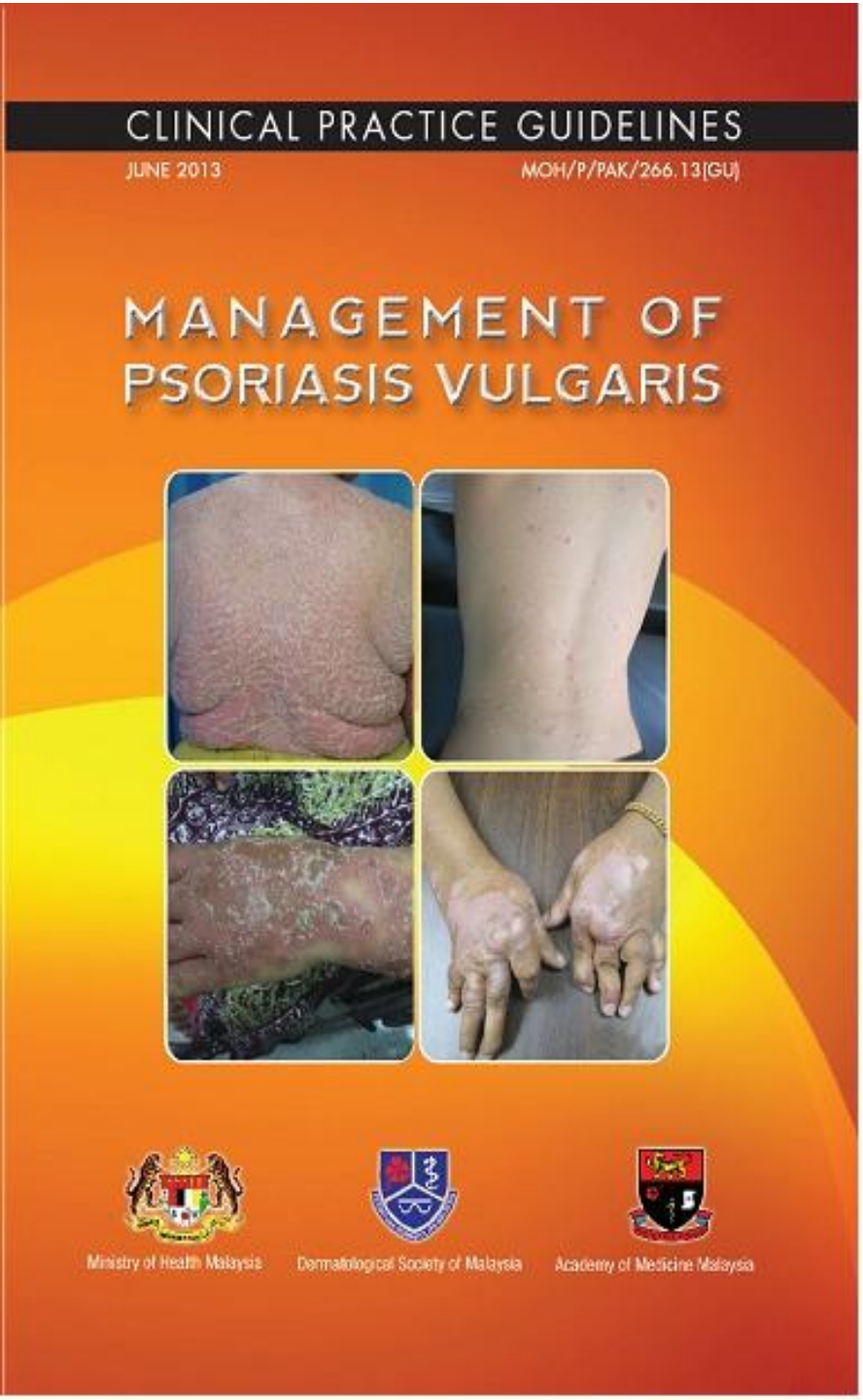

TREATMENT OF PSORIASIS IN PREGNANCY

Clinical Practice Guidelines Management of Psoriasis Development Group

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INTRODUCTION

- During pregnancy, psoriasis improves in 55%, worsen in 23% and remain static in 21%.

- It frequently flares in the immediate post-partum period

- Safety data for the use Psoriasis therapies in pregnant and lactating women is limited.

- In managing psoriasis in pregnant and lactating women, drug chosen should confer benefit to the mother and pose minimal risk to the foetus / baby

The FDA-assigned pregnancy categories as used in the Drug Formulary

Category	Interpretation
A	Controlled human studies show no risk Controlled studies in pregnant women fail to demonstrate a risk to the fetus in the first trimester with no evidence of risk in later trimesters. The possibility of fetal harm appears remote.
B	No evidence of risk in studies Either animal-reproduction studies have not demonstrated a fetal risk but there are no controlled studies in pregnant women, or animal-reproduction studies have shown an adverse effect (other than a decrease in fertility) that was not confirmed in controlled studies in women in the first trimester and there is no evidence of a risk in later trimesters
C	Risk cannot be ruled out Either studies in animals have revealed adverse effects on the fetus (teratogenic or embryocidal effects or other) and there are no controlled studies in women, or studies in women and animals are not available. Drugs should be given only if the potential benefits justify the potential risk to the fetus.
D	Positive evidence of risk There is positive evidence of human fetal risk, but the benefits from use in pregnant women may be acceptable despite the risk (eg, if the drug is needed in a life-threatening situation or for a serious disease for which safer drugs cannot be used or are ineffective).
X	Contraindicated in pregnancy Studies in animals or human beings have demonstrated fetal abnormalities or there is evidence of fetal risk based on human experience, or both, and the risk of the use of the drug in pregnant women clearly outweighs any possible benefit. The drug is contraindicated in women who are or may become pregnant.
N	FDA has not classified this drug

