



## CONSENSUS DOCUMENT

# Management of Psoriasis During Preconception, Pregnancy, Postpartum, and Breastfeeding: A Consensus Statement<sup>☆</sup>

I. Belinchón,<sup>a,\*</sup> M. Velasco,<sup>b,1</sup> M. Ara-Martín,<sup>c</sup> S. Armesto Alonso,<sup>d</sup>  
 O. Baniandrés Rodríguez,<sup>e</sup> L. Ferrándiz Pulido,<sup>f</sup> M. García-Bustinduy,<sup>g</sup>  
 J.A. Martínez-López,<sup>h</sup> N. Martínez Sánchez,<sup>i</sup> A. Pérez Ferriols,<sup>j</sup> E. Pérez Pascual,<sup>k</sup>  
 R. Rivera Díaz,<sup>l</sup> R. Ruiz-Villaverde,<sup>m</sup> R. Taberner Ferrer,<sup>n</sup> A. Vicente Villa,<sup>o</sup>  
 J.M. Carrascosa<sup>p</sup>

<sup>a</sup> Servicio de Dermatología, Hospital General Universitario de Alicante-ISABIAL-UMH, Alicante, Spain

<sup>b</sup> Servicio de Dermatología, Hospital Universitario Arnau de Vilanova, Valencia, Spain

<sup>c</sup> Servicio de Dermatología, Hospital Clínico Lozano Blesa, Zaragoza, Spain

<sup>d</sup> Servicio de Dermatología, Hospital Universitario Marqués de Valdecilla, Santander, Spain

<sup>e</sup> Servicio de Dermatología, Hospital Universitario Gregorio Marañón, Madrid, Spain

<sup>f</sup> Servicio de Dermatología, Hospital Universitario Virgen Macarena, Sevilla, Spain

<sup>g</sup> Servicio de Dermatología, Hospital Universitario de Canarias, Santa Cruz de Tenerife, Spain

<sup>h</sup> Servicio de Reumatología, Hospital Universitario Fundación Jiménez Díaz, Madrid, Spain

<sup>i</sup> Servicio de Ginecología-Obstetricia, Hospital Universitario La Paz, Madrid, Spain

<sup>j</sup> Servicio de Dermatología, Hospital General de Valencia, Valencia, Spain

<sup>k</sup> Servicio de Ginecología-Obstetricia, Hospital General Universitario de Alicante-ISABIAL, Alicante, Spain

<sup>l</sup> Servicio de Dermatología, Hospital Universitario 12 de Octubre, Madrid, Spain

<sup>m</sup> Servicio de Dermatología, Hospital Universitario San Cecilio, Granada, Spain

<sup>n</sup> Servicio de Dermatología, Hospital Son Llàtzer, Palma de Mallorca, Spain

<sup>o</sup> Servicio de Dermatología, Hospital Sant Joan de Déu, Esplugues de Llobregat, Barcelona, Spain

<sup>p</sup> Servicio de Dermatología, Hospital Universitario Germans Trias i Pujol, Badalona, Barcelona, Spain

Received 17 April 2020; accepted 2 October 2020

### KEYWORDS

Psoriasis;  
 Fertility;  
 Pregnancy;

### Abstract

**Objective:** To develop evidence- and experience-based recommendations for the management of psoriasis during preconception, pregnancy, postpartum, and breastfeeding.

**Methods:** The nominal group technique and the Delphi method were used. Fifteen experts (12 dermatologists, 2 of whom were appointed coordinators; 1 rheumatologist; and 2

<sup>☆</sup> Please cite this article as: Belinchón I, Velasco M, Ara-Martín M, Armesto Alonso S, Baniandrés Rodríguez O, Ferrándiz Pulido L et al. Consenso sobre las actuaciones a seguir durante la edad fértil, el embarazo, el posparto y la lactancia en pacientes con psoriasis. Actas Dermosifiliogr. 2021;112:225–241.

\* Corresponding author.

E-mail address: [belinchon\\_isa@gva.es](mailto:belinchon_isa@gva.es) (I. Belinchón).

<sup>1</sup> Both authors contributed equally to this work.

Postpartum;  
Breastfeeding;  
Delphi process;  
Recommendations

gynecologists) were selected to form an expert panel. Following a systematic review of the literature on fertility, pregnancy, postpartum, and breastfeeding in women with psoriasis, the coordinators drew up a series of preliminary recommendations for discussion by the panel at a nominal group meeting. The experts defined the scope, sections, and intended users of the statement and prepared a final list of recommendations. Consensus was obtained using a Delphi process in which an additional 51 dermatologists rated their level of agreement with each recommendation on a scale of 1 (total disagreement) to 10 (total agreement). Consensus was defined by a score of 7 or higher assigned by at least 70% of participants. Level of evidence and strength of recommendation were reported using the Oxford Center for Evidence-Based Medicine categories. The final statement was approved by the expert panel.

**Results:** The resulting consensus statement includes 23 recommendations on preconception (fertility and contraception), pregnancy (planning, pharmacological management, and follow-up), and breastfeeding (management and follow-up). Consensus was achieved for all recommendations generated except one.

**Conclusions:** These recommendations for the better management of psoriasis in women of childbearing age could improve outcomes and prognosis.

© 2020 AEDV. Published by Elsevier España, S.L.U. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

## PALABRAS CLAVE

Psoriasis;  
Fertilidad;  
Embarazo;  
Posparto;  
Lactancia;  
Método Delphi;  
Recomendaciones

## Consenso sobre las actuaciones a seguir durante la edad fértil, el embarazo, el posparto y la lactancia en pacientes con psoriasis

### Resumen

**Objetivo:** Desarrollar recomendaciones basadas en la mejor evidencia y experiencia sobre el manejo de pacientes con psoriasis durante la edad fértil, el embarazo, el posparto y la lactancia.

**Métodos:** Se siguió la metodología de grupos nominales y Delphi. Se seleccionó un grupo director de expertos (12 dermatólogos —de los cuales 2 fueron los coordinadores—, 1 reumatólogo, 2 ginecólogos). Se realizó una revisión sistemática de la literatura sobre fertilidad, embarazo, posparto y lactancia en pacientes con psoriasis. Con esta información los coordinadores generaron una serie de recomendaciones preliminares. Todo ello se presentó y discutió con el resto de expertos en una reunión de grupo nominal donde se definió el alcance, los usuarios, los apartados del documento, y donde se generaron las recomendaciones definitivas. El grado de acuerdo con las recomendaciones se votó siguiendo la metodología Delphi, que se extendió a 51 dermatólogos más, según una escala de 1 (total desacuerdo) a 10 (total acuerdo), definiéndose el acuerdo como una puntuación  $\geq 7$  por al menos el 70% de los participantes. El nivel de evidencia y el grado de recomendación se clasificaron según el modelo del Center for Evidence Based Medicine de Oxford. El documento completo final fue aprobado por el panel de expertos.

**Resultados:** Se generaron 23 recomendaciones sobre el periodo pre-concepcional (fertilidad y anticoncepción), el embarazo (planificación, manejo farmacológico y seguimiento) y la lactancia (manejo y seguimiento). Todas las recomendaciones menos una alcanzaron el nivel de acuerdo definido.

**Conclusiones:** En los pacientes con psoriasis en edad fértil estas recomendaciones pueden mejorar el manejo, los resultados y el pronóstico.

© 2020 AEDV. Publicado por Elsevier España, S.L.U. Este es un artículo Open Access bajo la licencia CC BY-NC-ND (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

## Introduction

Psoriasis is a very common disease<sup>1,2</sup> with 2 peaks in incidence—one between age 15 and 30 years and the other between 50 and 60 years—although the disease first manifests before age 40 years in more than 75% of cases.<sup>3,4</sup> In clinical practice, a large percentage of patients are of reproductive age, and psoriasis and/or its treatments can affect fertility, pregnancy, postpartum, and breastfeeding and vice versa.<sup>5–8</sup> Owing to its severity, or to pain or embarrassment in the case of genital involvement, psoriasis may be associated with fertility problems, both in men

and in women.<sup>9–11</sup> Some treatments of psoriasis, including tazarotene and acitretin,<sup>12,13</sup> are potentially teratogenic and are therefore contraindicated during pregnancy. It has also been reported that the disease worsens in 40% to 80% of patients a few weeks after delivery<sup>14</sup> and that the children of mothers who have been in treatment with monoclonal antibodies that cross the placenta during the third trimester are at greater risk of infection and, therefore, require specific monitoring and management.<sup>15</sup>

Awareness of these problems and a suitable approach to preventing them or treating them early and efficiently should form part of the knowledge and skills of health

professionals involved in the management of affected patients.<sup>16</sup> In addition, these problems are very relevant for psoriasis patients themselves.<sup>16</sup>

The objective of this consensus statement is to generate a series of recommendations aimed at improving management of patients of reproductive age with psoriasis. The statement covers fertility, pregnancy, postpartum, and breastfeeding. We believe that the recommendations are of considerable interest for health professionals involved in treating patients with psoriasis, namely, dermatologists, gynecologists, primary care physicians, and nurses.

## Methods

### Study Design

This document was promoted by the Psoriasis Working Group of the Spanish Academy of Dermatology and Venereology (Academia Española de Dermatología y Venereología [AEDV]). The consensus statement was drafted following the nominal group technique and the Delphi method, with the help of a systematic review of the literature.<sup>17</sup> The project was managed in full agreement with the principles set out in the Declaration of Helsinki and in line with current norms of Good Clinical Practice.

### Selection of Participants

The participants selected formed a multidisciplinary group comprising 12 dermatologists (2 of whom were the coordinators), 1 rheumatologist, and 2 gynecologists with experience and interest in the subject area. With help from methodologists, the coordinators defined the objectives, scope, users, and sections of the document. It was decided to address 3 broad areas: (a) reproductive age; (b) pregnancy and postpartum; and (c) breastfeeding and perinatal care.

