

**ANNEX 1**  
**SUMMARY OF PRODUCT CHARACTERISTICS**

## **1. NAME OF THE MEDICINAL PRODUCT**

ALDARA 5% cream

## **2. QUALITATIVE AND QUANTITATIVE COMPOSITION**

Each sachet contains 12.5 mg of imiquimod in 250 mg cream (5 %).

100 mg of cream contains 5 mg of imiquimod.

Excipients:

Methyl hydroxybenzoate (E218)

Propyl hydroxybenzoate (E216)

Cetyl alcohol

Stearyl alcohol

For a full list of excipients, see section 6.1.

## **3. PHARMACEUTICAL FORM**

Cream.

White to slightly yellow cream.

## **4. CLINICAL PARTICULARS**

### **4.1 Therapeutic indications**

Imiquimod cream is indicated for the topical treatment of :

- External genital and perianal warts (condylomata acuminata) in adults.
- Small superficial basal cell carcinomas (sBCCs) in adults.
- Clinically typical, nonhyperkeratotic, nonhypertrophic actinic keratoses (AKs) on the face or scalp in immunocompetent adult patients when size or number of lesions limit the efficacy and/or acceptability of cryotherapy and other topical treatment options are contraindicated or less appropriate.

### **4.2 Posology and method of administration**

#### *Posology*

The application frequency and duration of treatment with imiquimod cream is different for each indication.

#### External genital warts in adults:

Imiquimod cream should be applied 3 times per week (example: Monday, Wednesday, and Friday; or Tuesday, Thursday, and Saturday) prior to normal sleeping hours, and should remain on the skin for 6 to 10 hours. Imiquimod cream treatment should continue until the clearance of visible genital or perianal warts or for a maximum of 16 weeks per episode of warts.

For quantity to be applied see 4.2 Method of administration.

#### Superficial basal cell carcinoma in adults:

Apply imiquimod cream for 6 weeks, 5 times per week (example: Monday to Friday) prior to normal sleeping hours, and leave on the skin for approximately 8 hours.  
For quantity to be applied see 4.2 Method of administration.

#### Actinic keratosis in adults

Treatment should be initiated and monitored by a physician. Imiquimod cream should be applied 3 times per week (example: Monday, Wednesday and Friday) for four weeks prior to normal sleeping hours, and left on the skin for approximately 8 hours. Sufficient cream should be applied to cover the treatment area. After a 4-week treatment-free period, clearance of AKs should be assessed. If any lesions persist, treatment should be repeated for another four weeks.

The maximum recommended dose is one sachet. The maximum recommended treatment duration is 8 weeks.

An interruption of dosing should be considered if intense local inflammatory reactions occur (see section 4.4) or if infection is observed at the treatment site. In this latter case, appropriate other measures should be taken. Each treatment period should not be extended beyond 4 weeks due to missed doses or rest periods.

If the treated lesion(s) show an incomplete response at the follow-up examination at 4-8 weeks after the second treatment period, a different therapy should be used (see section 4.4)

#### Information applicable to all indications:

If a dose is missed, the patient should apply the cream as soon as he/she remember and then he/she should continue with the regular schedule. However the cream should not be applied more than once a day.

#### Paediatric patients

Use in the paediatric patient population is not recommended. There are no data available on the use of imiquimod in children and adolescents in the approved indications.

Aldara should not be used in children with molluscum contagiosum due to lack of efficacy in this indication (see section 5.1).

#### *Method of administration*

#### External genital warts:

Imiquimod cream should be applied in a thin layer and rubbed on the clean wart area until the cream vanishes. Only apply to affected areas and avoid any application on internal surfaces. Imiquimod cream should be applied prior to normal sleeping hours. During the 6 to 10 hour treatment period, showering or bathing should be avoided. After this period it is essential that imiquimod cream is removed with mild soap and water. Application of an excess of cream or prolonged contact with the skin may result in a severe application site reaction (see sections 4.4, 4.8 and 4.9). A single-use sachet is sufficient to cover a wart area of 20 cm<sup>2</sup> (approx. 3 inches<sup>2</sup>). Sachets should not be re-used once opened. Hands should be washed carefully before and after application of cream.

Uncircumcised males treating warts under the foreskin should retract the foreskin and wash the area daily (see section 4.4).

#### Superficial basal cell carcinoma:

Before applying imiquimod cream, patients should wash the treatment area with mild soap and water and dry thoroughly. Sufficient cream should be applied to cover the treatment area, including one centimetre of skin surrounding the tumour. The cream should be rubbed into the treatment area until

the cream vanishes. The cream should be applied prior to normal sleeping hours and remain on the skin for approximately 8 hours. During this period, showering and bathing should be avoided. After this period it is essential that imiquimod cream is removed with mild soap and water. Sachets should not be re-used once opened. Hands should be washed carefully before and after application of cream.

Response of the treated tumour to imiquimod cream should be assessed 12 weeks after the end of treatment. If the treated tumour shows an incomplete response, a different therapy should be used (see section 4.4).

A rest period of several days may be taken (see section 4.4) if the local skin reaction to imiquimod cream causes excessive discomfort to the patient, or if infection is observed at the treatment site. In this latter case, appropriate other measures should be taken.

#### Actinic keratosis:

Before applying imiquimod cream, patients should wash the treatment area with mild soap and water and dry thoroughly. Sufficient cream should be applied to cover the treatment area. The cream should be rubbed into the treatment area until the cream vanishes. The cream should be applied prior to normal sleeping hours and remain on the skin for approximately 8 hours. During this period, showering and bathing should be avoided. After this period it is essential that imiquimod cream is removed with mild soap and water. Sachets should not be re-used once opened. Hands should be washed carefully before and after application of cream.

### **4.3 Contraindications**

Hypersensitivity to the active substance or to any of the excipients.

### **4.4 Special warnings and special precautions for use**

#### External genital warts, superficial basal cell carcinoma and actinic keratosis:

Avoid contact with the eyes, lips and nostrils.

Imiquimod has the potential to exacerbate inflammatory conditions of the skin.

Imiquimod cream should be used with caution in patients with autoimmune conditions (refer to section 4.5). Consideration should be given to balancing the benefit of imiquimod treatment for these patients with the risk associated with a possible worsening of their autoimmune condition.

Imiquimod cream should be used with caution in organ transplant patients (refer to section 4.5). Consideration should be given to balancing the benefit of imiquimod treatment for these patients with the risk associated with the possibility of organ rejection or graft-versus-host disease.

Imiquimod cream therapy is not recommended until the skin has healed after any previous drug or surgical treatment. Application to broken skin could result in increased systemic absorption of imiquimod leading to a greater risk of adverse events (refer to section 4.8 and 4.9)

The use of an occlusive dressing is not recommended with imiquimod cream therapy.

