

## Imiquimod Application: Patient Diary

This diary has been designed to help you record your daily imiquimod cream applications, as well as write down any other effects (good or bad) you may be experiencing. This information is really important to help your physician to collect all the information that is required for this trial. Please carefully read the instructions and follow them closely.

Please record any signs and symptoms on the diary which will be regularly reviewed by your doctor.

Below is your photograph; it shows your lentigo maligna and your physician has drawn an area around this. Please apply the imiquimod cream within the area indicated. Use this photograph to help guide you as to the application area and follow the instructions on the following page:

*Please affix photograph of the participant's marked treatment area here.*

## Application instructions

Please read carefully:

1. You will need to apply imiquimod cream to the affected area 5 days / week for a 12-week period. This diary is designed to record your daily applications, as well any other side effects you may experience.
2. Before applying the cream, wash your hands. It needs to be applied in the evening prior to going to sleep 5 days a week (Monday to Friday inclusive).
3. Apply the cream to the area the doctor has indicated on your photograph. Take care to apply the cream in a very thin layer only to the area that is indicated.
4. After applying the cream, rub it into your skin until it is absorbed properly and then leave it on your skin overnight (between 6 to 10 hours).
5. After applying the cream, please wash your hands.
6. When you wake the next morning, the cream should be washed off the skin using mild soap and water.
7. Leave the affected area uncovered and avoid cosmetics or other creams during the day.
8. Repeat steps 1 to 5 in the evening for 5 continuous days.

The use of cosmetics and of sunscreen has not been tested with imiquimod so please keep the area free of other products.

Exposure to natural or artificial sunlight should be minimised during your treatment with imiquimod. You may use a sunscreen after your treatment is completed. Please consult your doctor if you have further questions.

You will be seen by your doctor after 4 weeks of starting on the treatment. Please bring this diary with you to that appointment.

**IF YOU NEED TO CONTACT YOUR DOCTOR BECAUSE YOUR SKIN IS REACTING TOO MUCH,  
please contact the person named below:**

**Name:**

**Phone number:**

**Email:**

## What does a normal reaction look like?

Inflammation is a sign that the immune system is working in the area. A normal reaction may include some or all, of the following symptoms:

- Redness
- Dryness
- Itchiness
- Inflammation
- Crustiness
- Swelling

This is what a normal response looks like:



Examples of an inflammatory response:



See Annex 1 for more examples.

### Reactions outside of the target area

When the immune system cells increase in the target area, they may also take care of other sun damaged cells that can be outside of the area where you are applying imiquimod. You may get patches of strong reactions, which is completely normal and not a worry. Do not start applying cream on these areas as we need your immune system to focus on the cancer.

## Crust formation and removal

When the inflammatory state is strong it can cause blistering and crusting, which is normal. The skin generally heals quickly after a little break. Imiquimod cream doesn't penetrate the skin efficiently when there is crust on top, and crust can harbour bacteria, so we want you to help your body get rid of the crust when needed. Please see Annex 2 for instructions on **saltwater soaks** that you can do 1-2 times/day when needed.



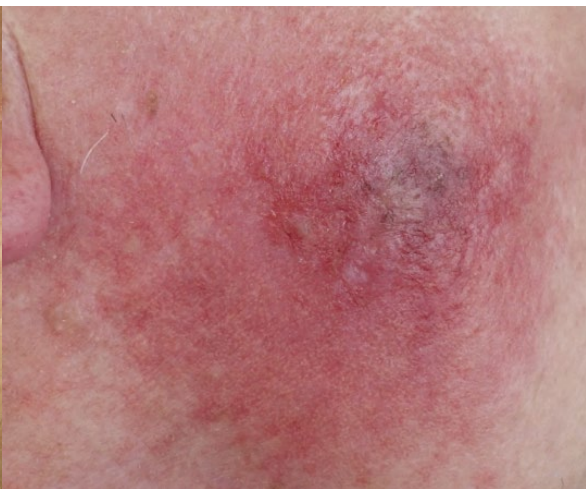
Example of crust formation



Skin after a 5-day break



Example of crust formation



Skin after a 4-day break

## Infection

It is unusual for an infection to develop as there is a lot of immune system present in the area, but it can happen. If you have excessive thick, yellow ooze and redness spreading well away from the area, increasing pain, or feel generally unwell, please contact your doctor.