### Systematic Review of the Literature and Preliminary Recommendations

A systematic review of the literature was performed to assess fertility, delivery, and breastfeeding in patients with psoriasis. An expert documentalist designed the search strategies for the PubMed, EMBASE, and Cochrane library databases (from baseline to November 2018) using Medical Subject Headings and free text terms. In order to be included, studies had to fulfil the following criteria: (1) they had to include patients with psoriasis; (2) they had to provide data on pregnancy, breastfeeding, and postpartum (e.g., prevalence, interventions, prognoses); and (3) they had to be a meta-analysis, systematic review of the literature, randomized clinical trial, or observational study. Two reviewers independently selected articles and collected data. Finally, a secondary search for articles was carried out. The quality of the studies was evaluated using the 2011 classification of the Oxford Centre for Evidence-Based Medicine.<sup>18</sup> This information enabled the coordinators to generate a series of preliminary recommendations.

### Meeting of the Nominal Group

The objectives, scope, users, and sections of the document were confirmed at the meeting of the nominal group. The results of the systematic literature review were then presented and discussed, as were the provisional recommendations. Finally, the definitive recommendations were established.

### Delphi Process

The definitive recommendations were assessed using the Delphi process to establish the level of agreement (LA) with them. This stage was carried out online. The recommendations were sent to the expert panel and to 120 dermatologists. The vote was based on a Likert-type scale ranging from 1 (completely disagree) to 10 (completely agree). Agreement was defined as a score of  $\geq 7$  from at least 70% of the participants. The recommendations with an LA < 70% were evaluated and, if applicable, re-edited and voted on in a second Delphi round. It was possible to include new recommendations in the first Delphi round.

### Edition of the Final Document

The definitive document was drafted based on the systematic review of the literature, the decisions of the nominal group, and the Delphi process. In addition to the LA, each of the recommendations was assigned a level of evidence (LE) and a grade of recommendation (GR) according to the recommendations for evidence-based medicine of the Oxford Centre for Evidence-Based Medicine.<sup>18</sup> The final version of the document was sent to the experts for a concluding evaluation and comments.

## Results

### Systematic Review of the Literature and Delphi Process

After elimination of duplicates, 610 references were recovered. Of these, 49 were eventually included (Fig. 1 and other results in Appendix A, Supplementary material).

A total of 23 recommendations were generated. The Delphi response rate was 50%. In the first Delphi round, the LA was sufficient for all recommendations but one. The recommendation for which a sufficient LA was not reached was excluded. The results are shown in Table 1.

### Preconception

#### Preconception Counseling

*Recommendation 1. Preconception counseling should be offered to all psoriasis patients of reproductive age (both men and women) (LE 2b; GR B; LA 82%).*

Preconception counseling should always be offered so that patients with psoriasis can make informed decisions together with the dermatologist and also to avoid, as far as possible, unnecessary delays in conception.

**Table 1** Definitive Recommendations and Results of the Delphi Process.

#	Recommendation	Mean	SD	Median	P25	P75	Min	Max	% $\geq 7$
1	Preconception counseling should be offered to all psoriasis patients of reproductive age (both men and women)	8.23	2.82	9	7.5	10	1	10	82%
2	The panel recommends regular assessment of the desire to become pregnant	8.66	2.82	9	8	10	1	10	87%
3	The panel advises evaluating and recommending, if applicable, an effective contraceptive method for as long as a pregnancy is not desirable	7.89	2.12	9	7	10	1	10	73%
4	The panel recommends referring the patient to a gynecologist for reproductive health counseling	6.23	1.41	6	5	8.5	1	10	46%
5	Planning for pregnancy should include an assessment of the gynecologic and dermatologic history, a laboratory analysis, assessment of current psoriasis and its treatment, assessment of comorbidities, and possible contraindications to pregnancy	8.64	4.24	9	8	10	1	10	93%
6	The panel recommends that patients be informed on an individual basis about maternal-fetal risk factors in pregnancy and about all aspects of follow-up of pregnancy, including postpartum	7.98	1.41	9	7.25	10	1	10	81%
7	The panel recommends that psoriasis be as well controlled as possible before the patient tries to become pregnant	7.62	2.83	9	7	9	1	10	78%
8	The panel recommends establishing the most effective and safest drug profile possible during pregnancy. This should be tailored to the individual patient	9.41	2.12	10	9	10	1	10	98%
9	Potentially teratogenic topical agents (anthralin, tazarotene, topical psoralen-UV-A) should be discontinued once pregnancy is confirmed. Topical drugs with a more favorable safety profile should be considered	9.6	1.41	10	9.75	10	5	10	98%
10	Potentially teratogenic systemic agents (acitretin, systemic retinoids, systemic psoralen-UV-A, apremilast, dimethyl fumarate, methotrexate) should be discontinued before conception. Drugs with a better safety profile should be considered	9.56	2.12	10	10	10	5	10	97%
11	In the case of women receiving biologic therapy, the panel recommends that this be maintained during the first and second trimesters. Together with the patient, the clinician should evaluate the risks and benefits of continuing these drugs during the third trimester. Patients taking certolizumab pegol can continue the drug throughout pregnancy only if it is considered clinically necessary	8.48	4.24	9	8	10	1	10	88%
12	Patients with psoriasis who require standard systemic treatment and/or biologics to control their disease must be followed up closely by an obstetrician once the pregnancy is confirmed	8.88	0.13	10	8	10	2	10	92%
13	The panel recommends strict follow-up and monitoring of pregnant women with psoriasis	8.10	1.41	9	7	10	1	10	83%
14	In the case of a flare-up, the panel recommends treating each case on an individual basis, taking into account type and severity, week of gestation, and available therapeutic options	9.75	0.10	10	10	10	8	10	100%
15	The panel recommends encouraging cooperation between specialties (e.g., dermatology, obstetrics, pediatrics)	9.50	0.12	10	9	10	5	10	98%

Table 1 (Continued)

#	Recommendation	Mean	SD	Median	P25	P75	Min	Max	% $\geq 7$
16	Emollients can be prescribed during breastfeeding	9.74	0	10	10	10	7	10	100%
17	With respect to topical treatments for psoriasis during breastfeeding, tazarotene is contraindicated. Other topical agents can be used providing that the benefits outweigh the risks, at minimum doses, and for as short a period as possible. The area of the nipple and areola should be avoided	9.16	0.71	10	9	10	3	10	97%
18	Topical PUVA is not recommended during breastfeeding. Narrowband UV-B phototherapy can be used	9.18	0.70	10	9	10	2	10	95%
19	Systemic corticosteroids can be used during breastfeeding as long as the benefits outweigh the risks They should be administered at minimum doses and for as short a time as possible	8.33	0.34	9	7.75	10	2	10	80%
20	Oral retinoids, apremilast, dimethyl fumarate, methotrexate, and ciclosporin A are not recommended during breastfeeding	9.16	3.54	10	9	10	1	10	95%
21	Certolizumab pegol has been approved for use during breastfeeding. For all other biologics, the panel recommends assessing the risks and benefits in each case	9.38	0.71	10	9	10	5	10	93%
22	Once the pregnancy has come to term, standard follow-up should be resumed in the dermatology clinic as soon as possible	8.91	1.41	10	9	10	2	10	88%
23	The newborn does not require special care, except if the mother has been exposed to biologics that cross the placenta and have been maintained beyond the second trimester	8.83	0.71	10	9	10	1	10	87%

Table 2 Areas to Be Covered in Preconception Counseling.

#	Area
1	Genetic counseling (heritability of psoriasis)
2	Impact of psoriasis and its treatment on fertility
3	Use of contraceptives (when and types)
4	Impact of psoriasis and its treatment (as well as the risk of not treating) during pregnancy (for mother and fetus) and postpartum
5	Impact of pregnancy and postpartum on psoriasis
6	Planning for pregnancy (e.g., justification, alternatives, and modifications of treatment before conception and during pregnancy, visit schedule, tests, vaccinations)
7	Measures for puerperium and breastfeeding
8	Management of the unexpected pregnancy

Psoriasis is not a contraindication for gestation, although pregnancy can affect psoriasis; in turn, psoriasis (and its treatment) may be a risk factor for the course of the pregnancy.<sup>4,14,19–25</sup>

Preconception counseling (Table 2) ranges from information on the impact of the disease on fertility and pregnancy to the approach to an unexpected pregnancy and genetic

counseling.<sup>26,27</sup> This in turn should be adjusted to the patient's characteristics and involve the partner where possible. Preconception counseling should be repeated periodically.

While psoriasis is not a frequently reported problem, its severity or the consequences of genital involvement (pain or embarrassment) mean that it may be associated with fertility problems.<sup>9,22,25,28–36</sup> Some of the drugs used to treat psoriasis may also affect fertility, although this has not been demonstrated.<sup>10,37–40</sup>

**Recommendation 2.** The panel recommends regular assessment of the desire to become pregnant (LE 5; GR D; LA 87%).

This recommendation applies to all patients of reproductive age (both sexes), especially those who are receiving or who are candidates for long-term systemic treatment.

**Recommendation 3.** The panel recommends evaluating and recommending, if applicable, an effective contraceptive method panel for as long as pregnancy is not desirable (LE 2b; GR B; LA 73%).

We should recommend the use of effective contraceptive methods to both men and women, for as long as a pregnancy is not envisaged or when it is preferable to postpone it (e.g., owing to the severity of the disease, initiation of a teratogenic treatment).