The excipients methylhydroxybenzoate (E218), propylhydroxybenzoate (E216), cetyl alcohol and stearyl alcohol may cause allergic reactions.

Rarely, intense local inflammatory reactions including skin weeping or erosion can occur after only a few applications of imiquimod cream. Local inflammatory reactions may be accompanied, or even

preceded, by flu-like systemic signs and symptoms including malaise, pyrexia, nausea, myalgias and rigors. An interruption of dosing should be considered.

Imiquimod should be used with caution in patients with reduced haematologic reserve (refer to section 4.8d).

#### External genital warts:

There is limited experience in the use of imiquimod cream in the treatment of men with foreskin-associated warts. The safety database in uncircumcised men treated with imiquimod cream three times weekly and carrying out a daily foreskin hygiene routine is less than 100 patients. In other studies, in which a daily foreskin hygiene routine was not followed, there were two cases of severe phimosis and one case of stricture leading to circumcision. Treatment in this patient population is therefore recommended only in men who are able or willing to follow the daily foreskin hygiene routine. Early signs of stricture may include local skin reactions (e.g. erosion, ulceration, oedema, induration), or increasing difficulty in retracting the foreskin. If these symptoms occur, the treatment should be stopped immediately. Based on current knowledge, treating urethral, intra-vaginal, cervical, rectal or intra-anal warts is not recommended. Imiquimod cream therapy should not be initiated in tissues where open sores or wounds exist until after the area has healed.

Local skin reactions such as erythema, erosion, excoriation, flaking and oedema are common. Other local reactions such as induration, ulceration, scabbing, and vesicles have also been reported. Should an intolerable skin reaction occur, the cream should be removed by washing the area with mild soap and water. Treatment with imiquimod cream can be resumed after the skin reaction has moderated. The risk of severe local skin reactions may be increased when imiquimod is used at higher than recommended doses (see section 4.2). However, in rare cases severe local reactions that have required treatment and/or caused temporary incapacitation have been observed in patients who have used imiquimod according to the instructions. Where such reactions have occurred at the urethral meatus, some women have experienced difficulty in urinating, sometimes requiring emergency catheterisation and treatment of the affected area.

No clinical experience exists with imiquimod cream immediately following treatment with other cutaneously applied drugs for treatment of external genital or perianal warts. Imiquimod cream should be washed from the skin before sexual activity. Imiquimod cream may weaken condoms and diaphragms, therefore concurrent use with imiquimod cream is not recommended. Alternative forms of contraception should be considered.

In immunocompromised patients, repeat treatment with imiquimod cream is not recommended.

While limited data have shown an increased rate of wart reduction in HIV positive patients, imiquimod cream has not been shown to be as effective in terms of wart clearance in this patient group.

#### Superficial basal cell carcinoma:

Imiquimod has not been evaluated for the treatment of basal cell carcinoma within 1 cm of the eyelids, nose, lips or hairline.

During therapy and until healed, affected skin is likely to appear noticeably different from normal skin. Local skin reactions are common but these reactions generally decrease in intensity during therapy or resolve after cessation of imiquimod cream therapy. There is an association between the complete clearance rate and the intensity of local skin reactions (e.g. erythema). These local skin reactions may be related to the stimulation of local immune response. If required by the patient's discomfort or the severity of the local skin reaction, a rest period of several days may be taken. Treatment with imiquimod cream can be resumed after the skin reaction has moderated.

The clinical outcome of therapy can be determined after regeneration of the treated skin, approximately 12 weeks after the end of treatment.  
As data on long-term clearance rates beyond 36 months post-treatment are not currently available, other appropriate therapeutic modalities should be considered for sBCC.

No clinical experience exists with the use of imiquimod cream in immunocompromised patients.

No clinical experience exists in patients with recurrent and previously treated BCCs, therefore use for previously treated tumours is not recommended.

Data from an open label clinical trial suggest that large tumours ( $>7.25 \text{ cm}^2$ ) are less likely to respond to imiquimod therapy.

The skin surface area treated should be protected from solar exposure.

### Actinic keratosis

Lesions clinically atypical for AK or suspicious for malignancy should be biopsied to determine appropriate treatment.

Imiquimod has not been evaluated for the treatment of actinic keratoses on the eyelids, the inside of the nostrils or ears, or the lip area inside the vermilion border.

There are very limited data available on the use of imiquimod for the treatment of actinic keratoses in anatomical locations other than the face and scalp. The available data on actinic keratosis on the forearms and hands do not support efficacy in this indication and therefore such use is not recommended.

Imiquimod is not recommended for the treatment of AK lesions with marked hyperkeratosis or hypertrophy as seen in cutaneous horns.

During therapy and until healed, affected skin is likely to appear noticeably different from normal skin. Local skin reactions are common but these reactions generally decrease in intensity during therapy or resolve after cessation of imiquimod cream therapy. There is an association between the complete clearance rate and the intensity of local skin reactions (e.g. erythema). These local skin reactions may be related to the stimulation of local immune response. If required by the patient's discomfort or the intensity of the local skin reaction, a rest period of several days may be taken. Treatment with imiquimod cream can be resumed after the skin reaction has moderated.

Each treatment period should not be extended beyond 4 weeks due to missed doses or rest periods.

The clinical outcome of therapy can be determined after regeneration of the treated skin, approximately 4-8 weeks after the end of treatment.

No clinical experience exists with the use of imiquimod cream in immunocompromised patients.

No data are available on re-treating actinic keratoses that have cleared after one or two courses of treatment and subsequently recur, and any such use is therefore not recommended.

Data from an open-label clinical trial suggest that subjects with more than 8 AK lesions showed a decreased rate of complete clearance compared to patients with less than 8 lesions.

The skin surface area treated should be protected from solar exposure.

#### **4.5 Interaction with other medicinal products and other forms of interaction**

No interaction studies have been performed. This includes studies with immunosuppressive drugs. Interactions with systemic drugs would be limited by the minimal percutaneous absorption of imiquimod cream.

Due to its immunostimulating properties, imiquimod cream should be used with caution in patients who are receiving immunosuppressive medication (see Section 4.4).

#### **4.6 Pregnancy and lactation**

For imiquimod no clinical data on exposed pregnancies are available. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/foetal development, parturition or postnatal development (see 5.3). Caution should be exercised when prescribing to pregnant women.

As no quantifiable levels (>5 ng/ml) of imiquimod are detected in the serum after single and multiple topical doses, no specific advice can be given on whether to use or not in lactating mothers.

