Pregnancy, breastfeeding, and family planning

The current ethical framework of GCP guidelines deems it unethical to perform clinical trials in pregnant women. Therefore, there is no high-level evidence data on the efficacy and safety in this patient population. On the other hand, AE is the most common general skin disease in pregnancy. AE may either (i) worsen in women with a chronic condition, or (ii) may be reactivated in patients with a past AE history or (iii) may occur in women with no AE history (atopic eruption of pregnancy, AEP). Worsening of AE is mostly reported during the second and third trimesters, while AEP typically occurs during the first trimester.[1] There are no major clinical differences between classical AE worsening and AEP. Physiological skewness of the immune system towards a Th2-dominated response during pregnancy as well as physical and psychological stress during this period may contribute to AE worsening during pregnancy. Little is known about treatment patterns during pregnancy, but patients and caregivers tend to reduce the use of topical and systemic therapies during pregnancy to avoid presumed harm to the fetus.[2] Consequently, undertreatment of AE during pregnancy may lead to serious QoL impairment but also to complications such as eczema herpeticum or staphylococcus aureus skin infections, and should therefore be avoided.

Pregnant women

In pregnant women with AE, we **recommend** TCS class II or III.	↑↑	100% 100 % Agreement (19/19) Expert Consensus
In pregnant women with AE, we **suggest** that TCI may preferably be used on the face and intertriginous areas and on abdominal, breast and thigh skin, where the risk of striae formation increases with excessive use of TCS.	↑	100% 100 % Agreement (19/19) Expert Consensus
In pregnant women with AE, when topical treatments are insufficient, we **recommend** narrow-band UVB (311 nm) or broad spectrum UVB therapy if NB-UVB is unavailable.	↑↑	100% 100 % Agreement (19/19) Expert Consensus

In pregnant women with AE, who are candidates for systemic treatment, we **suggest** ciclosporin.	↑	100%  (14/14) Expert Consensus
In pregnant women with AE, who are being treated with azathioprine and still need a systemic treatment, we **suggest** continuing azathioprine.	↑	100%  (14/14) Expert Consensus
In pregnant women with AE, we **recommend against** long term use of systemic corticosteroids - as we do in all AE patients.	↓↓	100%  (16/16) Expert Consensus
In pregnant women with AE, we **suggest** prednisolone only as short term rescue therapy for acute flares.	↑	
In pregnant women with AE, we **recommend against** the use of abrocitinib, baricitinib, upadacitinib, methotrexate and mycophenolate.	↓↓	100%  (15/15) Expert Consensus
In pregnant women with AE, we **cannot make a recommendation** regarding the use of dupilumab and tralokinumab during pregnancy due to the current lack of clinical data.	0	100%  (15/15) Expert Consensus

First line treatments

Emollients. Basic emollient therapy is key in the treatment of AE also during pregnancy and must be proposed to pregnant women with AE as a basic daily therapy. There is no firm evidence on which emollient should be used, but using one with a high lipid content and as few potentially harmful agents as possible is recommended. Using emollients in a wet wrap technique is encouraged.[3]

TCS. Reactive or proactive use of TCS class II or III is recommended. A Cochrane systematic review updated in 2015 including 14 studies (5 cohort and 9 case-control studies) with 1,601,515 study subjects has examined the risk of TCS use in pregnancy. Overall, it has been deemed safe, with no causal associations between maternal exposure to TCS of all potencies and pregnancy outcomes including mode of delivery, congenital abnormalities, preterm delivery, foetal death, and low Apgar score, although the use of very potent topical corticosteroids may be associated with low birthweight.[4] Proactive, twice weekly TCS application as maintenance therapy is regarded as safe, but caution is recommended when using potent TCS over large body surface areas, or sensitive areas as breast and thigh skin, on a more regular basis. Some experts suggest that class IV may be used as rescue therapy, or over longer periods on limited skin areas, but this is controversial. Fluticasone propionate should be avoided as it is the only TCS that is known not to be metabolized by the placenta.[1]

TCI. Reactive and proactive use of TCI may be preferable on the face and intertriginous areas, and on abdominal, breast and thigh skin, where the risk of striae formation increases with excessive use of TCS.

Antiseptics. Antiseptics, except triclosan, may be used by pregnant women if clinically needed to prevent recurring skin infections, but are not recommended as a general routine measure.

UV phototherapy. Therapy with narrow-band UVB (311 nm) and broad-spectrum UVB does not impose a risk to the fetus in pregnant woman. However, oral psoralen should not be used preconceptionally (3 months) or in pregnant women.

Second and third line treatments

Second and third line treatments are recommended in pregnant women with AE who are inadequately controlled with TCS class II or III.