Combined hormonal contraception is the most efficacious method,<sup>41</sup> except in the case of a contraindication.<sup>42</sup> How-

**Table 3** Planning the Pregnancy.

#	Action
1	<i>Complete gynecologic and obstetric history</i> Number of previous pregnancies (to term or not), route of delivery, number of induced and spontaneous abortions History of preeclampsia, HELLP syndrome, arterial hypertension, or thrombosis in previous pregnancies History of delayed growth or low birth weight Previous fertility problems
2	<i>Identification and evaluation of comorbidities</i> Metabolic syndrome (obesity, arterial hypertension, diabetes mellitus, hypercholesterolemia) Smoking and drinking Depression Other, depending on the patient
3	<i>Characteristics and severity of psoriasis (current and past)</i> Duration of psoriasis Type Location Severity
4	<i>Absolute and relative contraindications to pregnancy</i>
5	<i>Estimation of the risk of maternal-fetal complications during pregnancy</i> Individualized Age, activity, and damage caused by the disease itself and drugs Complications during previous pregnancies
6	<i>Treatments</i> Drugs used in the 3-36 months before deciding to become pregnant Time since the last dose of drugs that are contraindicated in pregnancy
7	<i>Complementary tests</i> Standard laboratory work-up (complete blood count, urine, biochemistry) Other, depending on the patient
8	<i>Re-evaluation of treatment options</i> In the case of clinical remission, maintenance of nonteratogenic drugs
9	<i>Information</i> Complications during pregnancy, puerperium, and breastfeeding Disease course Plan for action in the case of complications of the underlying disease and/or pregnancy Schedule for check-ups

Abbreviations: HELLP, hemolysis, elevated liver enzymes, low platelet count.

ever, the panel recommends tailoring the method to the individual case and referring the patient to a gynecologist or primary care if necessary.

While assisted reproduction is considered a gynecologic area, dermatologists who care for patients undergoing this process should be aware of the general aspects of the procedures in order to be able to provide appropriate information. The LA for the recommendation formulated with respect to this area (Recommendation 4, Table 1) was insufficient (see Discussion).

### Planning for Pregnancy

*Recommendation 4. The panel recommends referring the patient to a gynecologist for reproductive counseling (LE 5; GR D; LA 46%).*

*Recommendation 5. Planning for pregnancy should include an assessment of the gynecologic and dermatologic history, a laboratory analysis, assessment of current psoriasis and its treatment, assessment of comorbidities, and possible contraindications to pregnancy (LE 5; GR D; LA 93%).*

*Recommendation 6. The panel recommends that patients be informed on an individual basis about maternal-fetal risk factors in pregnancy and about all aspects of follow-up of the pregnancy, including postpartum (LE 5; GR D; LA 81%).*

*Recommendation 7. The panel recommends that psoriasis is controlled as well as possible before the patient tries to become pregnant (LE 2b; GR B; LA 78%).*

Pregnancy can affect psoriasis, and this (and its treatment) may be a risk factor for the course of the pregnancy.<sup>4,14,19-25</sup> Control of psoriasis and preconception use of drugs with a low risk for the fetus make it possible to reduce the risk of maternal-fetal complications. Therefore, it is essential to plan the pregnancy and ensure collaboration with a gynecologist and primary care physician.

Planning (Tables 3 and 4) should involve a personalized preconception assessment covering the patient's complete gynecologic and obstetric history, contraindications for pregnancy, and risk factors for maternal-fetal complications,<sup>22,25</sup> including the drugs used before and during pregnancy (Table 5).

**Table 4** Risk Factors for Maternal-Fetal Complications in Patients With Psoriasis.

<b>Previous Bad Obstetric History</b>
Severe preeclampsia
HELLP syndrome
Previous recurrent miscarriage
...
<b>Dependent on the Patient or on Psoriasis</b>
Age > 40 y
Family history of preeclampsia
Personal history of preeclampsia, multiple pregnancies, nulliparity, or diabetes
Obesity or arterial hypertension at the beginning of pregnancy
Moderate to severe psoriasis
Comorbidity
<b>Exposure to Teratogenic Drugs</b>
Between 6 and 36 mo before conception

Abbreviation: HELLP, hemolysis, elevated liver enzymes, low platelet count.

Psoriasis improves in 33%-60% of women during pregnancy,<sup>4,14,19</sup> remains unchanged in 25%, and worsens in 25%.<sup>14</sup> However, 40%-88% experience a flare-up after delivery.<sup>4,6,14,19,24,43–45</sup>

Data on the effect of psoriasis in pregnancy, childbirth, and the newborn are somewhat controversial.<sup>5,25,34,46–48</sup> Some studies associate poor results specifically with patients who have moderate to severe psoriasis.<sup>7,48</sup> At present, there are no data suggesting an association between psoriasis and the development of congenital malformations,<sup>7,49</sup> and while findings are heterogeneous, there does seem to be an association between psoriasis and the development of diabetes and gestational arterial hypertension.<sup>7,48</sup>

Finally, it is also essential to ensure that psoriasis is inactive for 3-4 months, using nonteratogenic drugs. If this is not possible, then the lowest degree of activity possible should be sought on an individual basis.

## Pregnancy and Follow-up

### Pregnancy

**Recommendation 8.** *The panel recommends establishing the most effective and safest pharmacological profile possible during pregnancy. This should be tailored to the individual patient (LE 5; GR D; LA 98%).*

Knowledge of safety of medications is one of the pillars of effective and safe medical and obstetric care (Table 5). However, we lack sufficient evidence to provide robust, explicit recommendations for all drugs.<sup>9,50,51</sup> Therefore, during pregnancy, drugs should be prescribed with caution, after performing a meticulous evaluation of the risks and benefits for each patient and taking informed decisions, which should be agreed with the patient.<sup>40</sup>

### Topical Drugs

**Recommendation 9.** *Potentially teratogenic topical agents (anthralin, tazarotene, topical psoralen-UV-A [PUVA]) should be discontinued once pregnancy is confirmed. Top-*

*ical drugs with a more favorable safety profile should be considered (LE 3a; GR C; LA 98%).*

The panel also considers it important to assess the risk-benefit ratio on an individual basis. In the case of topical drugs with a more favorable safety profile, these should be prescribed at the lowest dose possible over as small an area as possible for as short a time as possible. Occlusive dressings should be avoided (Table 5).

The only association reported for topical corticosteroids is between low birth weight and the use of high- and very-high-potency corticosteroids, especially when the duration of exposure and cumulative dose are considerable.<sup>15,52</sup> Topical calcineurin inhibitors<sup>15</sup> and calcipotriol have been shown to be safe. However, maternal vitamin D deficiency can be associated with a teratogenic risk. As for coal tar, there are no data to suggest teratogenicity or poor pregnancy outcome in humans, although cases of malformation have been reported in animals.<sup>15,53,54</sup> A moderate amount of topical salicylic acid (9%-25%) can be absorbed systemically, and it has been reported that use of this agent during the first trimester could be associated with an increased risk of gastroschisis.<sup>15,55</sup> It is important to note that phototherapy with narrowband UV-B radiation is safe during pregnancy.<sup>56</sup>

While teratogenicity and poor pregnancy outcome have not been reported with anthralin, this agent should be suspended 4 weeks before conception.<sup>15</sup> As for topical tazarotene, it is estimated that 6% is absorbed systemically<sup>57,58</sup>; in addition, systemic absorption may increase owing to individual factors, such as damage to the skin barrier. Although there are no data pointing to embryopathy, this drug is contraindicated during pregnancy. Similarly, topical PUVA drugs are not recommended during pregnancy.<sup>15</sup>

### Systemic Drugs

**Recommendation 10.** *Potentially teratogenic systemic agents (acitretin, systemic retinoids, systemic PUVA, apremilast, dimethyl fumarate, methotrexate) should be discontinued before conception. Prescription of topical and/or systemic and/or phototherapy with a better safety profile should be considered (LE 3a; GR C; LA 97%).*

No cases of congenital malformations or other relevant problems have been reported for systemic corticosteroids.<sup>59–61</sup>

Acitretin is a potent teratogen in humans.<sup>62,63</sup> It can be detected in blood 2 months after the last dose, although in some circumstances, such as the presence of alcohol, it can be converted to etretinate and be detected for 120 days. Therefore, it is usually recommended to suspend this drug for up to 2 years before conception. Cases should be managed on an individual basis.<sup>15,64,65</sup> Other oral retinoids, such as alitretinoin and isotretinoin are also contraindicated during pregnancy.<sup>39,40</sup>

Potential associations between systemic PUVA agents and teratogenic complications remain unclear<sup>15,66,67</sup>; therefore, these agents are contraindicated during pregnancy. Narrowband UV-B phototherapy, on the other hand, has proven to be safe during pregnancy.<sup>56</sup>

No data are currently available on the teratogenic potential of apremilast in humans, although abortion and low birth weight have been reported in animals; consequently, its use

**Table 5** Safety of Commonly Used Dermatologic Drugs With Respect to Fertility and Pregnancy.

Drug	MR	FR	FDA	AEMPS and Other Data	Ref
[0,1-6]Topical Corticosteroids	U	U	B-C	-No data on effect on the fetus or on other pregnancy outcomes in humans -If corticosteroids are necessary, topical agents should not be used extensively during pregnancy, that is, in large amounts, or over long periods, or over wide areas. Occlusive dressings should be avoided	98-100,116
Calcineurin inhibitors -Pimecrolimus -Tacrolimus	U	U	C	-No data on the effect on the fetus or on other pregnancy outcomes -Do not use during pregnancy, except when the potential benefit outweighs the potential risk for the fetus	117-120
Calcipotriol	U	U	C	-Animal studies have revealed cases of cleft palate and lack of lung maturation - No data on the effect on the fetus or on other outcomes of pregnancy in humans - Do not use during pregnancy, except when the potential benefit outweighs the potential risk for the fetus	104
Anthralin	U	U	C	-No animal or human data -Experts recommend suspending treatment for 4 wk before conception and avoiding it during pregnancy	
Coal tar	U	U	C	-AEMPS: not mentioned - Animal studies have revealed cases of cleft palate and lack of lung maturation -During pregnancy, the product should be used intermittently, at low concentrations and over a reduced body surface area. Coal tar should be avoided during the first trimester	53,54,101
Salicylic acid	U	U	C	-Experts recommend avoiding this agent at high doses (> 3%) and in large amounts (e.g., > 20 g/d). Occlusive dressings should also be avoided -AEMPS: not mentioned	
Retinoids (tazarotene)	U	U	X	-No data for humans -Contraindicated during pregnancy -AEMPS: not mentioned	13
Topical PUVA	U	U	C	- No data for humans -Experts recommend avoiding the drug during pregnancy -AEMPS: not mentioned	67
NBUVB	U	U	-	-Few data in humans (occasional case reports) -Experts consider that it can be used during pregnancy -AEMPS: not mentioned	56
[0,1-6]Systemic Corticosteroids			B-C	-AEMPS: No need to interrupt if administered at standard doses	59,60
Acitretin	U	U	X	-Teratogenic in humans -AEMPS: Contraindicated during pregnancy	12
Other retinoids	U	U	X	-Teratogenic in humans -AEMPS: Contraindicated during pregnancy	39,40
PUVA	U	U	C	-Possible teratogenic effect -Experts recommend avoiding the drug during pregnancy -AEMPS: not mentioned	15,66,67