## How do you know if your skin is not reacting enough?

We know that up to 1 in 5 people do not react as pictured in the photo. If that is the case and you do not see a similar reaction to the photo within the first 2 weeks of using the cream, it is important that the frequency of applying the cream is increased. See below.

### Instructions to increase imiquimod dose:

1. Apply imiquimod cream to the affected area **5 days per/week** and record the details in the diary.
2. If an inflammatory reaction (like in the photograph above) is not obtained after the first 10 days of treatment (5 days/week for the first 2 weeks), imiquimod application will be increased to **7 days a week** for the remainder of the treatment.
3. If an inflammatory reaction is not obtained after 1 week of daily imiquimod application (7 days/week), **then cover the area with a plastic bandage overnight** to increase the penetration of the cream. Remove the bandage each morning when you wake up and wash off the imiquimod cream as usual.
4. THEN, if an inflammatory reaction is not obtained after 1 week, please contact your doctor as you will need to be given **a vitamin A** cream to apply in the morning to the area to further sensitise the skin. Apply both the imiquimod (evening) and ReTrieve cream (morning) daily and cover with a bandage overnight for 7 days/week.
5. Once an inflammatory reaction has been induced, begin reducing the dose one step at a time so that the inflammation is maintained without any pain. For example, the first step would be to stop applying vitamin A cream in the morning, while continuing to apply the imiquimod and bandage overnight for 7 continuous days. If you do this and your inflammation is maintained, you may then stop applying the bandage overnight and revert to daily imiquimod application (7 days/week).
6. If there is still no inflammatory reaction after 7 days of daily imiquimod and Vit A cream application and bandaging overnight, please contact your doctor. Your methods of applying the creams will be reviewed and corrected as necessary. If you have been administering the cream correctly and for reasons unknown haven't responded, alternatives will be discussed.
7. Please record what happens on the diary when you start using the imiquimod cream and return it at the scheduled visit. You may need to apply the cream for longer than 12 weeks so that a total period of 11 weeks of inflammation is achieved. Your doctor will give you advice about this at the scheduled visit.
8. If the imiquimod treatment has not been creating an inflammatory response after 2 weeks, please do continue to apply the cream beyond 12 weeks as the aim is to obtain a total period of 11 weeks of inflammation.

**If you run out or need additional imiquimod cream, please contact your doctor.**



## How do you know if your skin is reacting too much?

### PAIN is too much!

In case you experience a severe skin reaction to the imiquimod cream, please temporarily stop using the cream. If you experience any symptoms such as pain or ulceration (see photo) please follow the procedure described below. If you experience any flu-like symptoms, please stop applying the cream and contact your doctor.



#### Instructions for reducing imiquimod dose:

1. If you experience pain or ulceration at or around the affected area, stop applying cream for **4 FULL days** to wait for the pain and ulceration to subside. (It may take longer than 4 days to subside – stop applying the cream for as long as necessary until the pain and ulceration is gone).
2. Following the break, recommence applying the imiquimod cream at a lower dose of 2 times/week (for example: only on **Monday** and **Thursday**, highlighted in pink on the diary) for the remaining treatment period until you complete the 12 weeks.
3. If an adequate inflammatory reaction is maintained with 2 days/week dosing, continue applying the imiquimod cream at the lower dose. **However, if the reduced dose leads to no more inflammation**, the imiquimod dose must be increased in order to obtain a proper inflammatory reaction. Please follow the 'Instructions to increase imiquimod dose' on page 5.
4. If the imiquimod treatment needs to be interrupted as a result of painful inflammatory reactions, please do not continue to apply the cream beyond 12 weeks as the aim is to obtain a total period of 11 weeks of inflammation.
5. Please write down your experiences on the diary and contact your doctor if you wish.