Systemic corticosteroids should not be used in the long-term in AE in general and even more so not during pregnancy, as it is associated with an increased risk of fetal complications, including gestational diabetes.[4] Only short courses of prednisolone (maximum 0.5mg/kg/d) may be used with strict indication.

Ciclosporin may be used off-label in severe uncontrolled AE during pregnancy if topical anti-inflammatory treatment alone or in combination with UV treatment fails, and there is a clear need for better long-term disease control. However, extra attention should be given to the renal function and blood pressure of the mother. There is no evidence of teratogenicity. Ciclosporin crosses the placenta[5] and should not be used during pregnancy, unless the potential benefit to the mother justifies the potential risk to the foetus.

AZA may be used off-label in pregnant women with severe uncontrolled AE, who are already receiving this treatment at the time of conception. There is no evidence for teratogenicity from studies with patients with inflammatory bowel diseases. Closely consulting an experienced obstetrician when prescribing this drug is strongly recommended.[1]

MTX and mycophenolate mofetil are teratogenic and therefore strictly contra-indicated during pregnancy.

We cannot recommend any of the novel systemic medications, as there is currently no clinical data available to inform about any potential drug-associated risks. On the other hand, pre-clinical data does not indicate that there would be a teratogenic potential of dupilumab or tralokinumab if given during pregnancy.

Abrocitinib, baricitinib and upadacitinib are contraindicated during pregnancy according to label. There is no clinical data but single case reports supporting its safety in pregnant women, but teratogenic effects have been described for both molecules in animal models

Antihistamines are of limited efficacy in AE (see chapter antipruritic treatment). In case of need, loratadine should preferentially be used because of the broad experience with this drug in pregnant women.

Due to lack of experience with crisaborole during pregnancy, this drug should not be used preconceptionally, in pregnancy or during lactation.

Specific consideration for breastfeeding women

In breastfeeding women with AE, we **recommend** TCS II or III.	↑↑	>75%  (14/15) Expert Consensus
In breastfeeding women with AE, we **suggest** prednisolone only as short-term rescue therapy for acute flares.	↑	
In breastfeeding women with AE, we **suggest against** abrocitinib, baricitinib, upadacitinib, azathioprine, ciclosporin and methotrexate.	↓	
In breastfeeding women with AE, we **cannot make a recommendation** regarding the use of dupilumab and tralokinumab due to the current lack of clinical data.	**0**	

TCS and TCI: No studies have examined the safety of TCS and TCI use during lactation but no harmful effect is suspected. Nevertheless, it is recommended to apply the topical treatment in the nipple region immediately after nursing the child, to allow the drug to be absorbed into the skin before the next feeding.[1]

Systemic corticosteroids: Treatment with a short course of a systemic corticosteroids during lactation is safe, since <0.1% of the mother's ingested dosage is secreted into breastmilk.

MTX, AZA, ciclosporin, and JAK inhibitors are secreted in breastmilk and may induce immunosuppression in the neonate. MTX, AZA, ciclosporin, and JAK inhibitors are generally not recommended for lactating mothers.[1]

Family planning

In parents with AE planning to have a child, we **recommend** TCS II or III or TCI.	↑↑	100%  (22/22) Expert Consensus

In women with AE planning to have a child, we **recommend** stopping methotrexate at least 3 months before conception.*	↑↑	>75%  (13/14) Expert Consensus
In men with AE planning to have a child, we **recommend** stopping methotrexate 3 months before conception.*	↑↑	

*EMA recommends 6 months as a means of precaution, the practice of the guideline group differs from this.

Preconception recommendations for women

TCS and TCI: Although the literature on this subject is very sparse, topical AE therapies in women wishing to conceive can be used without concern.

MTX: Local labels in different countries suggest a contraindication range spanning from 1 month to 6 months before conception. European Medicines Agency (EMA) recommends 6 months as a means of precaution. The practice of the guideline group differs from this and we recommend stopping methotrexate 3 months before conception.

Preconception recommendations for men

TCS and TCI : Although the literature on this subject is very sparse, topical AE therapies in men wishing to father a child can be used without concern.

Ciclosporin may be used in the treatment of AE in men at the time of conception, as there is no evidence for harm or decreased fertility.

MTX: Following the European S3-guideline on systemic treatment of psoriasis vulgaris a 3-month MTX pause prior to conception is recommended. However, (inadvertent) exposure beyond this time does not justify termination of pregnancy, because there is no evidence of male teratogenicity.[1]

AZA and baricitinib: there is no contraindication for the use of AZA and baricitinib in men wishing to father a child.

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