#### **4.7 Effects on ability to drive and use machines**

No studies on the effects on the ability to drive and use machines have been performed. From the undesirable effects noted in section 4.8, it is unlikely that treatment will have any effect on the ability to drive and use machines.

#### **4.8 Undesirable effects**

##### a) General Description:

##### External genital warts:

In the pivotal trials with 3 times a week dosing, the most frequently reported adverse drug reactions judged to be probably or possibly related to imiquimod cream treatment were application site reactions at the wart treatment site (33.7% of imiquimod treated patients). Some systemic adverse reactions, including headache (3.7%), influenza-like symptoms (1.1%), and myalgia (1.5%) were also reported.

Patient reported adverse reactions from 2292 patients treated with imiquimod cream in placebo controlled and open clinical studies are presented below. These adverse events are considered at least possibly causally related to treatment with imiquimod.

##### Superficial basal cell carcinoma:

In trials with 5 times per week dosing 58% of patients experienced at least one adverse event. The most frequently reported adverse events from the trials judged probably or possibly related to imiquimod cream are application site disorders, with a frequency of 28.1%. Some systemic adverse reactions, including back pain (1.1%) and influenza-like symptoms (0.5%) were reported by imiquimod cream patients.

Patient reported adverse reactions from 185 patients treated with imiquimod cream in placebo controlled phase III clinical studies for superficial basal cell carcinoma are presented below. These adverse events are considered at least possibly causally related to treatment with imiquimod.

##### Actinic keratosis

In the pivotal trials with 3 times per week dosing for up to 2 courses each of 4 weeks, 56% of imiquimod patients reported at least one adverse event. The most frequently reported adverse event

from these trials judged probably or possibly related to imiquimod cream was application site reactions (22% of imiquimod treated patients). Some systemic adverse reactions, including myalgia (2%) were reported by imiquimod treated patients.

Patient reported adverse reactions from 252 patients treated with imiquimod cream in vehicle controlled phase III clinical studies for actinic keratosis are presented below. These adverse events are considered at least possibly causally related to treatment with imiquimod.

b) Tabular Listing of adverse events:

Frequencies are defined as Very common ( $\geq 1/10$ ), Common ( $\geq 1/100$  to  $< 1/10$ ) and Uncommon ( $\geq 1/1,000$  to  $< 1/100$ ). Lower frequencies from clinical trials are not reported here.

|   | <b>External genital warts<br/>(3x/ wk, 16wks)<br/>N = 2292</b> | <b>Superficial basal cell carcinoma<br/>(5x/wk, 6 wks)<br/>N = 185</b> | <b>Actinic keratosis<br/>(3x/wk, 4 or 8 wks)<br/>N = 252</b> |
|---|--|--|--|
| <b>Infections and infestations:</b>                     |  |  |  |
| Infection   | Common   | Common   | Uncommon   |
| Pustules  |  | Common   | Uncommon   |
| Herpes simplex  | Uncommon   |  |  |
| Genital candidiasis                                     | Uncommon   |  |  |
| Vaginitis   | Uncommon   |  |  |
| Bacterial infection                                     | Uncommon   |  |  |
| Fungal infection  | Uncommon   |  |  |
| Upper respiratory tract infection                       | Uncommon   |  |  |
| Vulvitis  | Uncommon   |  |  |
| Rhinitis  |  |  | Uncommon   |
| Influenza   |  |  | Uncommon   |
| <b>Blood and lymphatic system disorders:</b>            |  |  |  |
| Lymphadenopathy   | Uncommon   | Common   | Uncommon   |
| <b>Metabolism and nutrition disorders:</b>              |  |  |  |
| Anorexia  | Uncommon   |  | Common   |
| <b>Psychiatric disorders:</b>                           |  |  |  |
| Insomnia  | Uncommon   |  |  |
| Depression  | Uncommon   |  | Uncommon   |
| Irritability  |  | Uncommon   |  |
| <b>Nervous system disorders:</b>                        |  |  |  |
| Headache  | Common   |  | Common   |
| Paraesthesia  | Uncommon   |  |  |
| Dizziness   | Uncommon   |  |  |
| Migraine  | Uncommon   |  |  |
| Somnolence  | Uncommon   |  |  |
| <b>Eye disorders</b>                                    |  |  |  |
| Conjunctival irritation                                 |  |  | Uncommon   |
| Eyelid oedema   |  |  | Uncommon   |
| <b>Ear and labyrinth disorders:</b>                     |  |  |  |
| Tinnitus  | Uncommon   |  |  |
| <b>Vascular disorders:</b>                              |  |  |  |
| Flushing  | Uncommon   |  |  |
| <b>Respiratory, thoracic and mediastinal disorders:</b> |  |  |  |
| Pharyngitis   | Uncommon   |  |  |



|  |             |             |             |
|--|-------------|-------------|-------------|
| Rhinitis   | Uncommon    |             |             |
| Nasal congestion   |             |             | Uncommon    |
| Pharyngo laryngeal pain                                      |             |             | Uncommon    |
| <b>Gastrointestinal disorders:</b>                           |             |             |             |
| Nausea   | Common      | Uncommon    | Common      |
| Abdominal pain   | Uncommon    |             |             |
| Diarrhoea  | Uncommon    |             | Uncommon    |
| Vomiting   | Uncommon    |             |             |
| Rectal disorder  | Uncommon    |             |             |
| Rectal tenesmus  | Uncommon    |             |             |
| Dry mouth  |             | Uncommon    |             |
| <b>Skin and subcutaneous tissue disorders:</b>               |             |             |             |
| Pruritus   | Uncommon    |             |             |
| Dermatitis   | Uncommon    | Uncommon    |             |
| Folliculitis   | Uncommon    |             |             |
| Rash erythematous  | Uncommon    |             |             |
| Eczema   | Uncommon    |             |             |
| Rash   | Uncommon    |             |             |
| Sweating increased   | Uncommon    |             |             |
| Urticaria  | Uncommon    |             |             |
| Actinic keratosis  |             |             | Uncommon    |
| Erythema   |             |             | Uncommon    |
| Face oedema  |             |             | Uncommon    |
| Skin ulcer   |             |             | Uncommon    |
| <b>Musculoskeletal and connective tissue disorders:</b>      |             |             |             |
| Myalgia  | Common      |             | Common      |
| Arthralgia   | Uncommon    |             | Common      |
| Back pain  | Uncommon    | Common      |             |
| Pain in extremity  |             |             | Uncommon    |
| <b>Renal and urinary disorders:</b>                          |             |             |             |
| Dysuria  | Uncommon    |             |             |
| <b>Reproductive system and breast disorders:</b>             |             |             |             |
| Genital pain male  | Uncommon    |             |             |
| Penile disorder  | Uncommon    |             |             |
| Dyspareunia  | Uncommon    |             |             |
| Erectile dysfunction   | Uncommon    |             |             |
| Uterovaginal prolapse  | Uncommon    |             |             |
| Vaginal pain   | Uncommon    |             |             |
| Vaginitis atrophic   | Uncommon    |             |             |
| Vulval disorder  | Uncommon    |             |             |
| <b>General disorders and administration site conditions:</b> |             |             |             |
| Application site pruritus                                    | Very common | Very common | Very common |
| Application site pain  | Very common | Common      | Common      |
| Application site burning                                     | Common      | Common      | Common      |
| Application site irritation                                  | Common      | Common      | Common      |
| Application site erythema                                    |             | Common      | Common      |
| Application site reaction                                    |             |             | Common      |
| Application site bleeding                                    |             | Common      | Uncommon    |
| Application site papules                                     |             | Common      | Uncommon    |
| Application site paraesthesia                                |             | Common      | Uncommon    |

