and benefits. Your doctor has weighed the risks of you taking MELATONIN against the benefits they expect it will have for you.

If you have any concerns about taking this medicine, ask your doctor or pharmacist.

Keep this leaflet with the medicine.

You may need to read it again.

WHAT MELATONIN IS USED FOR

MELATONIN is used to improve sleep quality and morning alertness in people with poor quality of sleep.

The active substance of MELATONIN, melatonin (not of plant or animal origin), belongs to a group of naturally occurring hormones produced in the body.

Melatonin works by controlling the circadian rhythms and increasing the ability to sleep.

This medicine is only available with a doctor's prescription.

Melatonin is not addictive.

BEFORE YOU TAKE MELATONIN

*When you must not take it*

Do not take MELATONIN if you are allergic to it or any of the ingredients listed at the end of this leaflet.

Symptoms of an allergic reaction may include shortness of breath, wheezing or difficulty breathing, swelling of the face, lips, tongue or other parts of the body, or rash, itching or hives on the skin.

Do not take MELATONIN if you have been drinking alcohol or intend to drink alcohol or believe that you may have alcohol in your blood stream. The effect of alcohol on melatonin has not been formally studied. It is recommended that alcohol should not be taken with melatonin because it reduces the effectiveness of melatonin on sleep. As alcohol is cleared from the body at a rate of approximately one unit per hour, one unit of alcohol (e.g., a glass of wine) taken at 5 pm should, theoretically, have been cleared from the body and therefore would not be able to interact with melatonin taken at 9 pm. However, metabolism differs between individuals and a firm recommendation on time of alcohol intake prior to melatonin cannot be made.

Do not take it after the expiry date printed on the pack.

If you take it after the expiry date has passed, it may not work as well. The expiry date refers to the last day of the month.

Do not take it if the packaging is torn or shows signs of tampering.

If you are not sure whether you should start taking MELATONIN talk to your doctor.

*Before you start to take it*

Tell your doctor if:

1. you have any allergies to any other medicines or any other substances, such as foods, preservatives or dyes

2. you have, or have had the following medical conditions:

• suffer from liver problems

• suffer from kidney problems

• you suffer from an autoimmune disease.

If you have not told your doctor about any of the above, tell him before you use MELATONIN.

*Taking other medicines*

Tell your doctor if you are taking any other medicines, including any that you buy without a prescription from your pharmacy, supermarket or health food shop. Some medicines may affect the way other medicines work.

Some medicines and MELATONIN may interfere with each other. These include:

• hypnotics and tranquilisers (e.g. benzodiazepines),

• fluvoxamine, thioridazine and imipramine (used to treat depression or psychiatric problems),

• oestrogen (contraceptives or hormone replacement therapy),

• cimetidine and psoralens (used to treat skin problems e.g. psoriasis)

• caffeine

The effect of adding MELATONIN to other medicines used to treat insomnia has not been examined. It is not known if MELATONIN will increase or decrease the effects of other treatments for insomnia.

Your doctor or pharmacist has more information on medicines to be careful with or avoid while taking MELATONIN.

HOW TO TAKE MELATONIN

*How much to take*

Take MELATONIN only when prescribed by your doctor.

Every night, take the number of tablets recommended by your doctor.

There is no evidence that taking more than the recommended dose will increase the effect of MELATONIN.

*How to take it*

Put the tablet under your tongue until it dissolves.

Do not crush, chew or divide your tablet.

If you crush, chew or divide the tablet they will not work properly.

Follow all directions given to you by your doctor carefully.

They may differ from the information contained in this leaflet.

If you do not understand the instructions on the bottle, ask your doctor or pharmacist for help.

*When to take it*

After food, 30 minutes before you go to bed.

*How long to take it*

It is important that you continue taking MELATONIN for as long as your doctor prescribes.

*If you forget to take it*

If you forget to take your melatonin, take another as soon as you remember, before going to bed or wait until it is time for your next dose.

Do not take a double dose to make up for a forgotten dose.

If you are not sure what to do, talk to your doctor or pharmacist.

If you have trouble remembering to take your MELATONIN, ask your pharmacist for some hints.

IF YOU TAKE TOO MUCH (OVERDOSE)

Immediately telephone your doctor or Poisons Information Centre (In Australia 13 11 26), or go to

accident and emergency at your nearest hospital, if you think that you or anyone else may have taken too much MELATONIN. Do this even if there are no signs of discomfort or poisoning.

