**CORE SAFETY PROFILE**

METHYLPREDNISOLONE ACEPONATE (MPA)

## 4.2 Posology and method of administration

MPA is to be applied thinly once daily to the affected areas and rubbed in lightly.

**MPA cream/ointment/fatty ointment:**
In general, the duration of use should not exceed **12 weeks in adults and 4 weeks in children**.
If the skin dries out excessively under protracted use of MPA cream, a switch should be made to one of the formulations with a higher fat content (MPA ointment or MPA fatty ointment).

**MPA Milk:**
In general, the duration of use should not exceed **2 weeks in adults.** In severely inflamed seborrhoic eczema, afflicted areas of the face should be treated not longer than **a week.** As a matter of principle, the duration of treatment should be **kept to a minimum with children.**
MPA Milk is not recommended for use in children below the age of 4 months due to insufficient data on safety.
If the skin dries out excessively under use of the MPA Milk, depending on the individual type of skin involved, an adjuvant neutral therapy (W/O emulsion or a single-phase fatty ointment) is recommended as a skin emollient.

**MPA solution:**
In general, the duration of use should not exceed **4 weeks**.
To date, no clinical data are available on the use of MPA solution in children.

## 4.3 Contra-indications

MPA must not be used in cases of hypersensitivity to the active substance or to any of the excipients, presence of tuberculous or syphilitic processes, viral infections (such as herpes or varicella), rosacea, perioral dermatitis, ulcera, acne vulgaris, atrophic skin diseases and vaccination skin reactions in the area to be treated.

MPA Milk must not be used on the eye and on deep open wounds.

Children under 4 months due to lack of experience.

Bacterial and mycotic skin diseases, cf. 4.4

## 4.4 Special warnings and precautions for use

Glucocorticoids must only be used at as low a dose as possible, especially in children, and only for as long as is absolutely necessary to achieve and maintain the desired therapeutic effect.

Additional, specific therapy is required in bacterially infected skin diseases and/or in fungal infections.

Local skin infections can be potentiated by topical glucocorticoid use.

A careful benefit/risk assessment is needed in the case of children between 4 months and 3 years.

When using MPA , care must be taken to avoid contact with the eyes, deep open wounds and mucosae.

Advantan Milk must not be applied to large areas (more than 40 % of body surface).

MPA must not be applied to intertriginous areas.

After application of MPA ointment to 60 % skin surface area under occlusive conditions for 22 hours, suppression of plasma cortisol levels and influence on circadian rhythm was observed in adult healthy volunteers. Therefore MPA should not be used under occlusive conditions.

Extensive application of topical corticosteroids to large areas of the body or for prolonged periods of time, in particular under occlusion, significantly increases the risk of side effects. Note that diapers can be occlusive.

When treating large areas of skin, particularly during pregnancy or lactation, the duration of treatment should be kept as short as possible as the possibility of absorption or a systemic effect cannot be completely excluded.

As with all other glucocorticoids unprofessional use can mask clinical symptomatology.

As known from systemic corticoids, glaucoma may also develop from using local corticoids (e.g. after large-dosed or extensive application over a prolonged period, occlusive dressing techniques, or application to the skin around the eyes).

Two excipients contained in MPA cream (cetostearyl alcohol and butyl hydroxytoluene) may cause local skin reactions (e.g., contact dermatitis). Butyl hydroxytoluene may also cause irritation in the eyes and mucous membranes.

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

As a consequence of absorption, treating large areas of skin or long term therapy could result in similar interactions to those occurring after systemic treatment. None so far known.

**4.6 Pregnancy and lactation**

There are insufficient data on the use of MPA in pregnant women. Animal experimental studies with methylprednisolone aceponate have shown embryotoxic and / or teratogenic effects at doses which exceed the therapeutic dose (cf. 5.3).

A number of epidemiological studies suggest that there could possibly be an increased risk of oral clefts among newborns of women who were treated with systemic glucocorticoids during the first trimester of pregnancy. Oral clefts are a rare disorder and if systemic glucocorticosteroids are teratogenic, these may account for an increase of only one or two cases per 1000 women treated while pregnant. Data concerning topical glucocorticosteroids use during pregnancy are insufficient, however, a lower risk might be expected since systemic availability of topically applied glucocorticosteroids is very low.