Table 5 (Continued)

Drug	MR	FR	FDA	AEMPS and Other Data	Ref
NBUVB	U	U	–	-Not associated with teratogenicity -AEMPS: not mentioned	56
Apremilast	U	U	C	-No data for humans -Cases of miscarriage reported in animals -AEMPS: Contraindicated during pregnancy	15
Dimethyl fumarate	U	U	C	-No data for humans -Experts recommend not using the drug during pregnancy -AEMPS: Contraindicated during pregnancy	9
Methotrexate	D	U	X	-Cases of miscarriage and congenital malformations reported in animals. This effect seems to be dose-dependent in humans and is associated mainly with high drug doses -AEMPS: Contraindicated during pregnancy	109
Ciclosporin A	U	U	C	-Case reports of low birth weight and preterm birth -AEMPS: Use if benefits outweigh risks	73–75
Infliximab	U	U	B	-No data showing an association with teratogenicity or poor pregnancy outcomes -AEMPS: Use if benefits outweigh risks	83,121
Adalimumab	U	U	B	-No data showing an association with teratogenicity or poor pregnancy outcomes -AEMPS: Use if benefits outweigh risks	15,83
Etanercept	U	U	B	- No data showing an association with teratogenicity or poor pregnancy outcomes -AEMPS: Not recommended	84
Certolizumab pegol	U	U	B	-Data similar to those for the general public -Approved by the EMA for use during pregnancy	81,82,122,123
Brodalumab	U	U	B	-Few data for humans -AEMPS: Preferably avoid	113
Secukinumab	U	U	B	-No data showing an association with teratogenicity or poor pregnancy outcomes -AEMPS: Preferably avoid	89
Ustekinumab	U	U	B	-Lack of data for humans -AEMPS: Preferably avoid	78,87,88,124
Ixekizumab	U	U	B	-Few data in humans -AEMPS: Preferably avoid	15
Guselkumab	U	U	B	-Few data in humans -AEMPS: Preferably avoid	125

Abbreviations: AEMPS, Agencia Española del Medicamento y Productos Sanitarios (Spanish Agency of Medicines and Medical Devices); D, doubtful; FDA, Food and Drug Administration; FR, fetal risk; MR, maternal risk; NBUVB, narrowband UV-B phototherapy; PUVA, psoralen-UV-A; U, unknown.

is contraindicated in pregnancy.<sup>15</sup> Similarly, the lack of data in humans for dimethyl fumarate means that this agent is not recommended.<sup>9</sup>

Animal data show that, in addition to causing abortion, methotrexate is a teratogenic drug. However, various observational studies suggest that defects are induced with doses of methotrexate greater than 10 mg/wk and that the critical period would be 6–8 weeks after conception.<sup>68–72</sup> This drug is currently contraindicated in pregnancy and should be suspended 3 months before conception.

Finally, ciclosporin A has been associated with a greater risk of low birth weight and preterm birth in pregnant women who have received solid organ transplants, but not with a greater risk of congenital abnormalities.<sup>73–75</sup>

### Biologic Therapy

*Recommendation 11. In the case of women receiving biologic therapy, the panel recommends that this be maintained during the first and second trimesters. Together with the patient, the clinician should evaluate the risks and benefits of continuing these drugs during the third trimester. Patients taking certolizumab pegol can continue the drug throughout pregnancy only if it is considered clinically necessary (LE 3a; GR C; LA 88%).*

In the case of monoclonal antibodies, transfer of immunoglobulin (Ig) G antibodies begins in the second trimester by means of binding to placental Fc receptors.<sup>9</sup> Nevertheless, not all monoclonal antibodies have the same affinity for binding to these receptors. IgG1 (adalimumab,

infliximab, secukinumab, ustekinumab, guselkumab), IgG2 (brodalumab), and IgG4 (ixekizumab) probably cross the placenta in a similar fashion.<sup>76-78</sup> Levels of infliximab have even been detected in newborns up to 6 months after birth. However, while etanercept has lower affinity<sup>79,80</sup>, reduced or no placental transfer has been reported mainly for certolizumab pegol (which lacks an Fc receptor).<sup>81,82</sup>

No associations have been reported for anti-TNF- $\alpha$  agents with respect to teratogenic capacity and poor pregnancy outcomes (including maternal infections).<sup>83,84</sup> Data on certolizumab pegol from prospective studies with more than 500 pregnant women do not show an increased risk of malformation or miscarriage.<sup>85,86</sup> Therefore, the regulatory agencies have approved certolizumab pegol for use during pregnancy and breastfeeding.

No or few data are available for brodalumab, ustekinumab,<sup>78,87,88</sup> secukinumab,<sup>89</sup> ixekizumab, and guselkumab.

### Follow-up

*Recommendation 12. Patients with psoriasis who require standard systemic treatments and/or biologics to control their disease must be followed up closely by an obstetrician once the pregnancy is confirmed (LE 5; GR D; LA 92%).*

Where possible, follow-up should be in a high-risk pregnancy unit (see section on multidisciplinary care, Recommendation 15).

*Recommendation 13. The panel recommends strict follow-up and monitoring of pregnant women with psoriasis (LE 5; GR D; LA 83%).*

As in the case of any other patient with psoriasis, pregnant women should be evaluated in terms of their disease.

The frequency of visits depends on the obstetric assessment and the type and status of psoriasis. In general, for a clinically stable patient with low or no disease activity, visits can be every 4-6 weeks during the first 2 trimesters, increasing in frequency from week 32 onward until term, depending on the individual characteristics of the patient. In the case of flare-ups or obstetric complications, the frequency is decided by the attending physicians. Direct and fast access must be ensured for clarification of doubts and resolution of dermatologic or obstetric complications.

Evaluation should be systematic and include a basic physical examination and measurement of arterial blood pressure and weight. The laboratory analysis should include a complete blood count and simple biochemistry work-up with urinalysis (manual and sedimentation). Severity and other disease-related variables are evaluated in line with daily clinical practice.

Finally, the panel considers that the dermatologist should be involved throughout follow-up, irrespective of whether the patient has been followed in a high-risk pregnancy unit or in a general obstetrics clinic.

*Recommendation 14. In the case of a flare-up, the panel recommends treating each case on an individual basis, taking into account type and severity, week of gestation, and available therapeutic options (LE 5; GR D; LA 100%).*

Therapy should be decided on an individual basis in each case and agreed with the patient and, if necessary, with the gynecologist-obstetrician.

When a pregnant patient with psoriasis develops an infection requiring treatment with antibiotics, the drug chosen should have a good safety profile in pregnancy.<sup>90</sup>

*Recommendation 15. The panel recommends encouraging cooperation between specialties (e.g., dermatology, obstetrics, pediatrics) (LE 5; GR D; LA 98%).*

Where possible, every attempt should be made to ensure multidisciplinary care of the patient involving gynecologists experienced in high-risk pregnancies and dermatologists. This approach is greatly facilitated by the electronic medical history. Coordination with the primary care physician is also recommended.

### Breastfeeding, Postpartum, and Perinatal Care

Psoriasis itself is not a contraindication for breastfeeding, although some of the drugs prescribed to treat it may be (Table 6).<sup>91</sup>

The risk of a postpartum flare-up is important. In addition, mothers are more likely to experience Koebner phenomena owing to the irritation caused by suction and contact with the baby. Psoriasis in the area of the nipple generally manifests as well-defined erythematous plaques with fine scale.<sup>92</sup>

In principle, breastfeeding does not interfere with administration of most vaccines to the mother (both inactivated and attenuated), despite the presence of maternal antibodies in milk.<sup>93-95</sup> An exception can be found in vaccines against smallpox and yellow fever. Since these vaccines have been associated with severe conditions in neonates, such as encephalitis, they are contraindicated.<sup>96,97</sup>

As during pregnancy, any decision taken during breastfeeding should be agreed upon with the patient.

*Recommendation 16. Emollients can be prescribed during breastfeeding (LE 4; GR C, LA 83%).*

There are no reports of emollients causing problems for neonates.

*Recommendation 17. With respect to topical treatments for psoriasis during breastfeeding, tazarotene is contraindicated. Other topical agents can be used providing that the benefits outweigh the risks, at minimum doses, and for as short a period as possible. The area of the nipple and areola should be avoided (LE 4; GR C; LA 97%).*

Despite the paucity of data, topical tazarotene is contraindicated. In general, no relevant problems have been reported for the other topical treatments, except for irritation of the baby's skin and 1 case of iatrogenic hypertension in a baby whose mother was receiving a high-dose corticosteroid that included the area of the nipple.<sup>15,98-104</sup>

*Recommendation 18. Topical PUVA is not recommended during breastfeeding. Narrowband UV-B phototherapy can be used (LE 4; GR C; LA 95%).*

While there are no data on the effect on the infant,<sup>13,104</sup> the experts recommend using another type of phototherapy. In this sense, narrowband UV-B phototherapy has proven safe during breastfeeding.<sup>56</sup>

*Recommendation 19. Systemic corticosteroids can be used during breastfeeding as long as the benefits outweigh the risks. They should be administered at minimum doses and for as short a time as possible (LE 4; GR D; LA 80%).*

Corticosteroids are excreted in low amounts in breast milk,<sup>105</sup> and there have been no reports of adverse events

