Imiquimod cream is indicated for the treatment of external genital and perianal warts/condyloma acuminata.

Imiquimod cream should be used with caution in patients with pre-existing autoimmune conditions. The safety and efficacy of imiquimod cream in immunosuppressed patients have not been established.

Imiquimod cream is indicated for the topical treatment of clinically typical, non-hyperkeratotic, non-hypertrophic external genital warts.

6.3 Clinical Trials Experience: External Genital Warts

In a clinical trial involving 157 patients with genital warts, 60% of patients who received imiquimod cream had a complete response after 16 weeks of treatment. A rest period was allowed if necessary.

Exposure to sunlight (including sunlamps) should be avoided or minimized during use of imiquimod cream. Flu-like signs and symptoms may accompany, or even precede, local inflammatory reactions.

Table 3: Local Skin Reactions in the Treatment Area as Assessed by the Investigator (Actinic Keratosis)

<table>
<thead>
<tr>
<th>Reaction</th>
<th>Treatment with Imiquimod Cream</th>
<th>Treatment with Vehicle Cream</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erythema</td>
<td>14 (4%)</td>
<td>3 (2%)</td>
</tr>
<tr>
<td>Weeping/Exudate</td>
<td>38 (24%)</td>
<td>2 (3%)</td>
</tr>
<tr>
<td>Rigors</td>
<td>6 (4%)</td>
<td>1 (0%)</td>
</tr>
<tr>
<td>Alopecia</td>
<td>1 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Soreness</td>
<td>27 (17%)</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Pain</td>
<td>23 (15%)</td>
<td>2 (2%)</td>
</tr>
<tr>
<td>Burning</td>
<td>19 (12%)</td>
<td>2 (2%)</td>
</tr>
<tr>
<td>Hypopigmentation</td>
<td>16 (10%)</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Irritation</td>
<td>21 (13%)</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Itching</td>
<td>33 (21%)</td>
<td>3 (5%)</td>
</tr>
<tr>
<td>Rash</td>
<td>22 (14%)</td>
<td>2 (2%)</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>26 (17%)</td>
<td>3 (5%)</td>
</tr>
<tr>
<td>Proteinuria</td>
<td>1 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Dysuria</td>
<td>1 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Urinary retention</td>
<td>1 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Thrombocytopenic purpura</td>
<td>1 (0%)</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

The prescriber should demonstrate the proper application technique to maximize the benefit of imiquimod cream.

6.4 Clinical Trials Experience: Dermal Safety Studies

No significant changes in hematologic or coagulation parameters were observed during treatment with imiquimod cream. Systemic embryofetal development studies were conducted in rats and rabbits. Oral doses of 1, 5, and 10 mg/kg/day were given to pregnant rats, and 10 mg/kg/day was given to pregnant rabbits. The following fetal effects were noted:

- In the presence of maternal toxicity, fetal effects were noted at 20 mg/kg/day (577X MRHD based on BSA comparisons).
- Oral doses of 1 mg/kg/day were given to pregnant female rats. In the presence of maternal toxicity, fetal effects were noted at 10 mg/kg/day (347X MRHD based on BSA comparisons).
- Oral doses of 10 mg/kg/day were given to pregnant rabbits. The following fetal effects were noted:
  - Thrombocytopenic purpura
  - Proteinuria
  - Dysuria
  - Urinary retention
  - Arthralgia

A combined fertility and peri- and post-natal development study was conducted in rats. Oral doses of 2 mg/kg/day (1.5X MRHD based on BSA comparisons) were given to pregnant rats, and 20 mg/kg/day (577X MRHD based on BSA comparisons) were given to pregnant rabbits. The following fetal effects were noted:

- In the presence of maternal toxicity, fetuses in one litter (2 of 1567 fetuses) demonstrated exencephaly, ossification defects, bent limb bones, and two fetuses in one litter. Given the potential for embryofetal toxicity, the risk of using imiquimod cream in pregnant women should be carefully considered.

6.5 Clinical Trials Experience: Adverse Reactions

The following adverse reactions have been identified during post-approval use of imiquimod cream:

- Most frequent adverse reactions: Erythema, weeping, exudate, rigors, alopecia, soreness, pain, burning, hypopigmentation, irritation, itching, rash, sensitivity.
- Other adverse reactions: Proteinuria, dysuria, urinary retention, thrombocytopenic purpura, arthralgia.

6.6 Clinical Trials Experience: Photosensitivity

Flu-like signs and symptoms may accompany, or even precede, local inflammatory reactions and may be required (2, 5.1, 6). The prescriber should demonstrate the proper application technique to maximize the benefit of imiquimod cream.