|                                 |          |          |          |
|---------------------------------|----------|----------|----------|
| Application site rash           |          | Common   |          |
| Fatigue                         | Common   |          | Common   |
| Pyrexia                         | Uncommon |          | Uncommon |
| Influenza-like illness          | Uncommon | Uncommon |          |
| Pain                            | Uncommon |          |          |
| Asthenia                        | Uncommon |          | Uncommon |
| Malaise                         | Uncommon |          |          |
| Rigors                          | Uncommon |          | Uncommon |
| Application site dermatitis     |          |          | Uncommon |
| Application site discharge      |          | Uncommon | Uncommon |
| Application site hyperaesthesia |          |          | Uncommon |
| Application site inflammation   |          | Uncommon |          |
| Application site oedema         |          | Uncommon | Uncommon |
| Application site scabbing       |          | Uncommon | Uncommon |
| Application site scar           |          |          | Uncommon |
| Application site skin breakdown |          | Uncommon |          |
| Application site swelling       |          | Uncommon | Uncommon |
| Application site ulcer          |          |          | Uncommon |
| Application site vesicles       |          | Uncommon | Uncommon |
| Application site warmth         |          |          | Uncommon |
| Lethargy                        |          | Uncommon |          |
| Discomfort                      |          |          | Uncommon |
| Inflammation                    |          |          | Uncommon |

c) Frequently occurring adverse events:

External genital warts:

Investigators of placebo controlled trials were required to evaluate protocol mandated clinical signs (skin reactions). These protocol mandated clinical sign assessments indicate that local skin reactions including erythema (61%), erosion (30%), excoriation/flaking/scaling (23%) and oedema (14%) were common in these placebo controlled clinical trials with imiquimod cream applied three times weekly (see section 4.4). Local skin reactions, such as erythema, are probably an extension of the pharmacologic effects of imiquimod cream.

Remote site skin reactions, mainly erythema (44%), were also reported in the placebo controlled trials. These reactions were at non-wart sites which may have been in contact with imiquimod cream. Most skin reactions were mild to moderate in severity and resolved within 2 weeks of treatment discontinuation. However, in some cases these reactions have been severe, requiring treatment and/or causing incapacitation. In very rare cases, severe reactions at the urethral meatus have resulted in dysuria in women (see section 4.4).

Superficial basal cell carcinoma:

Investigators of the placebo controlled clinical trials were required to evaluate protocol mandated clinical signs (skin reactions). These protocol mandated clinical sign assessments indicate that severe erythema (31%) severe erosions (13%) and severe scabbing and crusting (19%) were very common in these trials with imiquimod cream applied 5 times weekly. Local skin reactions, such as erythema, are probably an extension of the pharmacologic effect of imiquimod cream.

Skin infections during treatment with imiquimod have been observed. While serious sequelae have not resulted, the possibility of infection in broken skin should always be considered.

Actinic keratosis

In clinical trials of imiquimod cream 3 times weekly for 4 or 8 weeks the most frequently occurring application site reactions were itching at the target site (14%) and burning at the target site (5%). Severe erythema (24%) and severe scabbing and crusting (20%) were very common. Local skin reactions, such as erythema, are probably an extension of the pharmacologic effect of imiquimod cream. See 4.2 and 4.4 for information on rest periods.

Skin infections during treatment with imiquimod have been observed. While serious sequelae have not resulted, the possibility of infection in broken skin should always be considered.

**d) Adverse events applicable to all indications:**

Reports have been received of localised hypopigmentation and hyperpigmentation following imiquimod cream use. Follow-up information suggests that these skin colour changes may be permanent in some patients.

Clinical studies investigating the use of imiquimod for the treatment of actinic keratosis have detected a 0.4% (5/1214) frequency of alopecia at the treatment site or surrounding area. Postmarketing reports of suspected alopecia occurring during the treatment of sBCC and EGW have been received.

Reductions in haemoglobin, white blood cell count, absolute neutrophils and platelets have been observed in clinical trials. These reductions are not considered to be clinically significant in patients with normal haematologic reserve. Patients with reduced haematologic reserve have not been studied in clinical trials. Reductions in haematological parameters requiring clinical intervention have been reported from postmarketing experience.

Rare reports have been received of exacerbation of autoimmune conditions.

Rare cases of remote site dermatologic drug reactions, including erythema multiforme, have been reported from clinical trials. Serious skin reactions reported from postmarketing experience include erythema multiforme, Stevens Johnson syndrome and cutaneous lupus erythematosus.

## **4.9 Overdose**

When applied topically, systemic overdose with imiquimod cream is unlikely due to minimal percutaneous absorption. Studies in rabbits reveal a dermal lethal dose of greater than 5 g/kg. Persistent dermal overdosing of imiquimod cream could result in severe local skin reactions. Following accidental ingestion, nausea, emesis, headache, myalgia and fever could occur after a single dose of 200 mg imiquimod which corresponds to the content of approximately 16 sachets. The most clinically serious adverse event reported following multiple oral doses of  $\geq 200$  mg was hypotension which resolved following oral or intravenous fluid administration.

## **5. PHARMACOLOGICAL PROPERTIES**

### **5.1 Pharmacodynamic properties:**

Pharmacotherapeutic group: Chemotherapeutics for topical use, antivirals : ATC Code : D06BB10.

Imiquimod is an immune response modifier. Saturable binding studies suggest a membrane receptor for imiquimod exists on responding immune cells. Imiquimod has no direct antiviral activity. In animal models imiquimod is effective against viral infections and acts as an antitumour agent principally by induction of alpha interferon and other cytokines. The induction of alpha interferon and other cytokines following imiquimod cream application to genital wart tissue has also been demonstrated in clinical studies.