**Table 6** Safety of the Most Commonly Used Dermatologic Drugs During Breastfeeding.

Drug	Breastfeeding	Ref
<i>Topical</i> Corticosteroids	<p>Studies, AEMPS</p> <ul style="list-style-type: none"> <li>-Corticosteroids are a normal component of breast milk, with a mean concentration of 7 µg/L</li> <li>-Exposure of the baby via breast milk is minimal</li> <li>-A case of iatrogenic hypertension has been reported in a baby exposed to high-potency topical corticosteroids that had been applied directly on the nipple</li> <li>-Experts do not consider these agents to be problematic in breastfeeding</li> <li>-The AEMPS does not recommend topical corticosteroids during breastfeeding</li> </ul>	98–100
Calcineurin inhibitors -Pimecrolimus -Tacrolimus	<ul style="list-style-type: none"> <li>-When used topically, systemic absorption is slight owing to their molecular weight. Absorption is increased if applied to the area of the nipple</li> <li>-Experts consider these drugs to be safe</li> <li>-The AEMPS does not recommend these agents during breastfeeding or recommends that they be used with caution, avoiding the breast</li> </ul>	116–121
Calcipotriol	<ul style="list-style-type: none"> <li>-Systemic absorption is slight with topical calcipotriol, although this increases if applied on the area of the nipple</li> <li>-AEMPS: Caution should be exercised when prescribing to breastfeeding women. Avoid application to the breast</li> </ul>	103,104
Anthralin	<ul style="list-style-type: none"> <li>-No reports of problems with use during breastfeeding, except for irritation of the baby's skin</li> <li>-Experts consider anthralin to be safe</li> <li>-AEMPS: not mentioned</li> </ul>	15
Coal tar	<ul style="list-style-type: none"> <li>-Since treatment is generally used over a large body surface area, it is difficult to prevent the fetus from being exposed</li> <li>-No problems reported with coal tar, except irritation of the baby's skin</li> <li>-Experts consider coal tar to be a safe therapy</li> <li>-The AEMPS provides no specific information</li> </ul>	15,101,102
Salicylic acid	<ul style="list-style-type: none"> <li>-Given the possibility of Reye syndrome, the experts recommend avoiding applying this drug to the nipple, using it at low concentrations (e.g., 1%-2%) and in small doses (e.g., &lt;20 g/d) for short periods</li> <li>-Experts consider this agent to be safe</li> <li>-The AEMPS provides no specific information</li> </ul>	15
Retinoids (tazarotene)	<ul style="list-style-type: none"> <li>-No data in humans</li> <li>-Experts do not recommend this agent during breastfeeding</li> <li>-AEMPS: Tazarotene is contraindicated, adapalene can be used. Tretinoin can be used if the therapeutic benefit outweighs potential risks</li> </ul>	13
Topical PUVA	<ul style="list-style-type: none"> <li>-No data in humans for the effect on the infant</li> <li>-The experts recommend suspending or delaying breastfeeding for 5-24 h after the last dose</li> <li>-AEMPS: not mentioned</li> </ul>	67
NBUVB	<ul style="list-style-type: none"> <li>-Few data in humans (occasional case reports)</li> <li>-The experts consider that NBUVB can be used during breastfeeding</li> <li>-AEMPS: not mentioned</li> </ul>	
[0,1-3]Systemic Corticosteroids	<ul style="list-style-type: none"> <li>-Amounts of corticosteroids in breast milk are very low. In the case of mothers receiving doses of 10-80 mg/d, the relative doses found in nursing infants are 0.02% to 0.074% (0.002-0.059 mg), which represent 10% of the child's endogenous cortisol level</li> <li>-No major adverse events reported in infants</li> <li>-Wait 3-4 h after ingestion in order to minimize exposure</li> <li>-Reduced prolactin has been observed with dexamethasone</li> <li>-AEMPS: Prednisone is excreted in minimal amounts. No reports of harm to the child, although long-term treatment with high doses could affect adrenal function. Therefore, the infant should be monitored. Breastfeeding should be interrupted if very high doses are required for therapeutic reasons</li> </ul>	59,60,105,106,122

Table 6 (Continued)

Drug	Breastfeeding	Ref
Acitretin	-Information on maternal doses of acitretin and its transfer to breast milk is limited (0.65 mg/kg/d leads to excretion of low concentrations in breast milk, approximately 1%). However, there is some doubt over its cumulative toxic burden. Immaturity of the kidney and liver in the neonate could lead to problems with excretion	12,107
Other retinoids	-AEMPS: Contraindicated during breastfeeding	39,40
PUVA	-AEMPS: Contraindicated during breastfeeding -Excretion in breast milk, although no clear data on its effect on the infant -Experts recommend suspending or delaying breastfeeding for 5-24 h after the last dose (until 95% has been cleared in urine)	13,104
NBUVB	-AEMPS: not mentioned -No problems for infant	56
Apremilast	-AEMPS: not mentioned -Data in mice show that apremilast levels are 1.5-fold higher in milk than in blood	15,123
Dimethyl fumarate	-AEMPS: Given the paucity of available information at present, it is better to avoid apremilast during breastfeeding -Given the low molecular weight of this drug, levels in milk are likely to be approximately equivalent to those in maternal blood. Calculating the average level in maternal blood, the infant will receive roughly 3.5% of the dose adjusted for the mother's weight	108
Methotrexate	-AEMPS: Contraindicated during breastfeeding -At immunomodulatory doses (<0.4 mg/kg/wk), levels in breast milk are very low (proportion of breast milk to plasma, 0.08:1)	109
Ciclosporin A	-AEMPS: Contraindicated during breastfeeding -Ciclosporin is excreted in breast milk, although levels were not detectable in most infants studied. Commercial presentations contain ethanol, which should also be taken into account during breastfeeding	74,110
Infliximab	-AEMPS: Contraindicated during breastfeeding - Not generally detected in breast milk or at low doses	124
Adalimumab	-AEMPS: As human immunoglobulins are excreted in milk, women should not breastfeed for at least 6 months after treatment -Not generally detected in breast milk or at low doses, with concentrations in human milk of 0.1% to 1.0% of the maternal serum level	15,112
Etanercept	-AEMPS: Can be used during breastfeeding -Not generally detected in breast milk or at low doses	111
Certolizumab pegol	-AEMPS: Decide whether it is necessary to interrupt breastfeeding or interrupt treatment with etanercept after considering the benefit of breastfeeding for the child and the benefit of treatment for the mother. -Not generally detected in breast milk or detected at low doses	115
Brodalumab	-Approved for use in breastfeeding by the EMA -Transfer to breast milk unknown	15
Secukinumab	-AEMPS: Decide whether to interrupt breastfeeding or to interrupt/not start treatment with brodalumab after considering the benefit of breastfeeding for the infant and the benefit of treatment for the mother -In general, not detected in breast milk or at low doses.	15
Ustekinumab	-AEMPS: Decide whether breastfeeding is to be interrupted during treatment and for up to 20 wk after treatment or interrupt treatment, taking into account the benefit of breastfeeding for the child or the benefit of treatment for the mother -No data in humans	78,125
Ixekizumab	-AEMPS: The decision to interrupt breastfeeding during treatment and for up to 15 weeks after treatment or to suspend treatment should be taken after evaluating the beneficial effects of breastfeeding for the infant and the benefits of ustekinumab for the mother -No data on humans	15

(Continued)

Drug	Breastfeeding	Ref
Guselkumab	-No data in humans -AEMPS: Decide whether to interrupt breastfeeding during treatment and up to 12 weeks after the last dose or suspend treatment, once the benefit of breastfeeding and the benefit of treatment for the mother have been considered	126,127

Abbreviations: AEMPS, Agencia Española del Medicamento y Productos Sanitarios (Spanish Agency of Medicines and Medical Devices); EMA, European Medicine Agency; NBUVB, narrowband UV-B phototherapy.

in infants (although the studies analyzed show that the dose of corticosteroids taken by mothers was 5-10 mg/d).<sup>106</sup>

**Recommendation 20.** *Oral retinoids, apremilast, dimethyl fumarate, methotrexate, and ciclosporin A are not recommended during breastfeeding (LE 4; GR D; LA 95%).*

While oral retinoids are excreted in small amounts in breast milk, their possible cumulative toxicity remains unclear in newborns, whose immaturity may hamper their ability to eliminate these drugs.<sup>12,107</sup>

Apremilast is excreted in breast milk. While no studies have been performed in humans, the drug is contraindicated based on data from animal studies.<sup>56</sup> Dimethyl fumarate is also excreted in breast milk, possibly at doses equivalent to the plasma doses of the mother; therefore, it is not recommended during breastfeeding.<sup>108</sup>

Methotrexate is excreted in very low concentrations in breast milk, and there are no data to suggest problems for neonates. However, since methotrexate has the capacity to accumulate in tissue, excretion could be hampered by renal immaturity in the neonate.<sup>109</sup> Therefore, methotrexate is not recommended, as with ciclosporin A, which is also excreted, although levels in infants are almost undetectable.<sup>74,110</sup>

**Recommendation 21.** *Certolizumab pegol has been approved for use during breastfeeding. For all other biologics, the panel recommends assessing the risks and benefits in each case (LE 4; GR D; LA 93%).*

Since many monoclonal antibodies have a high molecular weight, they are excreted in breast milk in either very small amounts or not at all. Furthermore, most are digested in the newborn's gastrointestinal tract.<sup>15,111–114</sup> However, data on these agents are very scarce for newborns; therefore, prudence is recommended when prescribing.

Certolizumab pegol is excreted in breast milk either in very small amounts or not at all. No problems have been reported with neonates, and the drug is approved for use during breastfeeding.<sup>115</sup>

**Recommendation 22.** *Once the pregnancy has come to term, usual follow-up should be resumed in the dermatology clinic as soon as possible (LE 5; GR D; LA 88%).*

It is important to resume follow-up in the dermatology clinic as soon as possible after delivery, because there is a considerable risk of flare-ups at this time, mainly in patients whose disease was active during pregnancy, especially during the first trimester. Other factors associated with flare-ups include preterm delivery and low birth weight. The frequency of visits depends on the individual case.

Evaluation of the activity of psoriasis should be tailored in line with daily clinical practice.

Medications can be reintroduced or switched according to the patient's progress. This means, for example, that a patient in remission whose medication was suspended because she was pregnant does not require the drug to be reintroduced while she continues to be in remission.