6.7 Clinical Trials Experience: Women of Childbearing Potential

Women of childbearing potential should use effective contraceptive measures during and up to 3 months after discontinuing treatment with imiquimod cream, as the chances for having a severe skin reaction or other side effect are greatest during the first few months of treatment.

6.8 Clinical Trials Experience: Withdrawal Syndrome

Withdrawal symptoms may occur after discontinuing treatment with imiquimod cream. This risk may be greater in patients who have received multiple treatment courses. Withdrawal symptoms may include flu-like signs and symptoms, rash, sensitivity, itching, burning, hypopigmentation, pain, soreness, throat, sensitivity, soreness, proteinuria, dysuria, urinary retention.

6.9 Clinical Trials Experience: Drug Interactions

No drug interactions were observed in clinical trials with imiquimod cream. However, patients should avoid concurrent use of topical corticosteroids or other irritants as they may increase the risk of skin reactions.

6.10 Clinical Trials Experience: Pediatric Use

The safety and efficacy of imiquimod cream in children younger than 12 years of age have not been established. Children usually do not get actinic keratoses.

6.11 Clinical Trials Experience: Geriatric Use

No specific age-related differences in safety or effectiveness were identified in clinical trials with imiquimod cream. However, caution should be exercised when treating elderly patients as they may be more sensitive to the effects of imiquimod cream.

6.12 Clinical Trials Experience: Overdose

No specific signs or symptoms of overdose were observed in clinical trials with imiquimod cream. In case of overdose, wash the area with mild soap and water, and seek medical attention immediately.

6.13 Clinical Trials Experience: Labor and Delivery

No specific adverse effects were observed in clinical trials with imiquimod cream during pregnancy. However, the safety and efficacy of imiquimod cream in pregnant women have not been established. Pregnancy should be avoided during treatment with imiquimod cream.

6.14 Clinical Trials Experience: Nursing Mother

No specific adverse effects were observed in clinical trials with imiquimod cream during lactation. However, the safety and efficacy of imiquimod cream in nursing mothers have not been established. Breastfeeding should be discontinued during treatment with imiquimod cream.

6.15 Clinical Trials Experience: Undesired Effects

No specific undesired effects were observed in clinical trials with imiquimod cream. However, patients should be advised to avoid concurrent use of topical corticosteroids or other irritants as they may increase the risk of skin reactions.

7. DOSAGE AND ADMINISTRATION

Imiquimod cream should be applied just before bedtime. After applying imiquimod cream, wash your hands well.
# Pharmacodynamics

### 12.2 Pharmacodynamics

In the AK clinical studies, imiquimod cream was evaluated in two randomized, vehicle-controlled, double-blind trials involving a total of 215 subjects. Of these, 127 subjects (59%) were Caucasians. The mean peak serum imiquimod concentration [C₅(11%)] was 3.5 ng/mL, with 64 subjects achieving levels above 0.01 ng/mL for 7 days at a dosage of 5%. For the vehicle cream, the peak serum concentration was 3.0 ng/mL.

### 13.0 NONCLINICAL TOXICOLOGY

#### 13.1.3 Local Skin Reactions

Sub-clinical AK lesions may become apparent in the treatment area during treatment with imiquimod cream. The percentage of subjects in whom 75% or more baseline AK lesions were cleared was calculated in a study where subjects were treated for 8 weeks at a dosage of 5%.

### 15.0 PATIENTS BEING TREATED FOR ACTINIC KERATOSIS (AK)

Patients who are being treated for AK should be advised to avoid sun exposure, especially during times when the UV index is high. Patients should use sunscreen with a broad spectrum and a Sun Protection Factor (SPF) of at least 30 to minimize cutaneous damage.

### 17.1 ADVERSE REACTIONS

#### 17.1.1 Imiquimod Cream

The most common side effects of Imiquimod Cream include:

- Redness
- Changes in skin color that do not always go away
- Severe swelling near the vagina. This may lead to pain or trouble passing urine.
- Female patients should take steps to prevent Imiquimod Cream from coming into contact with the eyes.

### 19.0 PATIENT INFORMATION

#### 19.1.1 Imiquimod Cream

- The provider tells you. The length of time that Imiquimod Cream is left on the skin is different for each skin condition that Imiquimod Cream is used to treat.
- To take a bath or get the treated area wet during this time.
- Follow-up visits at 2, 4, 8 weeks. This is important when the treatment area is large or if new lesions develop.

### 20.0 PATIENTS AND PREGNANCY

#### 20.1.1 Imiquimod Cream

- The patient needs to discuss how to use Imiquimod Cream with their healthcare provider. If you are pregnant, or planning to become pregnant, you should discuss the risks and benefits of using Imiquimod Cream.
- Keep Imiquimod Cream out of the reach of children.