Increases in systemic levels of alpha interferon and other cytokines following topical application of imiquimod were demonstrated in a pharmacokinetic study.

#### External genital warts:

##### Clinical Efficacy

The results of 3 phase III pivotal efficacy studies showed that treatment with imiquimod for sixteen weeks was significantly more effective than treatment with vehicle as measured by total clearance of treated warts.

In 119 imiquimod-treated female patients, the combined total clearance rate was 60% as compared to 20% in 105 vehicle-treated patients (95% CI for rate difference: 20% to 61% ,  $p < 0.001$ ). In those imiquimod patients who achieved total clearance of their warts, the median time to clearance was 8 weeks.

In 157 imiquimod-treated male patients, the combined total clearance rate was 23% as compared to 5% in 161 vehicle-treated patients (95%CI for rate difference: 3% to 36% ,  $p < 0.001$ ). In those imiquimod patients who achieved total clearance of their warts, the median time to clearance was 12 weeks.

#### Superficial basal cell carcinoma:

##### Clinical efficacy:

The efficacy of imiquimod 5 times per week for 6 weeks was studied in two double-blind vehicle controlled clinical trials. Target tumours were histologically confirmed single primary superficial basal cell carcinomas with a minimum size of 0.5 cm<sup>2</sup> and a maximum diameter of 2 cm. Tumours located within 1 cm of the eyes, nose, mouth, ears or hairline were excluded. In a pooled analysis of these two studies, histological clearance was noted in 82% (152/185) of patients. When clinical assessment was also included, clearance judged by this composite endpoint was noted in 75% (139/185) of patients. These results were statistically significant ( $p < 0.001$ ) by comparison with the vehicle group, 3% (6/179) and 2% (3/179) respectively. There was a significant association between the intensity of local skin reactions (e.g. erythema) seen during the treatment period and complete clearance of the basal cell carcinoma.

Four-year data from a long-term open-label uncontrolled study indicate that an estimated 79.3% [95% CI (73.7%, 84.9%)] of all the subjects who initially received treatment became clinically clear and remained clear at 48 months. Data on recurrence rates beyond 48 months are not yet available.

#### Actinic keratosis:

##### Clinical efficacy:

The efficacy of imiquimod applied 3 times per week for one or two courses of 4 weeks, separated by a 4 week treatment-free period, was studied in two double-blind vehicle controlled clinical trials. Patients had clinically typical, visible, discrete, nonhyperkeratotic, nonhypertrophic AK lesions on the balding scalp or face within a contiguous 25 cm<sup>2</sup> treatment area. 4-8 AK lesions were treated. The complete clearance rate (imiquimod minus placebo) for the combined trials was 46.1% (CI 39.0%, 53.1%).

One-year data from two combined observational studies indicate a recurrence rate of 27% (35/128 patients) in those patients who became clinically clear after one or two courses of treatment. The recurrence rate for individual lesions was 5.6% (41/737). Corresponding recurrence rates for

vehicle were 47% (8/17 patients) and 7.5% (6/80 lesions). The rate of progression to squamous cell carcinoma (SCC) was reported in 1.6% (2/128 patients).

There are no data on recurrence and progression rates beyond 1 year.

Paediatric patients:

The approved indications genital warts, actinic keratosis and superficial basal cell carcinoma are conditions not generally seen within the paediatric population and were not studied.

Aldara Cream has been evaluated in four randomised, vehicle controlled, double-blind trials in children aged 2 to 15 years with molluscum contagiosum (imiquimod n = 576, vehicle n = 313). These trials failed to demonstrate efficacy of imiquimod at any of the tested dosage regimens (3x/week for  $\leq 16$  weeks and 7x/week for  $\leq 8$  weeks).

## 5.2 Pharmacokinetic properties

External genital warts, superficial basal cell carcinoma and actinic keratosis:

Less than 0.9% of a topically applied single dose of radiolabelled imiquimod was absorbed through the skin of human subjects. The small amount of drug which was absorbed into the systemic circulation was promptly excreted by both urinary and faecal routes at a mean ratio of approximately 3 to 1. No quantifiable levels ( $>5$  ng/ml) of drug were detected in serum after single or multiple topical doses.

Systemic exposure (percutaneous penetration) was calculated from recovery of carbon-14 from [ $^{14}C$ ] imiquimod in urine and faeces.

Minimal systemic absorption of imiquimod 5% cream across the skin of 58 patients with actinic keratosis was observed with 3 times per week dosing for 16 weeks. The extent of percutaneous absorption did not change significantly between the first and last doses of this study. Peak serum drug concentrations at the end of week 16 were observed between 9 and 12 hours and were 0.1, 0.2, and 1.6 ng/mL for the applications to face (12.5 mg, 1 single-use sachet), scalp (25 mg, 2 sachets) and hands/arms (75 mg, 6 sachets), respectively. The application surface area was not controlled in the scalp and hands/arms groups. Dose proportionality was not observed. An apparent half-life was calculated that was approximately 10 times greater than the 2 hour half-life seen following subcutaneous dosing in a previous study, suggesting prolonged retention of drug in the skin. Urinary recovery was less than 0.6% of the applied dose at week 16 in these patients.

Paediatric patients:

The pharmacokinetic properties of imiquimod following single and multiple topical application in paediatric patients with molluscum contagiosum (MC) have been investigated. The systemic exposure data demonstrated that the extent of absorption of imiquimod following topical application to the MC lesional skin of the paediatric patients aged 6-12 years was low and comparable to that observed in healthy adults and adults with actinic keratosis or superficial basal cell carcinoma. In younger patients aged 2-5 years absorption, based on  $C_{max}$  values, was higher compared to adults.

## 5.3 Preclinical safety data

Non-clinical data revealed no special hazard for humans based on conventional studies of safety pharmacology, mutagenicity and teratogenicity.

In a four-month rat dermal toxicity study, significantly decreased body weight and increased spleen weight were observed at 0.5 and 2.5 mg/kg; similar effects were not seen in a four month mouse dermal study. Local dermal irritation, especially at higher doses, was observed in both species.

A two-year mouse carcinogenicity study by dermal administration on three days a week did not induce tumours at the application site. However, the incidences of hepatocellular tumours among treated

animals were greater than those for controls. The mechanism for this is not known, but as imiquimod has low systemic absorption from human skin, and is not mutagenic, any risk to humans from systemic exposure is likely to be low. Furthermore, tumours were not seen at any site in a 2-year oral carcinogenicity study in rats.