<b>Date of starting treatment:</b>						
<b>Month 1 (Weeks 1 and 2)</b>						
How does your skin feel/appear?						
<b>Week 1</b>						
Day	Reaction? Y/N	Red? Y/N	Itchy? Y/N	Crusty? Y/N	Painful? Y/N See note	Comments
Monday						
Tuesday						
Wednesday						
Thursday						
Friday						
Saturday	Do not apply cream					
Sunday	Do not apply cream					
<b>Week 2</b>						
Monday						
Tuesday						
Wednesday						
Thursday						
Friday						
Saturday	Do not apply cream					
Sunday	Do not apply cream					

**Please note - You should not feel pain. If you are in pain, your skin is reacting too much please follow instructions on page 6.**

Week 3						
Monday						
Tuesday						
Wednesday						
Thursday						
Friday						
Saturday	Do not apply cream					
Sunday	Do not apply cream					

**After you have completed Week 3 – please answer these questions before continuing with treatment.**

1) Have you answered yes to any of the questions in a green box?

- **Yes, I have answered yes to green questions** – Your skin is reacting as we would expect keep applying the cream 5 days per week for the next 9 weeks.
- **Yes, but I have also answered yes to red questions** – Go to Question 2.

2) Have you answered yes to questions relating to pain?

- **Yes, my skin has been painful** – Your skin is reacting too much please follow the instructions for reducing dose (page 6).
- **No, my skin hasn't been painful** – Go to question 3.

3) Have you not yet experienced a reaction?

- **Yes, I have seen a reaction** – This is normal your skin is reacting as we would expect keep applying the cream 5 days per week for the next 9 weeks.
- **No, I haven't observed a reaction** – This is not uncommon please refer to the instructions to increase the dose on page 5 entitled 'Instructions to increase imiquimod dose'.



#### Instructions - Week 4

- **If you are reacting normally** – 5 days per week application = Apply on un-shaded days and those shaded pink.
- **If you are reducing your dose** – 2 days per week application = Apply on days shaded pink only. If pain continues, please contact your doctor.
- **If you are increasing your dose** – 7 days per week application = Apply every day. If at the end of this week you still have no reaction, contact your doctor.  
We need to give you another cream to help you react to imiquimod.

Week 4						
How does your skin feel/appear?						
Day	Reaction? Y/N	Red? Y/N	Itchy? Y/N	Crusty? Y/N	Painful? Y/N	Comments
Monday						
Tuesday						
Wednesday						
Thursday						
Friday						
Saturday						
Sunday						

### Instructions - Week 5

- **If you are reacting normally** – 5 days per week application = Apply on un-shaded days and those shaded pink.
- **If you are reducing your dose** – 2 days per week application = Apply on days shaded pink only. If pain continues, please contact your doctor.
- **If you are increasing your dose** – 7 days per week application = Apply every day. If at the end of this week you still have no reaction, contact your doctor.  
We need to give you another cream to help you react to imiquimod.

Week 5						
How does your skin feel/appear?						
Day	Reaction? Y/N	Red? Y/N	Itchy? Y/N	Crusty? Y/N	Painful? Y/N	Comments
Monday						
Tuesday						
Wednesday						
Thursday						
Friday						
Saturday						
Sunday						

### Instructions - Week 6

- **If you are reacting normally** – 5 days per week application = Apply on un-shaded days and those shaded pink.
- **If you are reducing your dose** – 2 days per week application = Apply on days shaded pink only. If pain continues, please contact your doctor.
- **If you are increasing your dose** – 7 days per week application = Apply every day. If at the end of this week you still have no reaction, contact your doctor.  
We need to give you another cream to help you react to imiquimod.

Week 6						
How does your skin feel/appear?						
Day	Reaction? Y/N	Red? Y/N	Itchy? Y/N	Crusty? Y/N	Painful? Y/N	Comments
Monday						
Tuesday						
Wednesday						
Thursday						
Friday						
Saturday						
Sunday						

### Instructions - Week 7

- **If you are reacting normally** – 5 days per week application = Apply on un-shaded days and those shaded pink.
- **If you are reducing your dose** – 2 days per week application = Apply on days shaded pink only. If pain continues, please contact your doctor.
- **If you are increasing your dose** – 7 days per week application = Apply every day. If at the end of this week you still have no reaction, contact your doctor.  
We need to give you another cream to help you react to imiquimod.