TOPICAL AGENTS AND PSORIASIS IN PREGNANCY

Topical agents and Psoriasis in Pregnancy (1)

- Emollients are safe in pregnancy

- **Topical corticosteroids** of various potencies showed no significant adverse event in pregnancy outcomes. However, high potency corticosteroids particularly on large body surface areas should be used with caution because of the possibility of low birth weight baby

- No sufficient published data to enable an accurate estimate of teratogenic risk **of tar-based** preparations in humans. Short-term use of **topical coal tar** is probably safe in second and third trimester of pregnancy

Topical agents and Psoriasis in Pregnancy (2)

- No information on the use of **anthralin (dithranol)** during pregnancy in humans or animals. Since there is no evidence of systemic absorption, dithranol is considered safe in pregnancy

- Use of **calcipotriol (calcipotriene)** is to be avoided in pregnancy because of systemic absorption

Topical agents & Psoriasis in Pregnancy (3)

- **Tacrolimus** is effective in the treatment of facial and intertriginous psoriasis. Systemic absorption of tacrolimus after topical administration is very low. Hence risk of teratogenicity is likely low if tacrolimus is used for limited disease although there is no published human data on it

- Topical **salicylic acid** is not recommended as studies are limited and topical absorption can be substantial

Phototherapy & Psoriasis in Pregnancy

- Both **NBUVB and BBUVB** are safe in pregnancy

- Insufficient evidence on the safety of **Psolaren-UVA (PUVA)** in pregnancy but in view of it's mutagenic potential, it is not recommended for use in pregnancy

SYSTEMIC THERAPIES FOR PSORIASIS IN PREGNANCY

Cyclosporine and Corticosteroids (1)

- **Cyclosporine and corticosteroids** are considered to be relatively safe but have to be used with caution

- No report of increase rate of congenital anomalies due to cyclosporine used but increased incidence of prematurity and intrauterine growth restriction (IUGR) has been reported

- Systemic corticosteroids are infrequently used for treatment of psoriasis except in pregnancy-induced generalised pustular psoriasis

Cyclosporine and Corticosteroids (2)

- Although long-term effects of multiple courses of prenatal corticosteroids on neurodevelopment and growth in humans are limited, repeated courses of corticosteroids should be used with caution

- A systemic review found a significant association between first-trimester corticosteroids and oral clefts (OR=3.4)

Acitretin (1)

- Acitretin (X), a systemic retinoid, is contraindicated in pregnancy due to high risk of teratogenicity (25.6 times higher than the general population)

- Pregnancy should be avoided in patient taking acitretin and for at least 2 years after stopping treatment or longer up to 3 years in patient who consumed alcohol

- Prescribing acitretin to any woman of childbearing potential warrants careful consideration

Acitretin (2)

- Prudent to document two negative urine or serum pregnancy tests before initiating therapy

- Patient should be advised to use two effective forms of contraception simultaneously for at least 1 month before initiation, during acitretin therapy, and for at least 2 - 3 years after discontinuing therapy

Methotrexate (1)

- Methotrexate (X) is contraindicated in pregnancy as it is associated with increased risk of spontaneous miscarriage, mental retardation and aminopterin/methotrexate syndrome

- Doses greater than 10 mg/week are necessary to produce aminopterin/methotrexate syndrome and the critical exposure period is between 6 and 8 weeks post-conception.

- The effect of exposure to methotrexate and aminopterin on foetus during the second and third trimesters is not known

Methotrexate (2)

- The potential foetal risk when the father is exposed to methotrexate at the time of conception (paternal conception) remains unclear
- Genotoxic effect of methotrexate on sperm and present of methotrexate in seminal fluid raises the theoretical potentials of teratogenicity
- No congenital malformation was observed in small case series and case reports of pregnancies after paternal exposure to low-dose methotrexate.
- Nevertheless, both men and women are to avoid conception for at least three months after taking methotrexate

Biologics

- Tumour necrosis factors (TNF) inhibitors (B) such as adalimumab, etanercept and infliximab should be used cautiously in pregnancy.

- Animal studies did not report any toxicity or teratogenicity but there is limited human data

Treatment in Lactating Women

- Topical agents such as emollients, low-moderate potency topical corticosteroids and dithranol are safe and can be used a first-line in treating psoriasis in lactating women
- Topical treatment should be applied after breastfeeding, and washed off thoroughly before the next feed
- It is also safe to use ultraviolet B phototherapy but PUVA should be avoided
- Systemic therapies like acitretin, methotrexate, cyclosporine and biologics are to be avoided in lactating women

Take Home Messages (1)

Treatment of a pregnant woman with psoriasis should take into consideration the benefit of the therapy to her and her foetus, and the availability of safe and effective alternatives

Malaysian CPG on the management of Psoriasis vulgaris
Pregnant and Lactating Women

RECOMMENDATION

- First-line treatment of psoriasis in pregnant and lactating patients should be topical emollient and low-mid potent topical corticosteroids. **(Grade C)**

- Ultraviolet B phototherapy may be offered when psoriasis is extensive or not controlled by topical treatments alone **(Grade C)**

Malaysian CPG on the management of Psoriasis vulgaris

Pregnant and lactating women

Recommendation

- Cyclosporine may be used in pregnant women with severe psoriasis **(Grade C)**
- Cyclosporine should not be used in psoriasis women who are breastfeeding **(Grade C)**
- Acitretin and methotrexate must not be used in pregnant and lactating women and should be avoided in those planning pregnancy **(Grade C)**
- Acitretin should be stopped two years before conception in women. **(Grade C)**
- Methotrexate should be stopped three months before conception in both women and men **(Grade C)**