Imiquimod cream was evaluated in a photocarcinogenicity bioassay in albino hairless mice exposed to simulated solar ultraviolet radiation (UVR). Animals were administered imiquimod cream three times per week and were irradiated 5 days per week for 40 weeks. Mice were maintained for an additional 12 weeks for a total of 52 weeks. Tumours occurred earlier and in greater number in the group of mice administered the vehicle cream in comparison with the low UVR control group. The significance for man is unknown. Topical administration of imiquimod cream resulted in no tumour enhancement at any dose, in comparison with the vehicle cream group.

## **6. PHARMACEUTICAL PARTICULARS**

### **6.1 List of excipients**

isostearic acid  
benzyl alcohol  
cetyl alcohol  
stearyl alcohol  
white soft paraffin  
polysorbate 60  
sorbitan stearate  
glycerol  
methyl hydroxybenzoate (E218)  
propyl hydroxybenzoate (E216)  
xanthan gum  
purified water.

### **6.2 Incompatibilities**

Not applicable.

### **6.3 Shelf life**

2 years.

### **6.4 Special precautions for storage**

Do not store above 25°C.  
Sachets should not be re-used once opened.

### **6.5 Nature and contents of container**

Boxes of 12 single-use polyester/aluminium foil sachets, containing 250 mg of cream.

### **6.6 Special precautions for disposal and other handling**

No special requirements.

## **7. MARKETING AUTHORISATION HOLDER**

Meda AB  
Pipers väg 2A  
170 73 Solna  
Sweden

**8. MARKETING AUTHORISATION NUMBER(S)**

EU/1/98/080/001

**9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

Date of first authorisation: 18/09/1998

Date of last renewal: 18/09/2003

**10. DATE OF REVISION OF THE TEXT**

## **ANNEX II**

- A. MANUFACTURING AUTHORISATION HOLDER  
RESPONSIBLE FOR BATCH RELEASE**
  
- B. CONDITIONS OF THE MARKETING AUTHORISATION**



**A. MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE**

Name and address of the manufacturer responsible for batch release

3M Health Care Limited, Derby Road, Loughborough, Leicester, LE11 0SF, United Kingdom.

**B CONDITIONS OF THE MARKETING AUTHORISATION**

• **CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE IMPOSED ON THE MARKETING AUTHORISATION HOLDER**

Medicinal product subject to medicinal prescription

• **CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT**

Not applicable

• **OTHER CONDITIONS**

### **ANNEX III**

## **A. LABELLING**

**PARTICULARS TO APPEAR ON THE OUTER PACKAGING**

**1. NAME OF THE MEDICINAL PRODUCT**

Aldara 5% cream  
imiquimod

**2. STATEMENT OF ACTIVE SUBSTANCE(S)**

Each sachet contains 12.5 mg of imiquimod in 250 mg cream (5 %).  
100 mg cream contains 5 mg imiquimod

**3. LIST OF EXCIPIENTS**

Excipients : isostearic acid, benzyl alcohol, cetyl alcohol, stearyl alcohol, white soft paraffin, polysorbate 60, sorbitan stearate, glycerol, methyl hydroxybenzoate (E218), propyl hydroxybenzoate (E216), xanthan gum, purified water.

See package leaflet for further information.

**4. PHARMACEUTICAL FORM AND CONTENTS**

Cream  
12 sachets. Each containing 250 mg of cream.

**5. METHOD AND ROUTE(S) OF ADMINISTRATION**

Read the package leaflet before use.  
For cutaneous use

**6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE REACH AND SIGHT OF CHILDREN**

Keep out of the reach and sight of children

**7. OTHER SPECIAL WARNING(S), IF NECESSARY**

For single use only. Discard any cream remaining in a sachet after use.

**8. EXPIRY DATE**

Exp.

**9. SPECIAL STORAGE CONDITIONS**

Do not store above 25°C

**10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE**

**11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER**

Meda AB  
Box 906  
170 09 Solna  
Sweden

**12. MARKETING AUTHORISATION NUMBER(S)**

EU/1/98/080/001

**13. BATCH NUMBER**

Lot

**14. GENERAL CLASSIFICATION FOR SUPPLY**

Medicinal product subject to medical prescription.

**15. INSTRUCTIONS ON USE**

**16. INFORMATION IN BRAILLE**

Aldara

**MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS**

**SACHET TEXT**

**1. NAME OF THE MEDICINAL PRODUCT AND ROUTE OF ADMINISTRATION**

Aldara 5% cream  
Imiquimod  
For cutaneous use

**2. METHOD OF ADMINISTRATION**

**3. EXPIRY DATE**

Exp.

**4. BATCH NUMBER**

Lot

**5. CONTENTS BY WEIGHT**

250 mg cream

**6. OTHER**

**B. PACKAGE LEAFLET**

## PACKAGE LEAFLET: INFORMATION FOR THE USER

### Aldara 5% cream Imiquimod

#### **Read all of this leaflet carefully before you start using this medicine.**

- Keep this leaflet. You may need to read it again.
- If you have any further questions, please ask your doctor or your pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

#### **In this leaflet:**

1. What Aldara cream is and what it is used for
2. Before you use Aldara cream
3. How to use Aldara cream
4. Possible side effects
5. How to store Aldara cream
6. Further information

## **1. WHAT IS ALDARA CREAM AND WHAT IT IS USED FOR**

Aldara cream may be used for three different conditions. Your doctor may prescribe Aldara cream for the treatment of:

- Warts (condylomata acuminata) on the surface of the genitals (sexual organs) and around the anus (back passage)
- Superficial basal cell carcinoma.  
This is a common slow-growing form of skin cancer with a very small likelihood of spread to other parts of the body. It usually occurs in middle-aged and elderly people, especially those who are fair-skinned and is caused by too much sun exposure. If left untreated, basal cell carcinoma can disfigure, especially on the face – therefore early recognition and treatment are important.
- Actinic keratosis  
Actinic keratoses are rough areas of skin found in people who have been exposed to a lot of sunshine over the course of their lifetime. Some are skin coloured, others are greyish, pink, red or brown. They can be flat and scaly, or raised, rough, hard and warty. Aldara should only be used for flat actinic keratoses on the face and scalp in patients with a healthy immune system where your doctor has decided that Aldara is the most appropriate treatment for you.

Aldara cream helps your body's own immune system to produce natural substances which help fight your basal cell carcinoma, actinic keratosis or the virus that has caused your warts.

## **2. BEFORE YOU USE ALDARA CREAM**

#### **Do not use Aldara cream :**

- If you are allergic to imiquimod (the active ingredient) or any of the ingredients of the cream.