**Recommendation 23.** *The neonate does not require special care, except if the mother has been exposed to biologics that cross the placenta and have been maintained beyond the second trimester (LE 5; GR D; SA 87%).*

Neonates who have been exposed to drugs (monoclonal antibodies) that cross the placenta during pregnancy may have a slightly increased risk of infection over a variable period of up to 6-9 months.<sup>15</sup> Therefore, in these cases, the newborn should be vaccinated with inactivated virus according to the vaccination schedule and with live virus only after 6 months. It is also recommended to perform laboratory testing during the first few weeks owing to the potential onset of neutropenia.

## Discussion

In the present document, which was promoted by the Psoriasis Working Group of the AEDV, we present a series of practical recommendations on fertility, pregnancy, postpartum, and breastfeeding for patients with psoriasis. The recommendations are based on the best currently available evidence.

We followed the nominal group method and the Delphi process, which are widely used for this type of document. Our approach was carried out with the participation of a nationally recognized multidisciplinary expert panel, who based the recommendations on a systematic review and their experience. We highlight the high level of agreement in the recommendations; only one did not reach the required level. In addition, the Delphi process was extended to a large group of dermatologists, thus reinforcing the validity of the recommendations.

The only recommendation for which the established level of agreement was not reached was that concerning referral to a gynecologist for reproductive counseling. This recommendation was rejected probably because the dermatologist felt responsible and able to counsel or at least inform the patient objectively and reliably about various aspects of reproduction. The present document will help in this task. After some reflection, it was decided not to reformulate the recommendation and, therefore, not to submit it for a second Delphi round.

The final objective of these recommendations is to improve outcomes in this area, but mainly in terms of pregnancy. In this sense, the expert panel would like to reinforce several messages. The first involves preconception counseling, which should be offered to all patients of reproductive age, irrespective of the treatment they receive. In addition, the professional's door should always remain open so that the patient feels confident asking about any aspect of pregnancy: a well-informed patient is more likely to reach the objectives set. The panel also considers it essential to plan pregnancy correctly. Ideally, the woman should become pregnant when psoriasis is controlled (or as well controlled as possible) and patients are receiving drugs considered safe for the pregnancy and the fetus. Thus, this planning may involve, for example, a change in treatment or an in-depth evaluation of psoriasis. Finally, the outcome of pregnancy is more likely to be successful in a context of multidisciplinary care based on teamwork and identification and comprehension of the possible specific risks for an individual patient.

In summary, explicit recommendations must be made to guide clinicians in the management of patients with psoriasis during reproductive age. Although evidence remains scarce in some areas, this document presents a series of recommendations that we believe could prove relevant and useful. Furthermore, the recommendations are simple and can be implemented without difficulty. The panel is convinced that following the recommendations provided here will improve management of affected patients and, therefore, their prognosis and that of their descendants.

## Funding

This project was funded by an unrestricted grant from UCB.

## Conflicts of Interest

MAM has given talks and provided consultancy services for and attended scientific meetings sponsored by AbbVie, Pfizer, MSD, Janssen, Novartis, Lilly, Almirall, Amgen, Cellgene, Leo, and UCB Pharma.

MGB has received clinical trial/study and speaking fees and grants for attending meetings and conferences from AbbVie, Novartis, LEO Pharma, Wyeth, MSD, Cellgene, Lilly, Janssen, and UCB Pharma.

OBR has received consultancy and speaking fees from Janssen-Cilag, AbbVie, Pfizer, Novartis, Lilly, Cellgene, Leo Pharma, UCB, and Almirall.

APF has received consultancy and speaking fees from AbbVie, Almirall, Leo, Lilly, Novartis, Pfizer, Cellgene, and Janssen.

JMC has received consultancy and speaking fees from Cellgene, Janssen, Lilly, Novartis, Leo Pharma, Pfizer, MSD, AbbVie, and Biogen Amgen.

RTF has received consultancy and speaking fees from Leo Pharma, Lilly, Janssen, Cellgene, Novartis, AbbVie, MSD, Pfizer, and Almirall.

IB has received consultancy and speaking fees from Cellgene, Janssen, Lilly, Novartis, Leo Pharma, Pfizer, MSD, AbbVie, and Amgen.

The remaining authors declare that they have no conflicts of interest.

## Acknowledgments

We are grateful to the following doctors for their participation in the Delphi process: Gloria Aparicio Español, Ana Batalla Cebey, Marta Ferran Farrés, Alba Calleja Algarra, Antonio Sahuquillo Torralba, Servando Eugenio Marrón Moya, Carlos Ferrándiz Foraster, Daniel Jesús Godoy Díaz, Carlos Muñoz Santos, Álvaro González-Cantero, Noemí Eiris Salvado, Laura Salgado Boquete, Conrad Pujol Marco, Vicenç Rocamora Duran, Anna López Ferrer, Carmen Rodríguez Cerdeira, Elena del Alcázar Viladomiu, Rosario Fátima Lafuente Urrez, Ana María Carrizosa Esquivel, Amparo Pérez Ferriols, Ander Zulaica Garate, Diana P. Ruiz Genao, Almudena Mateu Puchades, Ignacio Yanguas Bayona, Almudena Fernández Orland, José Carlos Moreno Giménez, Alberto Romero Maté, Alberto Conde Taboada, Beatriz Pérez Suárez, Miquel Ribera Pibernat, Eva Vilarrasa Rull, José Manuel Fernández Armenteros, Silvia Pérez Barrio, Miren Josune Michelena Eceiza, Cristina Rubio Flores, José Carlos Ruiz Carrascosa, Mónica Larrea García, Gregorio Carretero Hernández, José Luis Sánchez Carazo, Marc Julià Manresa, Luis Puig Sanz, Lourdes Rodríguez Fernández-Freire, Manuel Galán Gutiérrez, Alicia González Quesada, Estrella Simal Gil, Juan José Andrés Lencina, María Luisa Alonso Pacheco, Laura García Fernández, Mar Llamas Velasco, Pablo de la Cueva Dobao, Jaime Notario Rosa, Fco. Javier García Latasa de Aranibar.

We thank Dr Estibaliz Loza for her support and coordination of the methodology applied in the project.

## Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:<https://doi.org/10.1016/j.adengl.2020.10.031>.

## References

- Ferrandiz C, Carrascosa JM, Toro M. Prevalence of psoriasis in Spain in the age of biologics. *Actas Dermosifiliogr.* 2014;105:504–9.
- Parisi R, Symmons DP, Griffiths CE, Ashcroft DM, Identification, Management of P, et al. Global epidemiology of psoriasis: a systematic review of incidence and prevalence. *J Invest Dermatol.* 2013;133:377–85.
- Kimball AB, Leonardi C, Stahle M, Gulliver W, Chevrier M, Fakharzadeh S, et al. Demography, baseline disease characteristics and treatment history of patients with psoriasis enrolled in a multicentre, prospective, disease-based registry (PSO-LAR). *Br J Dermatol.* 2014;171:137–47.
- Tauscher AE, Fleischer AB Jr, Phelps KC, Feldman SR. Psoriasis and pregnancy. *J Cutan Med Surg.* 2002;6:561–70.
- Bandoli G, Chambers CD. Autoimmune conditions and comorbid depression in pregnancy: examining the risk of preterm birth and preeclampsia. *J Perinatol.* 2017;37:1082–7.
- Polachek A, Li S, Polachek IS, Chandran V, Gladman D. Psoriatic arthritis disease activity during pregnancy and the first-year postpartum. *Semin Arthritis Rheum.* 2017;46:740–5.
- Broms G, Haerskjold A, Granath F, Kieler H, Pedersen L, Berglind IA. Effect of Maternal Psoriasis on Pregnancy and Birth Outcomes: A Population-based Cohort Study from Denmark and Sweden. *Acta Derm Venereol.* 2018;98:728–34.