Based on these findings, a careful benefit/risk assessment is needed before MPA is used during pregnancy and lactation. In general, the use of topical preparations containing corticoids should be avoided during the first trimester of pregnancy.

If after careful benefit/risk assessment the use of MPA is indicated during the first trimester of pregnancy, MPA should not be applied on more than 20 % of body surface.

In particular, treating large areas, prolonged use or occlusive dressings should be avoided during pregnancy and lactation (cf. 4.3).

Nursing mothers should not be treated on the breasts.

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

MPA has no influence on the ability to drive and use machines.

### 4.8 Undesirable effects

Undesirable effects are added to the appropriate category according to the pooled analysis from clinical trials. Frequencies are defined according to MedDRA frequency convention.
Very common (≥1/10)
Common (≥1/100 to <1/10)
Uncommon (≥1/1,000 to <1/100)
Rare (≥1/10,000 to <1/1,000)
Very rare (<1/10,000), not known (cannot be estimated from the available data)

| SOC | Undesirable effect | Very common (≥1/10) | Common (≥1/100 to <1/10) | Uncommon (≥1/1,000 to <1/100) | Rare (≥ 1/10,000 to <1/1,000) | Very rare (<1/10,000) | Frequency unknown* |
|---|---|---|---|---|---|---|---|
| **Infections and infestations** | fungal skin infection | | | | C | | |
| **Immune system disorders** | drug hypersensitivity | | | C | | | |
| **Skin and subcutaneous tissue disorders** | eczema | | | M | | | |
| | skin exfoliation | | | M | | | |
| | skin fissures | | | M, FO | C | | |
| | acne | | C, O, FO | | | | M; S |
| SOC | Undesirable effect | Very common (≥1/10) | Common (≥1/100 to <1/10) | Uncommon (≥1/1,000 to <1/100) | Rare (≥ 1/10,000 to <1/1,000) | Very rare (<1/10,000) | Frequency unknown* |
| | pyoderma | | | | C | | |
| | telangiectasia | | | FO | C | | M; O; S |
| | skin atrophy | | | O | C | | S; M; FO |
| | ecchymosis | | | O | | | |
| | impetigo | | | O | | | |
| | skin greasy | | | O | | | |
| | seborrhea capitis | | | S | | | |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | hair loss | | | S | | | |
| | skin striae | | | | | | C; O; FO; M; S |
| | perioral dermatitis | | | | | | C; O; FO; M; S |
| | skin discoloration | | | | | | C; O; FO; M; S |
| | allergic skin reactions | | | | | | C; O; FO; S |
| **General disorders and administration site reaction** | application site burning | | M, C, O, FO, S | | | | |
| | application site pruritus | | C, O | M, FO, S | | | |
| | application site pain | | | M, FO, S | | | |
| | application site vesicles | | | M, C, O, FO | | | S |
| | application site pustules | | | M, FO | | | |
| | application site erosion | | | M | | | |
| | application site dryness | | | C, O, S | | | M |
| | application site erythema | | | C, O, FO | | | S; M |
| | application site folliculitis | | FO | C, S | | | O; M |
| | application site rash | | | C | | | |
| | application site paraesthesia | | | C | | | |
| | application site cellulitis | | | | C | | |
| | application site oedema | | | | C | | |
| | application site irritation | | | O, S | C | | |
| | application site eczema | | | O, S | | | |
| | oedema peripheral | | | O | | | |
| | application site papules | | | FO | | | |
| | localized feeling of warmth | | | S | | | |
| | hypertrichosis | | | | | | C; O; FO; S; M |

* Potential undesirable effects not observed in clinical studies.

Systemic effects due to absorption may occur when topical preparations containing corticoids are applied.

The most appropriate MedDRA term (MedDRA version 11.1) was used to describe a certain reaction and its synonyms and related conditions.

### 4.9 Overdose

Results from acute toxicity studies with methylprednisolone aceponate do not indicate that any risk of acute intoxication is to be expected following a single dermal application of an overdose (application over a large area under conditions favorable to absorption) or inadvertent ingestion.

Effects of the base component isopropanol are to be expected following inadvertent oral ingestion of **MPA solution**. Such effects may appear as symptoms of CNS depression after only a few millilitres.

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