#### **Take special care with Aldara cream:**



- If you have previously used Aldara cream or other similar preparations tell your doctor before starting this treatment.
- Tell your doctor if you have problems with your immune system.
- Do not use Aldara cream until the area to be treated has healed after previous drug or surgical treatment.
- Avoid contact with the eyes, lips and nostrils. In the event of accidental contact, remove cream by rinsing with water.
- Do not apply the cream internally.
- Do not use more cream than your doctor has advised.
- Do not cover the treated area with bandages or other dressings after you have applied Aldara cream.
- If the treated site becomes too uncomfortable, wash the cream off with mild soap and water. As soon as the problem has stopped you may restart to apply the cream.
- Tell your doctor if you have an abnormal blood count.

Because of the way Aldara works, there is a possibility that the cream may worsen existing inflammation in the treatment area.

- If you are being treated for genital warts follow these additional precautions:

Men with warts under the foreskin should pull the foreskin back each day and wash underneath it. If not washed daily the foreskin may be more likely to show signs of tightness, swelling and wearing away of the skin and result in difficulty in pulling it back. If these symptoms occur, stop the treatment immediately and call your doctor.

If you have open sores: do not start using Aldara cream until after the sores have healed.

If you have internal warts: do not use Aldara cream in the urethra (the hole from which urine is passed), the vagina (birth canal), the cervix (internal female organ), or anywhere inside your anus (rectum).

Do not use this medication for more than one course if you have problems with your immune system, either due to illness or because of the medicines you are already taking. If you think this applies to you talk to your doctor.

If you are HIV positive you should inform your doctor as Aldara cream has not been shown to be as effective in HIV positive patients. If you decide to have sexual relations while you still have warts, apply Aldara cream after - not before - sexual activity. Aldara cream may weaken condoms and diaphragms, therefore the cream should not be left on during sexual activity. Remember, Aldara cream does not protect against giving HIV or other sexually transmitted diseases to someone else.

- If you are being treated for basal cell carcinoma or actinic keratosis follow these additional precautions:

Do not use sunlamps or tanning beds, and avoid sunlight as much as possible during treatment with Aldara cream. Wear protective clothing and wide brimmed hats when outdoors.

Whilst using Aldara cream and until healed, the treatment area is likely to appear noticeably different from normal skin.

#### **Using other medicines:**

Please inform your doctor or pharmacist if you are taking or have recently taken any other medicines, including those obtained without a prescription.

There are no medicines known to be incompatible with Aldara cream.

#### **Pregnancy and breast-feeding:**

Ask your doctor or pharmacist for advice before taking any medicine.

You must tell your doctor if you are pregnant or intend to become pregnant. Your doctor will discuss the risks and benefits of using Aldara cream during pregnancy. Studies in animals do not indicate direct or indirect harmful effects in pregnancy.

Do not breast-feed your infant during treatment with Aldara cream, as it is not known whether imiquimod is secreted in human milk.

### **Important information about some of the ingredients of Aldara cream:**

Methyl hydroxybenzoate (E218) and propyl hydroxybenzoate (E216) may cause allergic reactions (possibly delayed). Cetyl and stearyl alcohol may cause local skin reactions (e.g. contact dermatitis).

### **3. HOW TO USE ALDARA CREAM**

Always use Aldara cream exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.

Wash hands carefully before and after applying the cream. Do not cover the treated area with bandages or other dressings after you have applied Aldara cream.

Open a new sachet each time you use the cream. Dispose of any cream left in the sachet after use. Do not save the opened sachet for use at a later date.

The treatment frequency and duration differ for genital warts, basal cell carcinoma and actinic keratosis (see specific instructions for each indication).



- **If you are being treated for genital warts:**

Application Instructions – (Mon, Wed and Fri)

1. Before going to bed, wash your hands and the treatment area with mild soap and water. Dry thoroughly.
2. Open a new sachet and squeeze some cream onto your fingertip.
3. Apply a thin layer of Aldara cream onto clean, dry wart area and rub gently into the skin until cream vanishes.
4. After application of the cream, throw away the opened sachet and wash hands with soap and water.
5. Leave Aldara cream on the warts for 6 to 10 hours. Do not shower or bathe during this time.
6. After 6 to 10 hours wash the area where Aldara cream was applied with mild soap and water.

Apply Aldara cream 3 times per week. For example, apply the cream on Monday, Wednesday and Friday. One sachet contains enough cream to cover a wart area of 20 cm<sup>2</sup> (approx. 3 square inches).

Men with warts under the foreskin should pull the foreskin back each day and wash underneath it (see section 2 “Take special care with Aldara cream.”)

Continue to use Aldara cream as instructed until your warts have completely gone (half the females who clear will do so in 8 weeks, half the males who clear will do so in 12 weeks but in some patients warts may clear as early as 4 weeks).

Do not use Aldara cream for more than 16 weeks in the treatment of each episode of warts.

If you have the impression that the effect of Aldara cream is too strong or too weak, talk to your doctor or pharmacist.

- **If you are being treated for basal cell carcinoma:**

Application Instructions – (Mon, Tues, Wed, Thurs and Fri)

1. Before going to bed, wash your hands and the treatment area with mild soap and water. Dry thoroughly.
2. Open a new sachet and squeeze some cream onto your fingertip.
3. Apply Aldara cream to the affected area and 1cm (approx. 0.5 inch) around the affected area. Rub gently into the skin until the cream vanishes.
4. After application of the cream, throw away the opened sachet. Wash hands with soap and water.
5. Leave Aldara cream on the skin for about 8 hours. Do not shower or bathe during this time.
6. After about 8 hours, wash the area where Aldara cream was applied with mild soap and water.

Apply sufficient Aldara cream to cover the treatment area and 1 cm (about ½ an inch) around the treatment area each day for 5 consecutive days each week for 6 weeks. For example, apply the cream from Monday to Friday. Do not apply the cream on Saturday and Sunday.

- **If you are being treated for actinic keratosis**

Application Instructions – (Mon, Wed and Fri)

1. Before going to bed, wash your hands and the treatment area with mild soap and water. Dry thoroughly.
2. Open a new sachet and squeeze some cream onto your fingertip.
3. Apply the cream to the affected area. Rub gently into the area until the cream vanishes.
4. After application of the cream, throw away the opened sachet. Wash hands with soap and water.
5. Leave Aldara cream on the skin for about 8 hours. Do not shower or bathe during this time.
6. After about 8 hours, wash the area where Aldara cream was applied with mild soap and water.

Apply Aldara cream 3 times per week. For example, apply the cream on Monday, Wednesday and Friday. One sachet contains enough cream to cover an area of 25 cm<sup>2</sup> (approx. 4 square inches). Continue treatment for four weeks. Four weeks after finishing this first treatment, your doctor will assess your skin. If the lesions have not all disappeared, a further four weeks of treatment may be necessary.

