For the use only of a Registered Medical Practitioner or a Hospital or a Laboratory.

Imiquimod Cream 5% w/w

Imiquad®

Cream

इमिक्वाड क्रीम

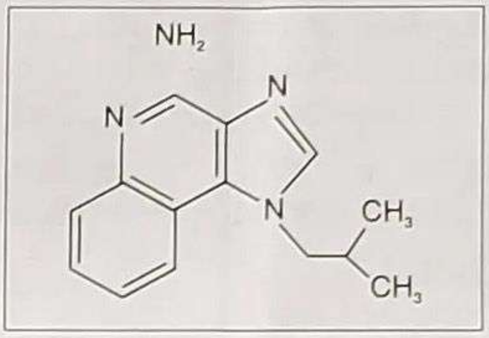
COMPOSITION: -

Each 0.25 g single use sachet contains:

Imiquimod	12.5 mg
Cream base	q.s.

DESCRIPTION:

Imiquad contains imiquimod cream 5% w/w. imiquimod, an imidazoquinoline amine, is and immune response modifier. Each gram of the 5% w/w cream contains 50 mg of imiquimod. The chemical name of imiquimod is 1-(2-methylpropyl)-1 H -imidazo [4, 5- c] quinoline-4-amine. Imiquimod has a molecular formula of $C_{14}H_{16}N_4$ and a molecular weight of 240.3. Its structural formula is:



CLINICAL PHARMACOLOGY:

Pharmacodynamics:

The exact mechanism of action of imiquimod in the topical treatment of external warts caused by human papillomavirus (HPV) has not been elucidated but may be related to the immunomodulating effects of the drug. Imiquad therapy induceds host messenger RNA (MRNA) encoding fore cytokines, including interferon alpha (IFN-α), at the treatment site and substatially decreases HPV DNA and HPV major capsid protein (L1) RNA. In vitro, imiquimod has no direct antiviral activity; however, the drug exhibits antiviral and antitumor effects in vivo. Imiquimod induces production of a variety of cytokines and apparently can, enhance cell-mediated cytolytic antiviral activity. The drug is a rapid and potent inducer of IFN-α, interleukin-1 alpha and beta (IL-1α and IL-1β), interleukin-6 (IL-6), Interleukin-8 (IL-8), tumor necrosis factor alfa (TNF-α), granulocyte-macrophage colony-stimulation factor (GM-CSF), granulocyte colony-stimulating factor (G-CSF), and macrrophage inflammatory protein-1α.

Pharmacokinetics :

Systemic absorption of imiquimod following topical application appears to be minimal. In healthy adults who received a single 5-mg dose of radiolabeled imiquimod administered as a topical cream, radioactivity was not detected in serum (lower) limit of detection: 1 ng/mL) and less than 0.9% of the radiolabeled dose was eliminated in urine and feces.

INDICATIONS AND USAGE:

Imiquad is indicated for the treatment of external genital and perianal warts in adult patients.

DOSAGE AND ADMINISTRATION:

Adult dose:

Imiquad is packaged in single-use packets which contain sufficient cream to cover a wart area of up to 20 cm^2. Imiquimod cream should be applied prior to normal sleeping hours, and left on the skin for 6-10 hours. Following the treatment period, cream should be removed by washing the treated area with mild soap and water. Imiquad cream should be applied 3 times per week, until there is total clerance of the genital/perianal warts or for a maximum of 16 weeks.

Because of the potential for adverse local reactions (e.g., erythema, erosion, excoriation/flaking, edema), the recommended dose, frequency of application, and duration of treatment of topical imiquimod should not be exceeded. Use of excessive amounts of the cream should be avoided. topical imiquimod therapy may be temporarily discontinued for several days if required because of the patient's discomfort or severity of local reactions, and then reinitiated after the reactions subside.

The technique for proper dose administration should be demonstrated by the prescriber to the patients. Hand washing before and after cream application is recommended. Patients should be instructed to apply the cream to external genital/perianal warts. A thin layer is applied to the wart area and rubbed in until the cream is no longer visiible. The application site is not to be occluded.

Pediatric use: Safety and efficacy of imiquimod topical cream in children younger than 12 years of age have not been established.

CONTRAINDICATIONS:

Patients with known hypersensitivity to imiquimod or any other ingredients of **Imiquad.**

WARNINGS AND PRECAUTIONS:

- Ø For external use only.
- Ø Eye contact should be avoided.
- Ø Imiquimod has not been evaluated for the treatment of urethral, intravaginal, cervical, rectal, or intraanal human papiliomavirus disease and is not recommended for these conditions.
- Ø There is no clinical experience with topical imiquimod therapy immediately following treatment with other cutaneously applied drugs; therefore, topical imiquimod administration is not recommended until genital/perianal tissue is healed from any pervious drug or surgical treatment.
- Ø Although adverse reactions to topical imiquimod usually consist of mild to moderate local skin reactions, severe skin reactions can occur. In addition, topical imiquimod has the potential to exacerbate inflammatory skin conditions. To minimize the potential for local reactions during topial imiquimod therapy, it is recommended that the treatment area by washed with mild soap and water 6-10 hours after each dose..
- Ø If a severe local reaction occurs, imiquimod should be washed form the treatment areas with mild soap and water. If necessary, the drug may be discontinued for several days and then reinitiated after these reaction subside. Nonocclusive dressing (e.g., cotton gauze, cotton underwear) may be used in the management of skin reactions.
- Ø Immunosuppressed individuals, including those with human immunodeficiency virus (HIV) infection, may have less of a response to treatment of genital and perianal HPV warts than

immunocompetent individuals and may have more frequent recurrences after treatment. In addition, biopsy to confirm a diagnosis of HPV warts may be required more frequently in immunosuppressed individuals since squamous cell carcinomas arising in or resembling HPV warts might occur more frequently in these individuals.

- Ø Topical imiquimod is not a cure, and patients should be informed that new HPV warts may develop during or after therapy with the drug.
- Ø The effect of topical imiquimod therapy on transmission of HPV is unknown. Patients should be instructed not to rely on condoms or diaphragms to prevent sexually transmitted diseases or pregnancy during topical imiquimod therapy since the cream may damage these devices and result in protective failure. Patients should be warned to avoid sexual contact (e.g., genital, anal, oral) while imiquimod is on the skin.
- Ø Patients also should be informed that changes in skin pigmentaion may occur at the application site and occasionally may be permanent.

CARCINOGENESIS, MUTAGENESIS IMPAIRMENT OF FERTILITY

Imiquimod was not mutagenic in several in vitro and in vivo tests, including the Ames test, mouse lymphoma assay, Chinese hamster ovary (CHO) chromosomal aberration assay, human lymphocyte chromosome aberration assay, SHE cell transformation assay, rat and hamster bone marrow cytogenetic tests, and mouse dominat lethal test. Carcinogenicity data on imiquimod are not available.

Studies in rats that received oral imiquimod doses up to 8 times the recommended human dose (based on mg/m2) throughout mating, gestation, parturition, and lactation have, lot revealed evidence of impaired fertility.

USE IN SPECIAL POPULATION:

Pregnancy: Teratogenic Effects:

Pregnancy Catagory B

There was no evidence of teratogenicity when imiquimod was administered orally in rats and rabbits. In rats receiving a maternally toxic of imiquimod equivalent to 28 times the human dose (based on mg/m2), reduced pup weights and delayed ossification were observed,, No adverse effects were demonstrated in offspring of pregnant hrats treated with oral imiquimod in doses 8 times the usual human dose. There are no adequate and controlled studies using imiquimod in pregnant women. Hence, use of **Imiquad** is not recommended in pregnant women.

Nursing Mothers:

It is not know whether topically applied **Imiquimod** is distributed into human milk. Hence, use of Imiquad cream is not recommended in lactating women.

Pediatric Use:

Safety and efficacy of imiquimod topical cream in children younger than 12 years of age have not been established.

ADVERSE REACTIONS:

Imiquad generally is well tolerated when applied topically. The most frequent adverse effects of the drug are mild to moderate local inflammatory reactions; these effects have been severe enough to require discontinuance of the drug in 1-4% of patients. Serious adverse systemic effects have not been reported to date with topical imiquimod.

Local and Dermatologic Effects: Adverse local reactions, including erythema, erosion, exoriation/flaking, and edema, commonly occur at the site of application of imiquimod and/or surrounding areas. These reactions usually are mild to moderate in severity; however, severe local reactions have been reported. Adverse local reactions occur more frequently and are more intense if the drug is administered once daily rather then according to the currently recommended 3 times weekly regimen. Local adverse effects that have been reported in more thant 1% of patients receiving topical imiquimod include pruritus, burning, pain, tenderness, soreness, sensitivity, stinging, rash, and hypopigmentation. Localized hyperpigmentation also has been reported. Skin color changes (i.e., hypopigmentation hyperpigmentation) may be permanent in some patients, Adverse dermatologic reactions like erythema, erosion, induration, ulceration, edema, bleeding , burning, itching, pain, tenderness, and tinea cruris have been reported at sites away from the site of application in some patients receiving topical imiquimod.

Systemic Effects: Adverse systemic effects such as headache, flu-like symptoms, myalgia, fatigue, fever, diarrhea, and fungal infection have been reported in patients receiving topical imiquimod.

OVERDOSAGE:

In rabbits, the minimum lethal dermal dose of imiquimod exceeds 1.6g/m^2. Overdosage of imiquimod following topical application in humans is unlikely since only minimal amounts of the drug are absorbed percutaneouslu; however, persistent topical overdosage may result in severe local skin reactions.

STORAGE:

Store below 25°C. Avoid freezing.

Keep out of reach of children.

PRESENTATION:

Imiquad is supplied in single-use sachets, which contain 0.25 g of the cream.

For further information please write to:

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