8. Danesh M, Murase JE. The immunologic effects of estrogen on psoriasis: A comprehensive review. *Int J Womens Dermatol*. 2015;1:104–7.
9. Brown SM, Aljefri K, Waas R, Hampton P. Systemic medications used in treatment of common dermatological conditions: safety profile with respect to pregnancy, breast feeding and content in seminal fluid. *J Dermatolog Treat*. 2018:1–17.
10. Gutierrez JC, Hwang K. The toxicity of methotrexate in male fertility and paternal teratogenicity. *Expert Opin Drug Metab Toxicol*. 2017;13:51–8.
11. Tugrul Ayanoglu B, Ozdemir ED, Turkoglu O, Alhan A. Diminished ovarian reserve in patients with psoriasis. *Taiwan J Obstet Gynecol*. 2018;57:227–30.
12. Rollman O, Pihl-Lundin I. Acitretin excretion into human breast milk. *Acta Derm Venereol*. 1990;70:487–90.
13. Briggs GG, Freeman RK, Yaffe SJ. *Drugs in pregnancy and lactation: a reference guide to fetal and neonatal risk*. Philadelphia (PA): Wolters Kluwer Health / Lippincott Williams & Wilkins; 2011.
14. Murase JE, Chan KK, Garite TJ, Cooper DM, Weinstein GD. Hormonal effect on psoriasis in pregnancy and post partum. *Arch Dermatol*. 2005;141:601–6.
15. Rademaker M, Agnew K, Andrews M, Armour K, Baker C, Foley P, et al. Psoriasis in those planning a family, pregnant or breastfeeding. The Australasian Psoriasis Collaboration. *Australas J Dermatol*. 2018;59:86–100.
16. Maccari F, Fougerousse AC, Esteve E, Frumholtz L, Parier J, Hurabielle C, et al. Crossed looks on the dermatologist's position and the patient's preoccupations as to psoriasis and pregnancy: preliminary results of the PREGNAN-PSO study. *J Eur Acad Dermatol Venereol*. 2019;33:880–5.
17. Fitch K, Bernstein S, Aguilar M, Burnand B, LaCalle J, Lazaro P, et al. [http://www.rand.org/content/dam/rand/pubs/monograph\\_reports/2011/MR1269.pdf](http://www.rand.org/content/dam/rand/pubs/monograph_reports/2011/MR1269.pdf), 2011.
18. CEBM. <http://www.cebm.net/index.aspx?o=1025>, 2011.
19. Boyd AS, Morris LF, Phillips CM, Menter MA. Psoriasis and pregnancy: hormone and immune system interaction. *Int J Dermatol*. 1996;35:169–72.
20. Farber EM, Nall ML. The natural history of psoriasis in 5,600 patients. *Dermatologica*. 1974;148:1–18.
21. Oumeish OY, Al-Fouzan AW. Miscellaneous diseases affected by pregnancy. *Clin Dermatol*. 2006;24:113–7.
22. Bandoli G, Johnson DL, Jones KL, Lopez Jimenez J, Salas E, Mirasoul N, et al. Potentially modifiable risk factors for adverse pregnancy outcomes in women with psoriasis. *Br J Dermatol*. 2010;163:334–9.
23. Traupe H, van Gurp PJ, Happle R, Boezeman J, van de Kerkhof PC. Psoriasis vulgaris, fetal growth, and genomic imprinting. *Am J Med Genet*. 1992;42:649–54.
24. Ben-David G, Sheiner E, Hallak M, Levy A. Pregnancy outcome in women with psoriasis. *J Reprod Med*. 2008;53:183–7.
25. Harder E, Andersen AN, Kamper-Jorgensen M, Skov L. No increased risk of fetal death or prolonged time to pregnancy in women with psoriasis. *J Invest Dermatol*. 2014;134:1747–9.
26. Gladman DD, Anhorn KA, Schachter RK, Mervart H. HLA antigens in psoriatic arthritis. *J Rheumatol*. 1986;13:586–92.
27. Swanbeck G, Inerot A, Martinsson T, Enerback C, Enlund F, Samuelsson L, et al. Genetic counselling in psoriasis: empirical data on psoriasis among first-degree relatives of 3095 psoriatic probands. *Br J Dermatol*. 1997;137:939–42.
28. Caldarola G, Milardi D, Grande G, Quercia A, Baroni S, Morelli R, et al. Untreated Psoriasis Impairs Male Fertility: A Case-Control Study. *Dermatology*. 2017;233:170–4.
29. El-Beheiry A, El-Mansy E, Kamel N, Salama N. Methotrexate and fertility in men. *Arch Androl*. 1979;3:177–9.
30. Heppt F, Colsman A, Maronna A, Uslu U, Heppt MV, Kiesewetter F, et al. Influence of TNF-alpha inhibitors and fumaric acid esters on male fertility in psoriasis patients. *J Eur Acad Dermatol Venereol*. 2017;31:1860–6.
31. Horn EJ, Chambers CD, Menter A, Kimball AB, International Psoriasis C. Pregnancy outcomes in psoriasis: why do we know so little? *J Am Acad Dermatol*. 2009;61:e5–8.
32. Saougou I, Markatseli TE, Papagoras C, Kaltsonoudis E, Voulgari PV, Drosos AA. Fertility in male patients with seronegative spondyloarthropathies treated with infliximab. *Joint Bone Spine*. 2013;80:34–7.
33. Schill WB, Hofmann C, Plewig G. [Semen analysis under photochemotherapy (PUVA-therapy) (author's transl)]. *Arch Dermatol Res*. 1979;264:153–60.
34. Yang Y-W, Chen C-S, Chen Y-H, Lin H-C. Psoriasis and pregnancy outcomes: a nationwide population-based study. *J Am Acad Dermatol*. 2011;64:71–7.
35. Ryan C, Sadlier M, De Vol E, Patel M, Lloyd AA, Day A, et al. Genital psoriasis is associated with significant impairment in quality of life and sexual functioning. *J Am Acad Dermatol*. 2015;72:978–83.
36. Cemil BC, Cengiz FP, Atas H, Ozturk G, Canpolat F. Sex hormones in male psoriasis patients and their correlation with the Psoriasis Area and Severity Index. *J Dermatol*. 2015;42:500–3.
37. Li DK, Liu L, Odouli R. Exposure to non-steroidal anti-inflammatory drugs during pregnancy and risk of miscarriage: population based cohort study. *BMJ*. 2003;327:368.
38. Hester KE, Harper MJ, Duffy DM. Oral administration of the cyclooxygenase-2 (COX-2) inhibitor meloxicam blocks ovulation in non-human primates when administered to simulate emergency contraception. *Hum Reprod*. 2010;25:360–7.
39. Millsop JW, Heller MM, Eliason MJ, Murase JE. Dermatological medication effects on male fertility. *Dermatol Ther*. 2013;26:337–46.
40. Grunewald S, Jank A. New systemic agents in dermatology with respect to fertility, pregnancy, and lactation. *J Dtsch Dermatol Ges*. 2015;13:277–89.
41. Ostensen M. Contraception and pregnancy counselling in rheumatoid arthritis. *Curr Opin Rheumatol*. 2014;26:302–7.
42. Clowse ME. Managing contraception and pregnancy in the rheumatologic diseases. *Best Pract Res Clin Rheumatol*. 2010;24:373–85.
43. Ostensen M. Pregnancy in psoriatic arthritis. *Scand J Rheumatol*. 1988;17:67–70.
44. Polachek A, Li S, Polachek IS, Chandran V, Gladman D. Psoriatic arthritis disease activity during pregnancy and the first-year postpartum. *Semin Arthritis Rheum*. 2017;46:740–5.
45. Ursin K, Lydersen S, Skomsvoll JF, Wallenius M. Disease activity of psoriatic arthritis during and after pregnancy: A prospective multicenter study. *Arthritis Care Res (Hoboken)*. 2019;71:1092–100.
46. Lima XT, Janakiraman V, Hughes MD, Kimball AB. The impact of psoriasis on pregnancy outcomes. *J Invest Dermatol*. 2012;132:85–91.
47. Seeger JD, Lanza LL, West WA, Fernandez C, Rivero E. Pregnancy and pregnancy outcome among women with inflammatory skin diseases. *Dermatology*. 2007;214:32–9.
48. Cohen-Barak E, Nachum Z, Rozenman D, Ziv M. Pregnancy outcomes in women with moderate-to-severe psoriasis. *J Eur Acad Dermatol Venereol*. 2011;25:1041–7.
49. Kimball AB, Crow JA, Ridley K, Shear NH. Pregnancy outcomes in women with moderate to severe psoriasis: The PSOLAR experience. *J Am Acad Dermatol*. 2014:AB179.
50. Yiu ZZ, Griffiths CE, Warren RB. Safety of biological therapies for psoriasis: effects on reproductive potential and outcomes in male and female patients. *Br J Dermatol*. 2014;171:485–91.
51. Yiu ZZ, Warren RB, Mrowietz U, Griffiths CE. Safety of conventional systemic therapies for psoriasis on reproductive potential and outcomes. *J Dermatolog Treat*. 2015;26:329–34.