Week 7						
How does your skin feel/appear?						
Day	Reaction? Y/N	Red? Y/N	Itchy? Y/N	Crusty? Y/N	Painful? Y/N	Comments
Monday						
Tuesday						
Wednesday						
Thursday						
Friday						
Saturday						
Sunday						

### Instructions - Week 8

- **If you are reacting normally** – 5 days per week application = Apply on un-shaded days and those shaded pink.
- **If you are reducing your dose** – 2 days per week application = Apply on days shaded pink only. If pain continues, please contact your doctor.
- **If you are increasing your dose** – 7 days per week application = Apply every day. If at the end of this week you still have no reaction, contact your doctor.  
We need to give you another cream to help you react to imiquimod.

Week 8						
How does your skin feel/appear?						
Day	Reaction? Y/N	Red? Y/N	Itchy? Y/N	Crusty? Y/N	Painful? Y/N	Comments
Monday						
Tuesday						
Wednesday						
Thursday						
Friday						
Saturday						
Sunday						

### Instructions - Week 9

- **If you are reacting normally** – 5 days per week application = Apply on un-shaded days and those shaded pink.
- **If you are reducing your dose** – 2 days per week application = Apply on days shaded pink only. If pain continues, please contact your doctor.
- **If you are increasing your dose** – 7 days per week application = Apply every day. If at the end of this week you still have no reaction, contact your doctor.  
We need to give you another cream to help you react to imiquimod.

Week 9						
How does your skin feel/appear?						
Day	Reaction? Y/N	Red? Y/N	Itchy? Y/N	Crusty? Y/N	Painful? Y/N	Comments
Monday						
Tuesday						
Wednesday						
Thursday						
Friday						
Saturday						
Sunday						



### Instructions - Week 10

- **If you are reacting normally** – 5 days per week application = Apply on un-shaded days and those shaded pink.
- **If you are reducing your dose** – 2 days per week application = Apply on days shaded pink only. If pain continues, please contact your doctor.
- **If you are increasing your dose** – 7 days per week application = Apply every day. If at the end of this week you still have no reaction, contact your doctor.  
We need to give you another cream to help you react to imiquimod.

Week 10						
How does your skin feel/appear?						
Day	Reaction? Y/N	Red? Y/N	Itchy? Y/N	Crusty? Y/N	Painful? Y/N	Comments
Monday						
Tuesday						
Wednesday						
Thursday						
Friday						
Saturday						
Sunday						

### Instructions - Week 11

- **If you are reacting normally** – 5 days per week application = Apply on un-shaded days and those shaded pink.
- **If you are reducing your dose** – 2 days per week application = Apply on days shaded pink only. If pain continues, please contact your doctor.
- **If you are increasing your dose** – 7 days per week application = Apply every day. If at the end of this week you still have no reaction, contact your doctor.  
We need to give you another cream to help you react to imiquimod.

Week 11						
How does your skin feel/appear?						
Day	Reaction? Y/N	Red? Y/N	Itchy? Y/N	Crusty? Y/N	Painful? Y/N	Comments
Monday						
Tuesday						
Wednesday						
Thursday						
Friday						
Saturday						
Sunday						