WHILE YOU ARE USING MELATONIN

*Things you must do*

If you are about to be started on any new medicine tell your doctor and pharmacist that you are taking MELATONIN.

Tell any other doctors, dentists and pharmacists who treat you that you are taking this medicine.

*Things you must not do*

Do not give MELATONIN to anyone else, even if they have the same condition as you.

Do not take more than the recommended dose unless your doctor tells you to.

Do not use this medicine to treat any other complaints unless your doctor tells you to.

*Things to be careful of*

MELATONIN rarely causes drowsiness, nevertheless it is not recommended to drive or operate machinery for 8 hours after you take it. Melatonin does not impair morning alertness, but if you suffer from drowsiness during the day you should consult your doctor.

SIDE EFFECTS

Tell your doctor or pharmacist as soon as possible if you do not feel well while you are taking MELATONIN.

MELATONIN has been shown to improve the sleep of most people, but it may have unwanted side effects in a few people. All medicines can have side effects. Sometimes they are serious, but most of the time they are not. You may need medical treatment if you get some of the side effects.

Ask your doctor or pharmacist to answer any questions you may have.

Tell your doctor if you notice any of the following and they worry you.

These are considered to be uncommon side effect in adults (i.e., likely to occur in fewer than 1 in 100 patients):

Irritability, nervousness, restlessness, insomnia, abnormal dreams, anxiety, migraine, lethargy, psychomotor hyperactivity (restlessness associated with increased activity), dizziness, somnolence (tiredness), high blood pressure, (upper) abdominal pain, indigestion, mouth ulceration, dry mouth, hyperbilirubinaemia (changes in the composition of your blood which could cause yellowing of the skin or eyes (jaundice), inflammation of the skin (dermatitis, night sweats, pruritis (itching), rash, dry skin, pain in extremities, menopausal symptoms, asthenia (feeling of weakness), chest pain, excretion of glucose in urine, excess proteins in the urine, abnormal liver function and weight increase.

The following events are considered to be rare (i.e., likely to occur in fewer than 1 in 1,000 adults):

Shingles, reduced number of white blood cells in the blood, decreased number of platelets in the blood, high level of fatty molecules in the blood, severe chest pain due to angina, feeling your heartbeat (palpitations). low serum calcium levels in the blood, low sodium levels in the blood, altered mood, aggression, agitation, crying, stress symptoms, disorientation, early morning awakening, increased sex drive, depressed mood, depression, loss of consciousness or fainting, memory impairment, disturbance in attention, dreamy state, restless legs syndrome, poor quality sleep, 'pins and needles' feeling (paresthesia) reduced visual acuity (visual impairment), blurred vision, watery eyes, dizziness when standing or sitting, vertigo, hot flushes, gastro-oesophageal reflux, gastrointestinal disorder, blistering in the mouth, tongue ulceration, gastrointestinal upset, vomiting, abnormal bowel sounds, flatulence (wind), salivary hypersecretion (excess saliva production), halitosis (bad breath), abdominal discomfort, gastric disorder, inflammation of the stomach lining, , eczema, erythema (skin rash), hand dermatitis, psoriasis, pruritic rash (itchy rash), nail disorder, arthritis, ,muscle spasms, neck pain, night cramps, increased duration of erection, inflammation of the prostate gland, tiredness, pain, thirst, passing large volumes or urine, presence of red blood cells in the urine, urination during the night, increased liver enzymes, abnormal blood electrolytes and abnormal laboratory tests.

Melatonin is not addictive.

Other side effects not listed above may also occur in some patients. Tell your doctor if you notice any other effects.

Do not be alarmed by this list of possible side effects. You may not experience any of them.

AFTER USING MELATONIN

*Storage*

Keep your tablets in the bottle until it is time to take them.

If you take the tablets out of the bottle they may not keep well.

Keep MELATONIN away from sunlight.

Keep the medicine at room temperature, between 15 and 25 degrees Celsius.

Do not store it or any other medicine in the bathroom, near a sink, or on a window-sill.

Do not leave it in the car.

Heat and damp can destroy some medicines.

Keep it where children cannot reach it.

A locked cupboard at least one-and-a-half metres above the ground is a good place to store medicines in general.

DISPOSAL

If your doctor tells you to stop taking the tablets or the tablets have passed their expiry date, do not take any more tablets

Return any unused medicine to the research team.