**If you use more Aldara cream than you should:**

Wash the extra away with mild soap and water. When any skin reaction has gone you may then continue with your treatment.

If you accidentally swallow Aldara cream please contact your doctor.

**If you forget to use Aldara cream:**

If you miss a dose, apply cream as soon as you remember and then continue in your regular schedule. Do not apply the cream more than once per day.

If you have any further questions on the use of this product, ask your doctor or pharmacist.

#### 4. POSSIBLE SIDE EFFECTS

The frequency of side effects is classified as follows:

Very common side effects (likely to occur in more than 1 in 10 patients)

Common side effects (likely to occur in fewer than 1 in 10 patients)

Uncommon side effects (likely to occur in fewer than 1 in 100 patients)

Rare side effects (likely to occur in fewer than 1 in 1,000 patients)

Very rare side effects (likely to occur in fewer than 1 in 10,000 patients).

Like all medicines, Aldara cream can cause side effects, although not everybody gets them.

Tell your doctor or pharmacist as soon as possible if you do not feel well while you are using Aldara cream.

Some patients have experienced changes in skin colour in the area where Aldara cream was applied.

While these changes have tended to improve with time, in some patients they may be permanent.

If your skin reacts badly when using Aldara cream, stop applying the cream, wash the area with mild soap and water and contact your doctor or pharmacist.

In some individuals a lowering of blood counts was noted. A lowering of blood counts might make you more susceptible to infections, make you bruise more easily or cause fatigue. If you notice any of these symptoms, tell your doctor.

Serious skin reactions have been reported rarely. If you experience skin lesions or spots on your skin that start out as small red areas and progress to look like mini targets, possibly with symptoms such as itching, fever, overall ill feeling, achy joints, vision problems, burning, painful or itchy eyes and mouth sores, stop using Aldara cream and tell your doctor immediately.

A small number of patients have experienced hair loss at the treatment site or surrounding area.

If any of the side effects gets serious, or if you notice any side effects not mentioned in this leaflet, please tell your doctor or pharmacist.

● If you are being treated for genital warts:

Many of the undesirable effects of Aldara cream are due to its local action on your skin.

**Very common** effects include redness (61% patients), wearing away of the skin (30% patients), flakiness and swelling. Hardening under the skin, small open sores, a crust that forms during healing, and small bubbles under the skin may also occur. You might also feel itching (32% patients), a burning sensation (26% patients) or pain in areas where you have applied Aldara cream (8% patients). Most of these skin reactions are mild and the skin will return to normal within about 2 weeks after stopping treatment.

**Commonly** some patients (4% or less) have experienced headache, **uncommonly** fevers and flu like symptoms joint and muscle pains; prolapse of the womb; pain on intercourse in females; erection difficulties; increase in sweating; feeling sick; stomach and bowel symptoms; ringing in the ears; flushing; tiredness; dizziness; migraine; pins and needles; insomnia; depression; loss of appetite; swollen glands; bacterial, viral and fungal infections (e.g. cold sores); vaginal infection including thrush; cough and colds with sore throat.

**Very rarely** severe and painful reactions have occurred, particularly when more cream has been used than recommended. Painful skin reactions at the opening of the vagina have very rarely made it difficult for some women to pass urine. If this occurs you should seek medical help immediately.

● If you are being treated for basal cell carcinoma:

Many of the undesirable effects of Aldara cream are due to its local action on your skin. Local skin reactions can be a sign that the drug is working as intended.

**Very Commonly** the treated skin may be slightly itchy.

**Common** effects include: pins and needles, small swollen areas in the skin, pain, burning, irritation, bleeding, redness or rash.

If a skin reaction becomes too uncomfortable during treatment, speak to your doctor. He/she may advise you to stop applying Aldara cream for a few days (i.e. to have a short rest from treatment). If there is pus (matter) or other suggestion of infection, discuss this with your doctor. Apart from reactions in the skin, other common effects include swollen glands and back pain.

**Uncommonly** some patients experience changes at the application site (discharge, inflammation, swelling, scabbing, skin breakdown, blisters, dermatitis) or irritability, feeling sick, dry mouth, flu-like symptoms and tiredness.

- If you are being treated for actinic keratosis

Many of the undesirable effects of Aldara cream are due to its local action on your skin. Local skin reactions can be a sign that the drug is working as intended.

**Very commonly** the treated skin may be slightly itchy.

**Common** effects include pain, burning, irritation or redness.

If a skin reaction becomes too uncomfortable during treatment, speak to your doctor. He/she may advise you to stop applying Aldara cream for a few days (i.e. to have a short rest from treatment). If there is pus (matter) or other suggestion of infection, discuss this with your doctor. Apart from reactions in the skin, other common effects include headache, anorexia, nausea, muscle pain, joint pain and tiredness.

**Uncommonly** some patients experience changes at the application site (bleeding, inflammation, discharge, sensitivity, swelling, small swollen areas in the skin, pins and needles, scabbing, scarring, ulceration or a feeling of warmth or discomfort), or inflammation of the lining of the nose, stuffy nose, flu or flu-like symptoms, depression, eye irritation, swelling of the eyelid, throat pain, diarrhoea, actinic keratosis, redness, swelling of the face, ulcers, pain in extremity, fever, weakness or shivering.

## 5. HOW TO STORE ALDARA CREAM

Keep out of the reach and sight of children.

Do not store above 25°C.

Do not use after the expiry date stated on the label.

Sachets should not be re-used once opened.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist to dispose of medicines no longer required. These measures will help to protect the environment.

## 6. FURTHER INFORMATION

### What Aldara cream contains:

- The active substance is imiquimod. Each sachet contains 250 mg cream (100 mg cream contains 5 mg imiquimod).

- The other ingredients are isostearic acid, benzyl alcohol, cetyl alcohol, stearyl alcohol, white soft paraffin, polysorbate 60, sorbitan stearate, glycerol, methyl hydroxybenzoate (E218), propyl hydroxybenzoate (E216), xanthan gum, purified water.

**What Aldara cream looks like and contents of the pack:**

- Each Aldara 5% cream sachet contains 250 mg of a white to slightly yellow cream.
- Each box contains 12 single-use polyester/aluminium foil sachets.

**MARKETING AUTHORISATION HOLDER:**

Meda AB  
Box 906  
170 09 Solna  
Sweden

**MANUFACTURER :**

3M Health Care Limited  
Derby Road  
Loughborough  
Leicestershire  
LE11 0SF, United Kingdom

For any information about this medicinal product, please contact the local representative of the Marketing Authorisation Holder.

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**This leaflet was last approved in (MM/YYYY)**