### **Instructions - Week 12**

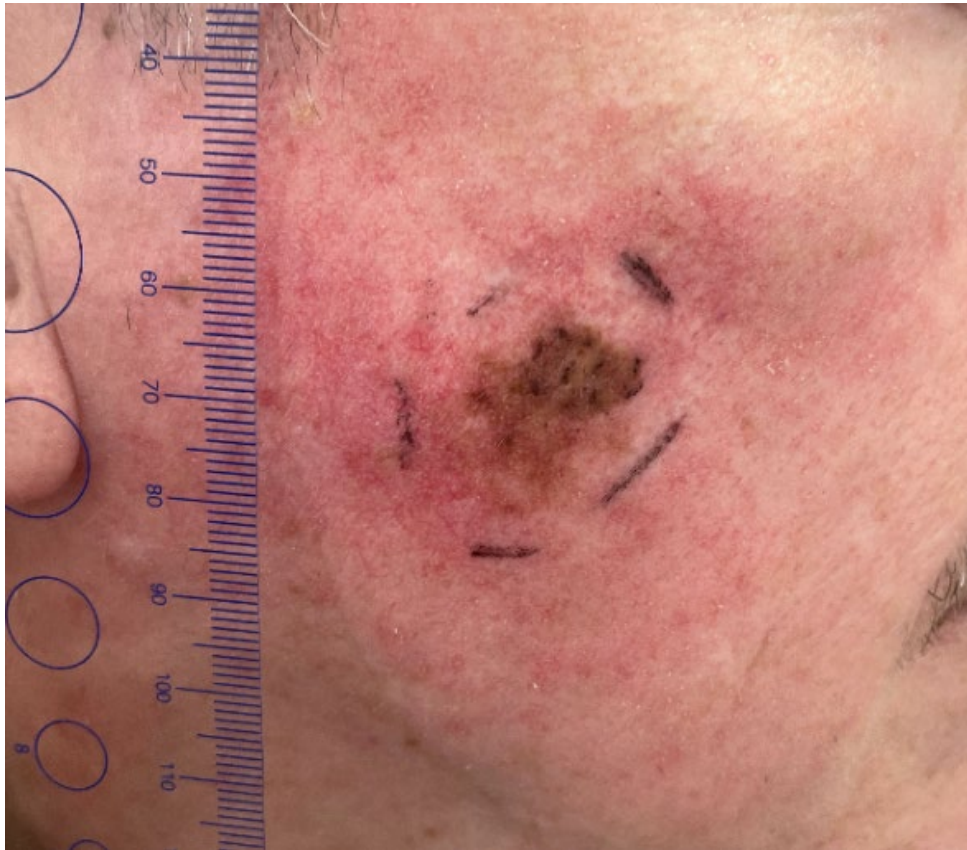
- **If you are reacting normally** – 5 days per week application = Apply on un-shaded days and those shaded pink.
- **If you are reducing your dose** – 2 days per week application = Apply on days shaded pink only. If pain continues, please contact your doctor.
- **If you are increasing your dose** – 7 days per week application = Apply every day. If at the end of this week you still have no reaction, contact your doctor.  
We need to give you another cream to help you react to imiquimod.

<b>Week 12</b>						
<b>How does your skin feel/appear?</b>						
<b>Day</b>	<b>Reaction? Y/N</b>	<b>Red? Y/N</b>	<b>Itchy? Y/N</b>	<b>Crusty? Y/N</b>	<b>Painful? Y/N</b>	<b>Comments</b>
Monday						
Tuesday						
Wednesday						
Thursday						
Friday						
Saturday						
Sunday						

**Your imiquimod treatment is now complete. Please return this diary at your next visit. Thank you for your help and cooperation.**

## ANNEX 1.

**LENTIGO MALIGNA** - Before and after 12 weeks treatment with imiquimod.





**Week 1**



**Week 2**



**Week 3**





**Week 4**



**Week 5**



**Week 6**



**Week 7**



**Week 8**



**Week 9**





**Week 10**



**Week 11**



**Week 12**

**LENTIGO MALIGNA** - Before and after 12 weeks treatment with imiquimod.







**Week 3**



**Week 4**



**Week 5**



**Week 6**



**Week 7**



**Week 8**



**Week 9**



**Week 10**



**Week 11**



**Week 12**

## **ANNEX 2**

### **SALTWATER SOAKS / CRUST REMOVAL**

#### **Salt solution:**

1. Boil a cup of water (250ml).
2. Add 1 teaspoon of table salt (2.5 grams) to make a solution of approximately 1 gram salt per 100 ml of water.
3. Stir and allow to cool.
4. Soak a clean cotton pad / gauze pad in the salty water and apply it to the treatment area.
5. Leave on for 10-15 minutes and then gently wipe away any ooze/crusts without making your skin bleed. Pat dry. If the crust isn't ready to come off, don't force it, but try again the next day.

The other option, if you are unable to do above method, is to have a long shower (10-15 min) and at the end of it, try to gently remove the crusts with a clean cotton pad/gauze.