52. Chi CC, Wang SH, Kirtschig G, Wojnarowska F. Systematic review of the safety of topical corticosteroids in pregnancy. *J Am Acad Dermatol.* 2010;62:694–705.
53. Franssen ME, van der Wilt GJ, de Jong PC, Bos RP, Arnold WP. A retrospective study of the teratogenicity of dermatological coal tar products. *Acta Derm Venereol.* 1999;79:390–1.
54. Zangar RC, Springer DL, Buschbom RL, Mahlum DD. Comparison of fetotoxic effects of a dermally applied complex organic mixture in rats and mice. *Fundam Appl Toxicol.* 1989;13:662–9.
55. Martinez-Frias ML, Rodriguez-Pinilla E, Prieto L. Prenatal exposure to salicylates and gastroschisis: a case-control study. *Teratology.* 1997;56:241–3.
56. Lam J, Polifka JE, Dohil MA. Safety of dermatologic drugs used in pregnant patients with psoriasis and other inflammatory skin diseases. *J Am Acad Dermatol.* 2008;59:295–315.
57. Heath MS, Sahni DR, Curry ZA, Feldman SR. Pharmacokinetics of tazarotene and acitretin in psoriasis. *Expert Opin Drug Metab Toxicol.* 2018;14:919–27.
58. Veraldi S, Rossi LC, Barbaresi M. Are topical retinoids teratogenic? *G Ital Dermatol Venereol.* 2016;151:700–5.
59. Ost L, Wettrell G, Bjorkhem I, Rane A. Prednisolone excretion in human milk. *J Pediatr.* 1985;106:1008–11.
60. Ostensen M, Motta M. Therapy insight: the use of antirheumatic drugs during nursing. *Nat Clin Pract Rheumatol.* 2007;3:400–6.
61. Reinisch JM, Simon NG, Gandelman R. Prenatal exposure to prednisone permanently alters fighting behavior of female mice. *Pharmacol Biochem Behav.* 1980;12:213–6.
62. de Die-Smulders CE, Sturkenboom MC, Veraart J, van Katwijk C, Sastrowijoto P, van der Linden E. Severe limb defects and craniofacial anomalies in a fetus conceived during acitretin therapy. *Teratology.* 1995;52:215–9.
63. Barbero P, Lotersztein V, Bronberg R, Perez M, Alba L. Acitretin embryopathy: a case report. *Birth Defects Res A Clin Mol Teratol.* 2004;70:831–3.
64. Maier H, Honigsmann H. Concentration of etretinate in plasma and subcutaneous fat after long-term acitretin. *Lancet.* 1996;348:1107.
65. Maradit H, Geiger JM. Potential risk of birth defects after acitretin discontinuation. *Dermatology.* 1999;198:3–4.
66. Stern RS, Lange R. Outcomes of pregnancies among women and partners of men with a history of exposure to methoxsalen photochemotherapy (PUVA) for the treatment of psoriasis. *Arch Dermatol.* 1991;127:347–50.
67. Gunnarskog JG, Kallen AJ, Lindelof BG, Sigurgeirsson B. Psoralen photochemotherapy (PUVA) and pregnancy. *Arch Dermatol.* 1993;129:320–3.
68. Feldkamp M, Carey JC. Clinical teratology counseling and consultation case report: low dose methotrexate exposure in the early weeks of pregnancy. *Teratology.* 1993;47:533–9.
69. Kozłowski RD, Steinbrunner JV, MacKenzie AH, Clough JD, Wilke WS, Segal AM. Outcome of first-trimester exposure to low-dose methotrexate in eight patients with rheumatic disease. *Am J Med.* 1990;88:589–92.
70. Beghin D, Cournot M-P, Vauzelle C, Elefant E. Paternal exposure to methotrexate and pregnancy outcomes. *J Rheumatol.* 2011;38:628–32.
71. Martinez Lopez JA, Loza E, Carmona L. Systematic review on the safety of methotrexate in rheumatoid arthritis regarding the reproductive system (fertility, pregnancy, and breastfeeding). *Clin Exp Rheumatol.* 2009;27:678–84.
72. Weber-Schoendorfer C, Hoeltzenbein M, Wacker E, Meister R, Schaefer C. No evidence for an increased risk of adverse pregnancy outcome after paternal low-dose methotrexate: an observational cohort study. *Rheumatology (Oxford).* 2014;53:757–63.
73. Lamarque V, Leleu MF, Monka C, Krupp P. Analysis of 629 pregnancy outcomes in transplant recipients treated with Sandimmun. *Transplant Proc.* 1997;29:2480.
74. Thiru Y, Bateman DN, Coulthard MG. Successful breast feeding while mother was taking cyclosporin. *BMJ.* 1997;315:463.
75. Bar Oz B, Hackman R, Einarson T, Koren G. Pregnancy outcome after cyclosporine therapy during pregnancy: a meta-analysis. *Transplantation.* 2001;71:1051–5.
76. Garty BZ, Ludomirsky A, Danon YL, Peter JB, Douglas SD. Placental transfer of immunoglobulin G subclasses. *Clin Diagn Lab Immunol.* 1994;1:667–9.
77. Irani V, Guy AJ, Andrew D, Beeson JG, Ramsland PA, Richards JS. Molecular properties of human IgG subclasses and their implications for designing therapeutic monoclonal antibodies against infectious diseases. *Mol Immunol.* 2015;67:171–82.
78. Klenke E, Osaba L, Nagore D, Rath T, Neurath Mf, Atreya R. Drug Levels in the Maternal Serum, Cord Blood and Breast Milk of a Ustekinumab-Treated Patient with Crohn's Disease. *J Crohns Colitis.* 2019;13:267–9.
79. Murashima A, Watanabe N, Ozawa N, Saito H, Yamaguchi K. Etanercept during pregnancy and lactation in a patient with rheumatoid arthritis: drug levels in maternal serum, cord blood, breast milk and the infant's serum. *Ann Rheum Dis.* 2009;68:1793–4.
80. Berthelsen BG, Fjeldsoe-Nielsen H, Nielsen CT, Hellmuth E. Etanercept concentrations in maternal serum, umbilical cord serum, breast milk and child serum during breastfeeding. *Rheumatology (Oxford).* 2010;49:2225–7.
81. Mariette X, Forger F, Abraham B, Flynn AD, Molto A, Flipo RM, et al. Lack of placental transfer of certolizumab pegol during pregnancy: results from CRIB, a prospective, postmarketing, pharmacokinetic study. *Ann Rheum Dis.* 2018;77:228–33.
82. Porter C, Armstrong-Fisher S, Kopotsha T, Smith B, Baker T, Kevorkian L, et al. Certolizumab pegol does not bind the neonatal Fc receptor (FcRn): Consequences for FcRn-mediated in vitro transcytosis and ex vivo human placental transfer. *J Reprod Immunol.* 2016;116:7–12.
83. Marchioni RM, Lichtenstein GR. Tumor necrosis factor-alpha inhibitor therapy and fetal risk: a systematic literature review. *World J Gastroenterol.* 2013;19:2591–602.
84. Berthelot JM, De Bandt M, Goupille P, Solau-Gervais E, Liote F, Goeb V, et al. Exposition to anti-TNF drugs during pregnancy: outcome of 15 cases and review of the literature. *Joint Bone Spine.* 2009;76:28–34.
85. Clowse MEB, Scheuerle AE, Chambers C, Afzali A, Kimball AB, Cush JJ, et al. Pregnancy Outcomes After Exposure to Certolizumab Pegol: Updated Results From a Pharmacovigilance Safety Database. *Arthritis Rheumatol.* 2018;70:1399–407.
86. Clowse ME, Wolf DC, Forger F, Cush JJ, Golembesky A, Shaughnessy L, et al. Pregnancy Outcomes in Subjects Exposed to Certolizumab Pegol. *J Rheumatol.* 2015;42:2270–8.
87. Cortes X, Borrás-Blasco J, Antequera B, Fernandez-Martinez S, Castera E, Martin S, et al. Ustekinumab therapy for Crohn's disease during pregnancy: a case report and review of the literature. *J Clin Pharm Ther.* 2017;42:234–6.
88. Rocha K, Piccinin MC, Kalache LF, Reichert-Faria A, Silva de Castro CC. Pregnancy during Ustekinumab Treatment for Severe Psoriasis. *Dermatology.* 2015;231:103–4.
89. Warren RB, Reich K, Langley RG, Strober B, Gladman D, Deodhar A, et al. Secukinumab in pregnancy: outcomes in psoriasis, psoriatic arthritis and ankylosing spondylitis from the global safety database. *Br J Dermatol.* 2018;179:1205–7.
90. Bookstaver PB, Bland CM, Griffin B, Stover KR, Eiland LS, McLaughlin M. A Review of Antibiotic Use in Pregnancy. *Pharmacotherapy.* 2015;35:1052–62.
91. Butler DC, Heller MM, Murase JE. Safety of dermatologic medications in pregnancy and lactation: Part II. Lactation. *J Am Acad Dermatol.* 2014;70:417 e1–10.
92. Barrett ME, Heller MM, Fullerton Stone H, Murase JE. Dermatoses of the breast in lactation. *Dermatol Ther.* 2013;26:331–6.



93. Sachs HC, Committee On D. The transfer of drugs and therapeutics into human breast milk: an update on selected topics. *Pediatrics*. 2013;132:e796–809.
94. Silfverdal SA, Ekholm L, Bodin L. Breastfeeding enhances the antibody response to Hib and Pneumococcal serotype 6B and 14 after vaccination with conjugate vaccines. *Vaccine*. 2007;25:1497–502.
95. Pisacane A, Continisio P, Palma O, Cataldo S, De Michele F, Vairo U. Breastfeeding and risk for fever after immunization. *Pediatrics*. 2010;125:e1448–52.
96. Centers for Disease C, Prevention. Transmission of yellow fever vaccine virus through breast-feeding - Brazil, 2009. *MMWR Morb Mortal Wkly Rep*. 2010;59:130–2.
97. Traiber C, Coelho-Amaral P, Ritter VR, Winge A. Infant meningoencephalitis caused by yellow fever vaccine virus transmitted via breastmilk. *J Pediatr (Rio J)*. 2011;87:269–72.
98. Kulski JK, Hartmann PE. Changes in the concentration of cortisol in milk during different stages of human lactation. *Aust J Exp Biol Med Sci*. 1981;59:769–78.
99. De Stefano P, Bongo IG, Borgna-Pignatti C, Severi F. Factitious hypertension with mineralocorticoid excess in an infant. *Helv Paediatr Acta*. 1983;38:185–9.
100. Westermann L, Hugel R, Meier M, Weichenthal M, Zillikens D, Glaser R, et al. Glucocorticosteroid-resistant pemphigoid gestationis: successful treatment with adjuvant immunoadsorption. *J Dermatol*. 2012;39:168–71.
101. Scheepers PT, van Houtum JL, Anzion RB, Harder R, Bos RP, van der Valk PG. Uptake of pyrene in a breast-fed child of a mother treated with coal tar. *Pediatr Dermatol*. 2009;26:184–7.
102. Sanitarios AEdMyP. Ficha técnica.Brea de Hulla; 2011.
103. Sanitarios AEdMyP; 2014 [https://cima.aemps.es/cima/doc.html/ft/64543/FT\\_64543.html](https://cima.aemps.es/cima/doc.html/ft/64543/FT_64543.html)
104. Briggs GG, Yaffe FR SJ. *Drugs in pregnancy and lactation*. 8th ed. Philadelphia (PA): Lippincott Williams & Wilkins; 2008.
105. Katz FH, Duncan BR. Letter: Entry of prednisone into human milk. *N Engl J Med*. 1975;293:1154.
106. Ito S, Blajchman A, Stephenson M, Eliopoulos C, Koren G. Prospective follow-up of adverse reactions in breast-fed infants exposed to maternal medication. *Am J Obstet Gynecol*. 1993;168:1393–9.
107. Sanitarios AEdMyP. Ficha técnica.acitretino; 2016.
108. Roll A, Reich K, Boer A. Use of fumaric acid esters in psoriasis. *Indian J Dermatol Venereol Leprol*. 2007;73:133–7.
109. Johns DG, Rutherford LD, Leighton PC, Vogel CL. Secretion of methotrexate into human milk. *Am J Obstet Gynecol*. 1972;112:978–80.
110. Nyberg G, Haljamae U, Frisenette-Fich C, Wennergren M, Kjellmer I. Breast-feeding during treatment with cyclosporine. *Transplantation*. 1998;65:253–5.
111. Ostensen M, Eigenmann GO. Etanercept in breast milk. *J Rheumatol*. 2004;31:1017–8.
112. Sanitarios AEdMyP. Ficha técnica.Adalimumab; 2008.
113. Sanitarios AEdMyP. Ficha técnica.Brodalumab; 2017.
114. Brodalumab. *Drugs and Lactation Database (LactMed)*. Bethesda (MD); 2006.
115. Clowse ME, Forger F, Hwang C, Thorp J, Dolhain RJ, van Tubergen A, et al. Minimal to no transfer of certolizumab pegol into breast milk: results from CRADLE, a prospective, postmarketing, multicentre, pharmacokinetic study. *Ann Rheum Dis*. 2017;76:1890–6.